Wagener, and Barker (KWB) classification [10]. The RA (−) group included subjects with a KWB grade I or lower, and RA (+) group included subjects with KWB grade II or higher. The subjects were divided into four groups to analyze the effects of noise exposure and KWB classification: (1) Noise (−) RA (−), (2) Noise (+) RA (−), (3) Noise (−) RA (+), and (4) Noise (+) RA (+).

2.6. Statistical analysis

Data were analyzed with the Statistical Analysis System (SAS) version 8.2 (SAS Procedures Guide, Version 8 (2000), Cary, NC: SAS Institute Inc.). Differences in the mean pure-tone thresholds at each frequency between the CA (+) and CA (−) groups based on noise exposure were compared using the general linear model (GLM) Procedure in SAS, with adjustments for age. Differences in the mean pure-tone thresholds at each frequency between RA (+) and RA (−) groups based on noise exposure were also compared after age adjustments. Finally, the main and interactive effects of noise and carotid atherosclerosis or noise and retinal atherosclerosis on audiometric thresholds were analyzed by an analysis of covariance (ANCOVA) using the GLM Procedure and controlling for age. The level of significance was set at $p < 0.05$.

3. Results

The mean age of the 773 subjects was 60.3 ± 11.6 years (range 40–83 years). The age distribution of the CA (+), (−) and Noise (+), (−) subjects is shown in Table 1. The same subjects are grouped by RA (+), (−) and Noise (+), (−) in Table 2. Among 773 subjects, 28% ($n = 218$) were exposed to occupational noise. Thirty percent of subjects had CA and 28% had RA. The rate of people with atherosclerosis, either CA or RA, increased with age.

The mean air conduction thresholds were compared in the Noise (−) and Noise (+) groups with either CA or RA (Table 3). In the Noise (+) group, a statistically significant deterioration in hearing was found in the CA (+) group compared with the CA (−) group at 500 and 1000 Hz (upper panel, Table 3). A statistically significant difference was observed between the RA (+) group and the RA (−) group at 125, 250, and 500 Hz in the Noise (+) group (lower panel, Table 3). Meanwhile CA or RA had no effects on hearing in the Noise (−) group. The presence of CA or RA exacerbated the hearing thresholds in noise-exposed subjects.

The ANCOVA analysis results on the main and interactive effects of noise and carotid atherosclerosis or noise and retinal arteriolosclerosis on the pure-tone threshold at each frequency are shown in Table 4. A significant main effect of CA on pure-tone threshold was observed at 8000 Hz. The effect of CA at other test frequencies was not statistically significant. A significant effect of noise and a strong effect of age were demonstrated at all measured frequencies. RA did not have a significant main effect on pure-tone thresholds at any of the test frequencies.

A significant combination effect of noise exposure and CA was found at 500 and 1000 Hz. A significant association between noise exposure and RA was found at 125, 250, and 500 Hz. Focusing on 500 Hz, the interactive effects of CA and noise exposure are graphically presented in Fig. 1a. In the CA (−) group, the mean air conduction thresholds at 500 Hz were 16.6 dB and increased to 18.0 dB with noise exposure. In the CA (+) group, the mean air conduction thresholds at 500 Hz were 16.3 dB and significantly increased to 21.3 dB with noise exposure ($p < 0.05$). There was a deleterious combination of CA and noise at a hearing threshold of 500 Hz. Similarly, the joint effects of RA and

Table 1
Number of subjects with and without carotid atherosclerosis (CA) and/or noise exposure by age.

Age	40–49 year	50–59 year	60–69 year	70+ year	Total
Noise (−), CA (−)	100 (62)	128 (60)	94 (47)	64 (32)	386 (50)
Noise (−), CA (+)	11 (7)	36 (17)	47 (24)	75 (38)	169 (22)
Noise (+), CA (−)	48 (30)	38 (18)	37 (18)	29 (15)	152 (20)
Noise (+), CA (+)	2 (1)	11 (5)	23 (11)	30 (15)	66 (8)
	161 (100)	213 (100)	201 (100)	198 (100)	773 (100)

The column percentages are indicated in parentheses.

Table 2
Number of subjects with and without retinal atherosclerosis (RA) and/or noise exposure by age.

Age	40–49 year	50–59 year	60–69 year	70+ year	Total
Noise (−), RA (−)	103 (64)	137 (64)	97 (48)	59 (30)	396 (51)
Noise (−), RA (+)	8 (5)	27 (13)	44 (22)	80 (40)	159 (21)
Noise (+), RA (−)	46 (29)	42 (20)	44 (22)	33 (17)	165 (21)
Noise (+), RA (+)	4 (2)	7 (3)	16 (8)	26 (13)	53 (7)
	161 (100)	213 (100)	201 (100)	198 (100)	773 (100)

The column percentages are indicated in parentheses.

