

ORIGINAL ARTICLE

## Contributing factors to hearing of diabetic patients in an in-hospital education program

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### Abstract

**Conclusion:** In patients with poorly controlled diabetes mellitus (DM), hearing disturbance was associated with renal dysfunction and diabetic neuropathy, represented by decreases in median nerve compound action potential amplitude. **Methods:** The evaluation was conducted using 43 subjects who were hospitalized for the purpose of DM education. The mean age was 58.1 years (range 21–82 years). The mean HbA1c was 9.5%. The mean DM duration was 11.0 years. Renal function, retina condition, and nerve conduction were evaluated in relation to DM complications (nephropathy, retinopathy, and neuropathy). Nerve conduction studies were used to obtain detailed information on the condition of the peripheral nerves. After otological inspection, pure-tone audiometry, auditory steady-state response (ASSR), and distortion-product otoacoustic emissions (DPOAEs) were measured. Stepwise multiple linear regression was used to analyze the results in the better ear and worse ear. **Results:** Decreases in median nerve compound action potential amplitude were associated with deterioration in pure-tone audiometry and ASSR. Diabetic neuropathy, creatinine clearance, diabetic nephropathy, and retinopathy were related to hearing in ASSR and/or DPOAEs.

**Keywords:** Hearing loss, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, auditory steady-state response, distortion-product otoacoustic emissions, nerve conduction study, median nerve compound action potential amplitude

### Introduction

Diabetes mellitus (DM) is a metabolic disease that produces complications of vascular and neurologic malfunction in those with the disorder. Several studies have reported that patients with DM have greater hearing loss compared with people without DM [1–12]. Some DM-related factors that affected hearing have been reported. Bainbridge et al. found that among 5140 participants in the National Health and Nutrition Examination Survey, those with DM

had greater hearing loss than those without [1]. They reported that associations with low/mid-frequency hearing impairment were observed for low levels of high-density lipoprotein and for poor health, and associations with high-frequency hearing impairment were found for history of coronary heart disease and for peripheral neuropathy [2]. Uchida et al. examined 2306 adults who participated in a population-based study of aging. They reported that diabetes detrimentally affected hearing in community-dwelling middle-aged and elderly people, and that the effect of diabetes

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on higher-frequency hearing might be stronger in middle age [3]. Kakarlapudi et al. [4] examined the electronic medical records of >12 000 patients with DM and >53 000 age-matched controls. They reported that sensorineural hearing loss was more common in patients with DM and that hearing loss correlated with the extent of elevated creatinine concentration [4]. Because of the wide range of DM control, some authors focused on patients with poorly controlled DM and reported prolonged auditory brainstem response latencies but did not attempt to identify the contributing factors [10,11].

There are several theories as to how DM may cause hearing loss. Most authors agree that microangiopathy of the inner ear is the main cause of hearing loss in diabetics, as reported in animal and temporal bone studies [12–15]. The other possible theory is that diabetes can cause hearing loss due to the VIII nerve neuropathy. The purposes of the present study were to investigate the factors that relate to hearing loss in patients with poorly controlled DM and to obtain clues to understanding the hearing loss of patients with DM by means of pure-tone audiometry, auditory steady-state response (ASSR), and distortion product otoacoustic emissions (DPOAEs).

## Material and methods

### Subjects

The subjects were 46 adults who were hospitalized in the Department of Endocrinology and Diabetes of Nagoya University Hospital for the purpose of DM education between October 2009 and April 2011. Demographic characteristics, personal history, family history, lifestyle habits, and medical history were obtained from detailed questionnaires completed before the examination. After otological inspection, hearing tests were performed on all participants. Three patients with conductive hearing loss were excluded from data analysis. Forty-three subjects between 21 and 82 years of age were finally included in the study. Twenty-four participants were men and 19 patients were women. Three patients had type 1 DM and 40 had type 2 DM.

### Dependent variables

Pure-tone audiometry was performed by laboratory technicians using an AA-79 diagnostic audiometer (Rion, Tokyo, Japan) in a soundproof compartment. Air-conduction audiometric measurement thresholds at octave intervals from 125 to 8000 Hz and at the inter-octave frequencies 3000 and 6000 Hz were obtained using 5 dB steps. Four pure-tone averages (500, 1000,

2000, and 4000 Hz thresholds) were calculated and used to determine the better ear and worse ear in order not to overlook subjects with at least one affected ear.