Table 3
Adjusted mean air conduction pure-tone thresholds (dB) for age in the better-hearing ear of subjects with and without occupational noise exposure and carotid atherosclerosis (CA) or retinal atherosclerosis (RA).

		125Hz	250Hz	500Hz	1000Hz	2000Hz	4000Hz	8000Hz
Noise (−)	CA (−)	25.1 (24.2-26.0)	21.0 (20.0-21.9)	16.6 (15.6-17.5)	13.5 (12.4-14.5)	19.2 (18.0-20.5)	26.7 (25.2-28.2)	37.3 (35.6-39.0)
	CA (+)	25.5 (24.1-26.8)	21.3 (19.8-22.7)	16.3 (14.8-17.7)	13.4 (11.8-15.1)	20.1 (18.2-22.0)	28.3 (26.0-30.5)	40.6 (38.0-43.2)
Noise (+)	CA (−)	27.3 (25.9-28.7)	22.7 (21.3-24.2)	18.0 (16.5-19.4)*	14.8 (13.2-16.5)*	22.7 (20.8-24.7)*	35.3 (33.0-37.7)	44.0 (41.4-46.7)
	CA (+)	27.6 (25.4-29.7)	23.6 (21.3-25.9)	21.3 (19.0-23.5)	18.5 (16.0-21.1)	26.0 (23.0-29.0)	36.8 (33.2-40.4)	45.5 (41.4-49.6)
Noise (−)	RA (−)	25.2 (24.3-26.1)	21.1 (20.2-22.1)	16.6 (15.7-17.5)	13.4 (12.3-14.4)	19.3 (18.0-20.5)	27.0 (25.5-28.4)	37.6 (36.0-39.3)
	RA (+)	25.3 (23.9-26.7)	20.9 (19.4-22.4)	16.2 (14.7-17.7)	13.7 (12.0-15.4)	20.1 (18.1-22.1)	27.7 (25.3-30.1)	39.9 (37.2-42.6)
Noise (+)	RA (−)	26.4 (25.0-27.7)*	21.8 (20.4-23.2)*	18.0 (16.6-19.4)*	15.4 (13.8-17.0)*	23.1 (21.2-24.9)	34.8 (32.6-37.0)	43.6 (41.0-46.1)
	RA (+)	30.6 (28.2-33.0)	26.7 (24.2-29.2)	22.1 (19.7-24.6)	17.6 (14.8-20.5)	25.8 (22.5-29.1)	38.8 (34.8-42.8)	47.3 (42.7-51.8)

The 95% confidence intervals are indicated in parenthesis. *Statistically significant ($p < 0.05$).

noise exposure at 500 Hz are graphically presented in Fig. 1b. In the RA (−) group, the mean air conduction thresholds at 500 Hz were 16.6 dB and increased to 18.0 dB with noise exposure. In the RA (+) group, the mean air conduction thresholds at 500 Hz were 16.2 dB and significantly increased to 22.1 dB with noise exposure ($p < 0.05$). The combination of RA and noise was deleterious at a 500 Hz-hearing threshold.

4. Discussion

In the current study, a significant main effect of CA on pure-tone threshold was observed at 8000 Hz, and RA has no significant main effect on pure-tone thresholds at any of the test frequencies.

While vascular disturbance is believed to affect hearing through a diminished cochlear blood supply, there are only a few previous findings available regarding the association of systemic macro- or micro-vascular changes (e.g., carotid atherosclerosis and retinal arteriolosclerosis, respectively) and hearing in the general population. John et al. reported that the carotid intima-media thickness was associated with hearing disorder in the analysis of 2619 individuals from a general population sample in north-eastern Germany aged 45–81 years, even after adjustment for cigarettes per day, waist circumference, diabetes, exposure to noise, age and sex [11]. Hearing disorder was assessed by self-statements in their study, and the author mentioned it as the main limitation. Although self-statements are valid and often used in general population surveys [12], audiologic measurements provide highly advantageous information such as the affected frequency and the extent of hearing loss. Liew et al. examined the relation of retinal micro-vascular abnormalities and hearing measured by audiometry among 1511 individuals (ages 54+ years) from the Blue Mountains Eye

Table 4
Results from ANCOVA. *F*-values for the pure-tone threshold at each frequency. Objective variable: pure-tone threshold at each frequency.