ASSRs were acquired using an Audera system (Grason-Stadler, Eden Prairie, MN, USA). All subjects were tested in a supine position within a soundproof and electrically shielded room. The only instructions were for the patient to relax and avoid excessive movements. The ASSRs were collected by means of surface electrodes, with a vertex-mastoid montage ipsilateral to the stimulated ear. The electrode impedance before the recordings was <5 k $\Omega$ . For each ASSR-EEG time window, the amplitude and phase were computed and reported as vectors. The analysis algorithm automatically stopped the acoustic stimulation when a significant probability value was reached. It also stopped the acoustic stimulation after the acquisition of 64 time windows when the analysis had failed to reach the expected probability criterion. Vector phase analysis relies on a measurement known as the squared phase coherence (PC2), with values between 0 and 1. The PC2 values were statistically evaluated through a circular variance to test for the chosen probability criterion resulting in positive response detection (usually with a confidence level of 97%). The ASSR threshold is automatically defined as the lowest stimulus intensity (dB HL) capable of generating a statistically significant response in the band of interest (i.e. 250–8000 Hz). The hearing threshold in the Audera is estimated by linear regression in which the values of the ASSR potential are used to predict the hearing threshold. The details of the linear regression model are similar to those reported by Rance et al. [16]. The data were collected with a custom ASSR protocol using acoustic stimuli at octave intervals from 500 to 4000 Hz, all modulated at 46 Hz. Recordings were started at an intensity level of 50 dB HL and then changed by descending and ascending steps of 10 dB until the minimal intensity corresponding to a significant ASSR was determined.

DPOAEs were obtained using an ILO 292-USB (ILO V6) system (Otodynamics, Herts, UK). All measurements were performed in a soundproof room. The acoustic stimuli were paired tones delivered simultaneously through the probe. The tones had an intensity of 70 dB SPL and an automatically determined ratio between frequency f1 and f2 (1.22). Five pairs of stimuli were used, corresponding to the following frequency values for f2: 1001, 2002, 3088, 4004, and 6165 Hz. Noise estimates were based on two standard deviations above the mean noise floor. Ears were included only if all of the DPOAE amplitudes at five test points were greater than –20 dB SPL. DPOAE amplitudes at the five f2 test frequencies were used in the statistical analyses.

### Independent variables

Age (years), sex (graded: 1, male; 0, female), body mass index (BMI: kg/m<sup>2</sup>), DM duration (years), medical history (insulin treatment, hypertension, hyperlipidemia, cardiovascular disease, and cerebrovascular accident), and history of occupational noise exposure were obtained from the medical records and self-reported questionnaire. Occupational noise was defined in our questionnaires as background noise in a work environment over which the worker could not hold a conversation in a normal voice. Former and current noise exposures were combined. Biochemical parameters were measured routinely. These parameters included HbA1c level (%), serum creatinine concentration (mg/dl), creatinine clearance (ml/min), microalbuminuria, and proteinuria. Fasting blood sugar concentration (mg/dl) was measured in venous blood collected early in the morning after a fast of  $\geq 12$  h.

Nerve conduction (NC) studies were performed using a Nicolet Viking Electrodiagnostic System (Nicolet Instrument Corp., Madison, WI, USA) and the values were used as independent variables. The nerves on one side of the body were usually studied. Motor nerve studies included the median, ulnar, peroneal, and tibial nerves. The following parameters were measured: compound muscle action potential (CMAP) amplitude (mV), conduction velocity (CV) (m/s), and latency and F-wave minimal latency (ms) (median and tibial nerves only). Sensory nerve studies were performed in the median, ulnar, and sural nerves. The following parameters were measured: sensory nerve action potential (SNAP) amplitude (mV), CV (m/s) to positive peak (first negative-going deflection), and negative latency (ms). The stimulus duration was 0.2 ms for median and ulnar studies, and 0.3 ms for peroneal, tibial, and sural nerve studies. For all studies, the strength was always tested for a maximum response.

Nephropathy was defined as present if there was microalbuminuria or proteinuria, and/or the patient was undergoing regular dialysis. An ophthalmological evaluation was performed to determine whether there was evidence of diabetic retinopathy and was graded: 0, no evidence of diabetic retinopathy; 1, simple diabetic retinopathy; 2, pre-proliferative diabetic retinopathy; or 3, proliferative diabetic retinopathy. Neuropathy was defined as present if there were two or more nerves with abnormalities in the NC studies.

### Statistical analysis

Statistical analyses were conducted using IBM Statistics (SPSS) version 20 (IBM Corporation,

Armonk, NY, USA). *p* values < 0.05 were considered significant.

Stepwise multiple linear regression was used to assess the DM-related and -unrelated factors that affected hearing. In the multiple linear regression analysis, the respective thresholds of pure-tone audiometry at nine frequencies, those of ASSR at four frequencies, and the respective amplitudes of DPOAEs at the five f2 test frequencies were the dependent variables, and the investigation factors were independent variables. Age, sex, BMI, DM duration, HbA1c level, fasting blood sugar and serum creatinine concentrations, creatinine clearance, presence of DM complications (nephropathy, retinopathy, and neuropathy), grade of diabetic retinopathy (grade 0–3), medical history (insulin treatment, hypertension, hyperlipidemia, cardiovascular disease, and cerebrovascular accident), occupational noise exposure, and median nerve CMAP amplitude were included as the investigation factors. DM complications (nephropathy, retinopathy, and neuropathy), medical history (insulin treatment, hypertension, hyperlipidemia, cardiovascular disease, and cerebrovascular accident), and occupational noise exposure were treated as binary variables (presence = 1, absence = 0). The significance of the multiple linear regressions was evaluated using the F-test. A variable was added to the model if its associated *p* value for the F test was <0.05 and removed if its *p* value was >0.1. Hearing between better and worse ear, and between ears with and without nephropathy, retinopathy or neuropathy were compared using the *t* test. The relationships between hearing and NC values were analyzed using Pearson's correlation.

### Results

Demographic and biochemical data for the patients are presented in Table I. Most patients (76.7%) were older than 50 years. Almost all patients (93.0%) had type 2 DM and 48.8% used insulin. HbA1c level, which reflects the control of DM, was poor. Half of the patients exhibited neuropathy.

The thresholds of pure-tone audiometry and ASSR, and DPOAE amplitudes are presented in Table II. A gently down-sloping configuration characterized most pure-tone audiograms. The hearing difference between the better ear and worse ear was significant for most pure-tone audiometry thresholds (500–6000 Hz), as shown by the *t* test. No significant differences in ASSR and DPOAEs were observed between the better and worse ear at any of the test frequencies. In measurements of DPOAEs, noise levels were not different significantly between the better and worse ear at any of the test frequencies, although not shown in Table II.

Table I. Demographic and clinical data ( $n = 43$ ).

Characteristic	Value
Age (years)	58.1 (15.1)
Sex (male/female)	24/19
Body mass index ( $\text{kg}/\text{m}^2$ )	25.2 (5.1)
Type of DM (type 1/type 2)	3/40
Duration of diabetes (years)	11.0 (7.9)
Medical history of insulin treatment	48.8%
Diabetic nephropathy	30.2%
Diabetic retinopathy	39.5%
Grade of diabetic retinopathy (0/1/2/3)	26/9/4/4
Diabetic neuropathy	51.2%
Fasting blood sugar ( $\text{mg}/\text{dl}$ )	156.2 (44.2)
HbA1c (%)	9.5 (2.0)
Serum creatinine ( $\text{mg}/\text{dl}$ )	0.8 (0.3)
Creatinine clearance ( $\text{ml}/\text{min}$ )	98.9 (46.0)
Medical history of hypertension	65.1%
Medical history of hyperlipemia	55.8%
Medical history of cardiovascular disease	14.0%
Medical history of cerebrovascular accident	16.3%
History of occupational noise exposure	20.9%

Figures in parentheses are standard deviations.

Regarding pure-tone audiometry, hearing thresholds were significantly correlated with median nerve CMAP amplitude in both the better and worse ears at all test frequencies except for 250 Hz in the worse ear. There were also significant correlations between ASSR thresholds and median nerve CMAP amplitudes at four frequencies in the worse ear. DPOAE amplitudes were also significantly correlated with median nerve CMAP amplitude at 1001, 3088, and the 5 frequencies average in the better ear. Meanwhile the other NC studies parameters did not correlate sufficiently with hearing like median nerve CMAP amplitude.