	125 Hz		250 Hz		500 Hz		1000 Hz		2000 Hz		4000 Hz		8000 Hz	
	F	df	*F*	df	*F*	df	*F*	df	*F*	df	*F*	df	*F*	df
Noise	9.7*	1	6.9*	1	11.8*	1	9.0*	1	18.8*	1	54.2*	1	21.7*	1
CA	0.2	1	0.3	1	0.8	1	1.3	1	2.2	1	1.6	1	3.9*	1
Noise × CA	0.0	1	0.1	1	5.1*	1	4.2*	1	1.3	1	0.0	1	0.4	1
Age	144.1*	1	127.9*	1	138.8*	1	193.7*	1	313.9*	1	521.8*	1	683.4*	1
Noise	10.3*	1	7.4*	1	12.1*	1	9.1*	1	19.2*	1	55.1*	1	22.4*	1
RA	2.7	1	2.0	1	1.1	1	0.9	1	1.6	1	1.6	1	3.3	1
Noise × RA	6.6*	1	9.3*	1	7.5*	1	0.9	1	0.7	1	1.5	1	0.2	1
Age	134.6*	1	123.1*	1	139.3*	1	193.3*	1	312.0*	1	514.4*	1	671.2*	1

Explanatory variables: (upper panel) noise, CA, noise × CA, age, (lower panel) noise, RA, noise × RA, age.
* Statistically significant ($p < 0.05$).

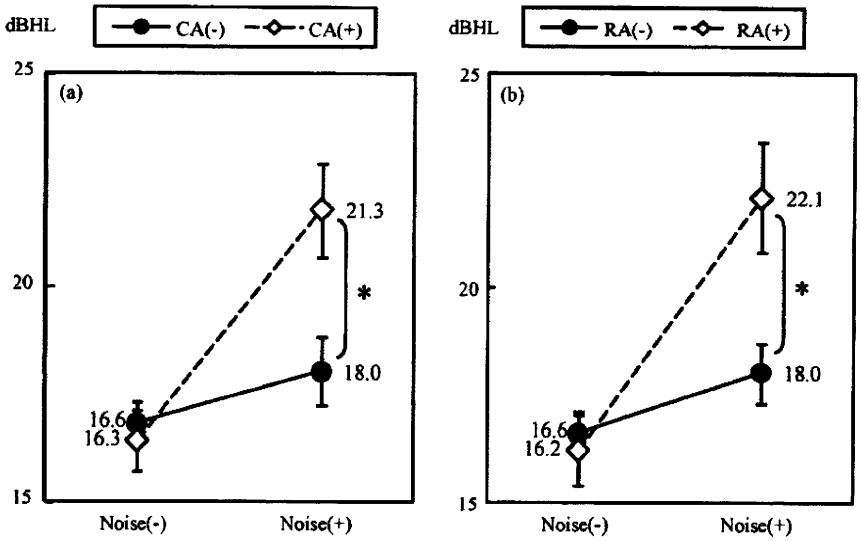

Fig. 1. (a) Comparative plotting of mean pure-tone thresholds at 500 Hz by occupational noise exposure and carotid atherosclerosis (CA) with adjustments for age. (b) Comparative plotting of mean pure-tone thresholds at 500 Hz by occupational noise exposure and retinal atherosclerosis (RA) with adjustments for age. Error bars show the standard error of the mean. Asterisk shows statistically significant difference ($p < 0.05$).

Study population [13]. They concluded that in an older population, retinopathy, a sign of retinal micro-vascular damage, was associated with hearing loss in women, particularly low-frequency losses.

We found that a significant main effect of CA was present at 8000 Hz even after controlling for the strong association of noise and age with hearing. The proximal portion of the cochlea, where high-frequency sounds are transduced, is vulnerable to many factors, such as age, noise exposure, ototoxic drugs, and therefore these risk factors are more frequently associated with high-frequency hearing loss [14]. As is shown in Table 4, F-values for noise and age at high-frequency thresholds were extremely high. Despite this disadvantageous condition, an independent effect of CA has persisted without being masked by the enormous effects of noise and age. The data suggest that the impact of arterial sclerosis on hearing is limited but significantly hazardous.

The interactive effects of noise exposure and arterial sclerosis were greater at low-frequency thresholds than at high-frequency thresholds. Possible interpretation is that the blood supply of the cochlea is most distal at the apex where low-frequency sounds are transduced [15,16]. It is also likely that diffuse vascular lesions affect low-frequency hearing [14]. Another explanation is that, because the respective effects of noise and age are enormous for high-frequency hearing loss, the interactive effects of noise and arterial sclerosis may be so small as to be masked by these predominant effects on high-frequency hearing loss.

An epidemiological approach has been performed to investigate the association between vascular risk factors and hearing loss. Hypertension and cardiovascular disease have been thought to have some relation to hearing loss [17,18]. Gates et al. reported that low-frequency hearing (250–1000 Hz) was related to cardiovascular disease events in both genders, especially women [17]. They proposed that noise-induced hearing loss may overshadow the effects of cochlear micro-vascular disease in men, while micro-vascular disease plays a greater role in low-frequency hearing loss in women. In this analysis, we assessed the impact of arterial sclerosis on hearing in men, taking account of the contribution of noise exposure. Our findings suggest that arterial sclerosis plays a role in hearing loss in men, and that the combined effects of noise exposure and arterial sclerosis in the cochlea could be synergistic. Determining if these combined risks also affect women will require additional studies.

Certain limitations should be noted. First, the present investigation on noise exposure was qualitative and not quantitative. The extent that noise affects cochlear blood flow appears to be heavily influenced by the length and intensity of noise exposure [19]. The variability in individual noise exposure could not be accounted for in this analysis. Second, neither the common carotid artery IMTs nor the stage of KWB classification is a direct indicator of cochlear blood flow. The inner ear artery (labyrinthine artery), which is usually a branch of the anterior inferior cerebellar artery (AICA), nourishes the inner ear, which is composed of the cochlea and the vestibular apparatus [16]. To date, there are no studies that have reported a useful and easily accessible marker for cochlear blood flow, and it was difficult to find direct evidence of impaired cochlear blood flow. This is because the cochlea, unlike the ocular fundus, is surrounded by bone, which prevents the direct observation of blood vessels [16].

We used both intima-media thickness of the carotid artery and narrowing of the retinal arterioles as indicators of

cochlear blood flow. The IMT of the common carotid artery provides an index of general atherosclerosis in other vascular regions and has been shown to be associated with most atherosclerosis risk factors [20]. Recently, an increase in the carotid IMT has been directly associated with an increased risk of myocardial infarction and stroke in older adults with no history of cardiovascular disease [21]. The retinal microcirculation offers a unique opportunity to assess correlates and consequences of systemic micro-vascular disease in a non-invasive fashion, suggesting that retinal micro-vascular changes may reflect structural and functional damage elsewhere in end-organ tissues. Narrowing of the retinal arterioles has been associated with persistently elevated blood pressure and inflammation and predicts stroke independently of other risk factors [22,23]. Both the IMT of the common carotid artery, a marker of early atherosclerosis, and retinal arteriolar narrowing, a marker of arteriolosclerosis, are associated with a higher risk and greater pathogenesis of general atherosclerosis throughout the body. The advantages of these two markers have been shown when predicting vascular pathology, such as ischemic stroke and cardiovascular disease, even though the vascular source of each marker is different from that of the target organ; therefore, the IMT and the stage of KWB classification are representative and non-invasive risk indicators of arterial sclerosis. In the present study, both atherosclerosis and arteriolosclerosis were associated with increased effects of noise exposure on hearing, implying that these vascular markers could predict the pathology of cochlear blood flow.

The advantages of the current analysis are that it is a large, population-based study with a careful assessment of study factors and outcome factors. In addition, we used two risk indicators to assess arterial sclerosis; IMT and the stage of KWB classification.

Whether there is a relationship between impaired cochlear blood flow and damage in a hearing frequency domain remains an important question. However, our findings suggest that reduced blood flow does contribute to hearing loss as the impact of arterial sclerosis at high-frequency, and as the interactive effects of noise exposure and arterial sclerosis at low frequencies. Underlying arterial sclerosis potentially results in increased susceptibility for many risk factors for hearing loss. Early recognition of arterial sclerosis found in carotid artery and retinal changes might be contributory to the hearing prognosis after middle age, especially for noise-exposed men.

5. Conclusions

The main effect of arterial sclerosis and the combined effect with noise exposure on hearing were investigated in a community-dwelling middle-aged and elderly sample of men. A significant main effect of CA on pure-tone threshold was observed at 8000 Hz. The presence of CA and RA aggravated the hearing thresholds in noise-exposed subjects, especially at low frequencies. The present study suggests that the impact of arterial sclerosis alone was limited but significantly hazardous on hearing, and that the harmful effects of noise exposure on hearing were enhanced by arterial sclerosis. Early recognition of general atherosclerosis might be contributory to the hearing prognosis after middle age, especially for noise-exposed men.