Table III shows the results of the multiple linear regression analysis to investigate the factors that affected hearing. This analysis showed that median nerve CMAP amplitude was an independent predictor of pure-tone hearing thresholds at 250 and 500 Hz in the better ear, and at 500 Hz and the 8 frequencies average in the worse ear. Aging was associated with deterioration in pure-tone audiometry, ASSR, and DPOAEs over a wide range, as shown in Table III. In pure-tone audiometry, sex, BMI, and hyperlipidemia were also significantly related to hearing. For ASSRs and DPOAEs, fasting blood sugar, medical history of insulin treatment, creatinine clearance, serum creatinine, diabetic nephropathy, grade of

Table II. Thresholds of pure-tone audiometry and ASSR (dB HL) and amplitudes of DPOAEs (dB SPL) of the subjects.

	Hz	Better ear		Worse ear	
Pure-tone audiometry	125	21.6	(7.5)	21.9	(9.8)
	250	19.8	(7.8)	20.3	(9.5)
	500**	16.7	(8.0)	19.5	(9.8)
	1000**	17.6	(10.9)	20.0	(11.6)
	2000***	19.5	(12.6)	23.4	(11.5)
	3000**	20.2	(14.3)	23.6	(15.4)
	4000***	26.2	(17.8)	31.3	(17.1)
	6000*	25.6	(19.2)	27.6	(22.3)
	8000	36.4	(22.9)	37.6	(24.3)
	Average***	22.6	(11.2)	25.0	(11.9)
ASSR	500	9.4	(13.1)	13.1	(13.0)
	1000	22.5	(10.4)	20.5	(12.5)
	2000	27.4	(14.3)	32.0	(13.8)
	4000	31.2	(16.7)	32.4	(18.7)
	Average	22.6	(10.6)	24.4	(11.2)
DPOAEs	1001	0.0	(8.1)	-0.8	(8.0)
	2002	4.0	(5.9)	2.8	(7.8)
	3088	-3.2	(8.7)	-0.6	(7.4)
	4004	1.5	(7.6)	-1.4	(9.1)
	6165	-1.4	(10.8)	-4.2	(10.7)
	Average	0.2	(6.6)	-0.8	(6.6)

Values are shown as mean (SD) for dB HL/dB SPL. ASSR, auditory steady-state response; DPOAEs, distortion product otoacoustic emissions.

Asterisks show the results of comparisons between audiological values of better and worse ear: \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

diabetic retinopathy, diabetic neuropathy, and cerebrovascular accident were significantly related to hearing.

The difference in the mean pure-tone audiometry thresholds with or without DM nephropathy, retinopathy, and neuropathy was analyzed using the  $t$  test. A statistically significant difference was observed between the group with neuropathy and the group without neuropathy at 6000 and 8000 Hz in the better ear and at 3000, 4000, 6000, and 8000 Hz in the worse ear (Table IV). Meanwhile there was no statistically significant difference in hearing between with or without nephropathy and retinopathy.

## Discussion

Many investigators have studied the adverse impact of DM on hearing using various study designs. In the present study, we collected data on a wide range of DM-related variables including DM severity and



Table III. Results from stepwise multiple linear regression (significant independent variables are shown).

		Frequency (Hz) of hearing level for dependent variable	Better ear		Worse ear	
			Independent variable	SPRC	Independent variable	SPRC
Pure-tone audiometry	125		Age	0.413**	Age	0.519**
			Sex	-0.376**		
			Body mass index	-0.357*		
	250		Median nerve CMAP amplitude	-0.535***	Age	0.462**
	500		Median nerve CMAP amplitude	-0.513**	Median nerve CMAP amplitude	-0.461**
					Age	0.303*
	1000		Age	0.640***	Age	0.544***
			Hyperlipidemia	0.271*		
	2000		Age	0.714***	Age	0.704***
	3000		Age	0.736***	Age	0.663***
	4000		Age	0.708***	Age	0.733***
	6000		Age	0.747***	Age	0.797***
	8000		Age	0.764***	Age	0.772***
	Average		Age	0.797***	Age	0.684***
ASSR	500		Fasting blood sugar	-0.461**	Median nerve CMAP amplitude	-0.244*
					Diabetic nephropathy	0.708**
					Serum creatinine	-0.462*
	1000		Age	0.360*	(No factor was found)	
	2000		(No factor was found)		Median nerve CMAP amplitude	-0.462**
					Cerebrovascular accident	-0.379*
	4000		Creatinine clearance	-0.418*	Body mass index	-0.446**
			Age	0.358*		
	Average		Age	0.390*	Median nerve CMAP amplitude	-0.446**
DPOAEs	1001		Age	-0.472**	Age	-0.440*
			Cerebrovascular accident	-0.306*		
	2002		Age	-0.474**	(No factor was found)	
	3088		Age	-0.433**	(No factor was found)	
			Insulin treatment	-0.378**		
			Diabetic neuropathy	-0.365*		
			Serum creatinine	0.278*		
	4004		Age	-0.602***	Body mass index	0.438*
			Insulin treatment	-0.312*	Sex	-0.390*
	6165		Age	-0.791***	Age	-0.683***
			Grade of diabetic retinopathy	-0.210*	Fasting blood sugar	-0.436***

Table III. (Continued).

Frequency (Hz) of hearing level for dependent variable	Better ear		Worse ear	
Average	Sex	-0.191*	Cerebrovascular accident	0.347**
			Creatinine clearance	0.326**
	Age	-0.747***	Age	-0.612**
	Insulin treatment	-0.263*	Fasting blood sugar	-0.322*
	Fasting blood sugar	-0.235*		

Stepwise multiple linear regression was used to assess the diabetes mellitus (DM)-related and -unrelated factors that affected hearing. Dependent variables: the respective thresholds of pure-tone audiometry at nine frequencies, those of ASSR at four frequencies, and the respective amplitudes of DPOAEs at the five f2 test frequencies. Investigation factors for independent variables: age, sex (male = 1, female = 0), body mass index, DM duration, HbA1c level, fasting blood sugar and serum creatinine concentrations, creatinine clearance, presence of DM complications (nephropathy, retinopathy, and neuropathy) (presence = 1, absence = 0), grade of diabetic retinopathy (grade 0–3), medical history (insulin treatment, hypertension, hyperlipidemia, cardiovascular disease, and cerebrovascular accident) (presence = 1, absence = 0), occupational noise exposure (presence = 1, absence = 0), and median nerve CMAP amplitude. The significance of the multiple linear regressions was evaluated using the F-test. A variable was added to the model if its associated *p* value for the F test was >0.05 and removed if its *p* value was <0.1. ASSR, auditory steady-state response; CMAP, compound muscle action potential; DPOAEs, distortion product otoacoustic emissions; SPRC, standardized partial regression coefficient.

\**p* < 0.05, \*\**p* < 0.01, \*\*\**p* < 0.001.

complications, prevalence, and comorbid medical conditions to understand more clearly the association between DM and hearing.

Our multiple linear regression results showed that a decrease in median nerve CMAP amplitude was associated with deterioration of pure-tone audiometry and ASSR. To our knowledge, this is the first reported study to show such a relationship. DM neuropathy was associated with various changes in the NC studies. The most prominent effects were observed in the sural nerve SNAP amplitude and CV, and tibial nerve F-wave minimal latency. It is thought that DM mainly harms the peripheral nerves, especially inferior limb sensory nerves. Pathology in the median nerve of the hand often goes unrecognized. When peripheral neuropathies occur in the upper limbs, the diabetic neuropathy is already well advanced in the legs and feet [17]. This fact means that the function of the median motor nerve could be an indicative factor reflecting the advance of diabetic neuropathy, and this characteristic of the median nerve might present a relationship with hearing.

Our multiple linear regression results showed that age had a strong effect on hearing in the three auditory assessments, especially in pure-tone audiometry. Bainbridge et al. found that people with DM exhibited greater hearing loss than those without DM, especially in those younger than 69 years [1]. Austin et al. examined 165 patients with DM and 137 people without DM and reported that those younger than 50 years had greater hearing loss compared with those older than 50 years [18]. Our patients had had DM for a relatively long period, and their HbA1c levels indicated poor control; however, most of our patients

were older than 50 years (mean age 58.1 years). In these patients, the effects of aging might have affected hearing more and may have hidden the effects of DM.

It is well known that the interrelationships between nephropathy, retinopathy, and neuropathy were definite. In the present study, among these major DM complications, neuropathy correlated significantly with pure-tone audiometry thresholds at high frequencies in the *t* test. However, in the multiple linear regression analysis, the significant relationship between hearing and neuropathy was observed only in DPOAEs (at 3088 in the better ear). In the multivariate approach, a decrease in median nerve CMAP amplitude was associated with deterioration of hearing and the aging effect was prominent for any of the auditory-dependent variable. Potentially collinearity between those two factors and neuropathy may affect the result of the multiple linear regression analysis. As previously noted, Bainbridge et al. reported that peripheral neuropathy was related to hearing impairment at high frequencies for people with diabetes [2]. It was supposed that the effect of neuropathy could be modest but significant. A link between diabetic neuropathy and diabetes-related hearing loss was implied.

The results of the multiple linear regression analysis showed other DM-related and -unrelated factors that might affect hearing. It was shown that sex, BMI, and hyperlipidemia were related to hearing in pure-tone audiometry. Decrease in BMI was associated with deterioration in the three auditory assessments. It is generally known that decrease of BMI is associated with DM complications. This association may

Table IV. Mean pure-tone audiometry thresholds with or without diabetes mellitus (DM) neuropathy.

Ear	Hz	With diabetic neuropathy		Without diabetic neuropathy	
Better ear	125	23.0	(7.3)	20.8	(7.5)
	250	20.5	(7.9)	19.7	(7.9)
	500	18.4	(7.5)	15.8	(8.4)
	1000	18.4	(10.6)	17.1	(11.9)
	2000	21.6	(12.2)	17.6	(13.6)
	3000	24.1	(13.2)	16.6	(15.3)
	4000	30.9	(15.7)	22.1	(19.5)
	6000*	31.4	(18.2)	19.2	(19.8)
	8000*	43.6	(21.4)	28.9	(23.3)
	Average	25.8	(10.2)	19.8	(12.1)
Worse ear	125	23.6	(10.9)	20.3	(8.6)
	250	20.7	(10.3)	20.8	(8.9)
	500	21.6	(9.4)	18.7	(9.4)
	1000	20.5	(12.3)	19.7	(11.6)
	2000	24.5	(11.2)	22.6	(12.5)
	3000*	28.6	(13.3)	18.4	(16.7)
	4000*	36.6	(15.4)	25.8	(18.2)
	6000*	35.7	(19.9)	18.9	(22.9)
	8000*	46.4	(23.9)	29.2	(22.6)
	Average	28.7	(11.3)	21.6	(12.0)

Values are shown as mean (SD) in dB HL.

Asterisks show the results of the each audiological value comparison with or without diabetic neuropathy: \* $p < 0.05$ .

explain the relationship between BMI and hearing. For ASSRs and DPOAEs, it was shown that fasting blood sugar, medical history of insulin treatment, creatinine clearance, serum creatinine, diabetic nephropathy, grade of diabetic retinopathy, and cerebrovascular accident were related to hearing. Regarding fasting blood sugar, Austin et al. also reported that serum glucose and HbA1c levels were associated with hearing loss [18]. Hirose suggested that the severity of DM or the serum glucose level may be related to hearing loss [19]. Medical history of insulin treatment was related to deterioration of hearing in DPOAEs. Some authors reported the relationship between insulin treatment and hearing [18,20]; however, further work is needed to explore this relationship.

Renal-related factors showed the relationship with hearing. Diabetic retinopathy and decrease in creatinine clearance were associated with deterioration of ASSR thresholds and DPOAE amplitudes. On the other hand, elevated serum creatinine concentration was associated with maintained ASSR at 500 Hz. Kakarlapudi et al. reported that elevation in creatinine

concentration to  $>2.5$  mg/dl was associated with hearing loss [4]. In the present study, the serum creatinine concentration ranged from 0.3 to 1.5 mg/dl (average 0.8 mg/dl). The maintained creatinine concentration may depend partly on reduction of the muscle volume in our subjects compared with relatively high creatinine concentration in well-muscled people. Taken together, renal dysfunction or DM nephropathy was related to DM hearing loss.

Some limitations of the present study should be mentioned. Our study focused on patients with poorly controlled DM and did not include a control group. Most of the patients were older than 50 years; their mean age was 58.1 years. It is possible that aging may have affected hearing more in these patients and may have hidden the effect of DM in this study. Despite these limitations, however, we examined in detail DM-related factors that affect hearing and found relationships between some DM-related factors and hearing. These results may provide clues for understanding DM-associated hearing loss better.

## Conclusions

In patients with poorly controlled DM, hearing disturbance was associated with decreases in median nerve compound action potential amplitude. Renal dysfunction may be related to DM hearing loss. Among the three major DM complications, pure-tone thresholds showed a modestly significant relationship only with neuropathy. A link between diabetic neuropathy and diabetes-related hearing loss was implied.

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## References

- [1] Bainbridge KE, Hoffman HJ, Cowie CC. Diabetes and hearing impairment in the United States: audiometric evidence from the National Health and Nutrition Examination Survey, 1999 to 2004. *Ann Intern Med* 2008;149:1–10.
- [2] Bainbridge KE, Hoffman HJ, Cowie CC. Risk factors for hearing impairment among U.S. adults with diabetes:

- National Health and Nutrition Examination Survey 1999–2004. *Diabetes Care* 2011;34:1540–5.
- [3] Uchida Y, Sugiura S, Ando F, Nakashima T, Shimokata H. Diabetes reduces auditory sensitivity in middle-aged listeners more than in elderly listeners: a population-based study of age-related hearing loss. *Med Sci Monit* 2010;16:63–8.
  - [4] Kakarlapudi V, Sawyer R, Staecker H. The effect of diabetes on sensorineural hearing loss. *Otol Neurotol* 2003;24:382–6.
  - [5] Konrad-Martin D, Austin DF, Griest S, McMillan GP, McDermott D, Fausti S. Diabetes-related changes in auditory brainstem responses. *Laryngoscope* 2010;120:150–8.
  - [6] Cullen JR, Cinnamon MJ. Hearing loss in diabetics. *J Laryngol Otol* 1993;107:179–82.
  - [7] Frisina ST, Mapes F, Kim S, Frisina DR, Frisina RD. Characterization of hearing loss in aged type II diabetics. *Hear Res* 2006;211:103–13.
  - [8] FuVaughan N, James K, McDermott D, Griest S, Fausti S. A 5-year prospective study of diabetes and hearing loss in a veteran population. *Otol Neurotol* 2006;27:37–43.
  - [9] Sunkum AJ, Pingile S. A clinical study of audiological profile in diabetes mellitus patients. *Eur Arch Otorhinolaryngol* 2013;270:875–9.
  - [10] Lisowska G, Namyslowski G, Morawski K, Strojek K. Early identification of hearing impairment in patients with type 1 diabetes mellitus. *Otol Neurotol* 2001;22:316–20.
  - [11] Diaz de Leon-Morales LV, Jauregui-Renaud K, Garay-Sevilla ME, Hernandez-Prado J, Malacara-Hernandez JM. Auditory impairment in patients with type 2 diabetes mellitus. *Arch Med Res* 2005;36:507–10.
  - [12] Fukushima H, Cureoglu S, Schachern PA, Kusunoki T, Oktay MF, Fukushima N, et al. Cochlear changes in patients with type 1 diabetes mellitus. *Otolaryngol Head Neck Surg* 2005;133:100–6.
  - [13] Fukushima H, Cureoglu S, Schachern PA, Paparella MM, Harada T, Oktay MF. Effects of type 2 diabetes mellitus on cochlear structure in humans. *Arch Otolaryngol Head Neck Surg* 2006;132:934–8.
  - [14] Wackym PA, Lintchicum FH. Diabetes mellitus and hearing loss: clinical and histopathological relationships. *Am J Otol* 1986;7:176–82.
  - [15] Jorgensen MB, Buch NH. Studies on inner ear functions and cranial nerves in diabetics. *Acta Otolaryngol* 1961;53:350–64.
  - [16] Rance G, Rickards FW, Cohen LT, Burton MJ, Clark GM. Steady-state evoked potentials: a new tool for the accurate assessment of hearing in cochlear implant candidates. *Adv Otorhinolaryngol* 1993;48:44–8.
  - [17] Lewko J, Polityńska B, Kochanowicz J, Zarzycki W, Mariak Z, Górska M, et al. Median nerve conduction impairment in patients with diabetes and its impact on patients' perception of health condition: a quantitative study. *Diabetol Metab Syndr* 2013;5:16.
  - [18] Austin DF, Konrad-Martin D, Griest S, McMillan GP, McDermott D, Fausti S. Diabetes-related changes in hearing. *Laryngoscope* 2009;119:1788–96.
  - [19] Hirose K. Hearing loss and diabetes: you might not know what you're missing. *Ann Intern Med* 2008;149:54–5.
  - [20] Asma A, Azmi MN, Mazita A, Marina MB, Salina H, Norlaila M. A single blinded randomized controlled study of the effect of conventional oral hypoglycemic agents versus intensive short-term insulin therapy on pure tone audiometry in type II diabetes mellitus. *Indian J Otolaryngol Head Neck Surg* 2011;63:114–18.