Conflicts of interest

There are no conflicts of interest.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Spatiotemporal components of the 3-D gait analysis of community-dwelling middle-aged and elderly Japanese: Age- and sex-related differences

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Aim: To describe age- and sex-related differences in gait patterns of community-living men and women using 3-D gait analysis.

Methods: Subjects (n = 2006) aged 40–84 years participated in the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA). Spatiotemporal components, including velocity, step length, step frequency, and double support time during a gait cycle, were calculated from 3-D coordinates and vertical force data. Velocity, step length and step frequency were normalized by leg length and acceleration due to gravity, and double support time was normalized to gait cycle duration.

Results: Spatiotemporal walking variables of brisk velocity and step length were significantly greater in men than in women, while comfortable velocity and comfortable and brisk step frequencies and double support times were greater in women than in men. Age-related changes were marked at 70–84 years in most spatiotemporal variables in both sexes during comfortable walking. During brisk walking, age-related changes were observed from a younger age than during comfortable walking, and there were sex-related differences.

Conclusion: The age-related gait alteration was obvious among those aged 70 years and older, and it accelerated markedly in women's brisk walking intensity. **Geriatr Gerontol Int 2011; 11: 39–49.**

Keywords: aging, gait, sex, velocity, walking.

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Author contributions: W. D. designed the study, obtained the funding, analyzed data and drafted the original article; R. K. interpreted data and advised on revising the article; K. H. Y. supervised data processing and prepared the article; and F. A. and H. S. originated the study, created the gait analysis program, supervised all aspects of its implementations, and contributed to obtaining the funding and revising the article. All authors conducted epidemiological studies on geriatric disease and human aging in Obu, Aichi, Japan, and read and approved the manuscript.

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Introduction

Age-related impairment of ambulatory ability is a critical component for inhibiting activities of daily living (ADL). For instance, decreased gait velocity observed in elderly is an indicator of common distinct diseases[1,2] and falls,[3–6] which lead to functional dependence[7–11] or death.[12] The prevalence and incidence of gait disorders increase with age in elderly persons.[13,14] The early presence of dynamic postural stability may provide more essential information for preserving adequate mobility, delaying the onset of functional decline and encouraging early appropriate lifestyle changes to promote active healthy aging.[6,8,10,11,15]

Previous studies examined age-related changes in spatiotemporal gait parameters including velocity, step length, step frequency (cadence) and selected stride time variables (single and double support time and swing time).[7,8,10,16–21] These performance-based gait variables were often measured by a 3-D gait system that computes the motions of the body center of mass (COM) and each segment, which can accurately evaluate the control of dynamic balance during walking.[22,23] The COM velocity on the 3-D gait system identified the effect of age on older gait in limited comparison between young and older groups.[24–26] It showed that the 3-D analyses conducted have not determined from which age group the accelerated decline of gait started. The collection of data using a large sample size with a broad age range could resolve the issue.

Age-related gait studies have recruited either men or women, or both sexes have been analyzed together: a few studies previously focused on sex-related changes on gait pattern with advancing age. Callisaya *et al.*[8] revealed the effects of sex and age on gait velocity in elderly men and women aged 60–86 years. The results of other studies of various age ranges and groups[17,19,27] to determine which sex shows an earlier age of accelerated gait velocity decrease have differed. The conflicts may partly depend on the sampling and subject characteristics.

Therefore, to understand the aging process in gait measures across the adult lifespan, a large sample size ranging from young or middle-aged to elderly men and women should be warranted. We decided to reinvestigate the previous findings. In the present study, the gait of elderly subjects was investigated based on comfortable and brisk spatiotemporal gait parameters with a 3-D gait analysis system; a large number of subjects were recruited. We found the age-related changes in gait by sex among middle-aged and elderly men and women in Japan. This may contribute to a beneficial effect on assessing gait in elderly people and making an adequate walking exercise program suitable for targeted age groups.

Methods

Study sampling

The present gait analysis is part of the third phase of the National Institute for Longevity Sciences Longitudinal Study of Aging (NILS-LSA); this study includes medical, physiological, nutritional and psychological examinations. The study began in November 1997 (the first phase), and the third phase lasted from May 2002 to May 2004. The subjects were age- and sex-stratified random samples of the population, aged 40–84 years, who lived in Obu-shi and Higashiura-cho, Aichi, Japan. These participants were chosen from the residents registered with local governments. All subjects lived or had lived at their home in the community and had Japanese nationality.[28] The NILS-LSA was approved by the Ethics Committee of the National Center for Geriatrics and Gerontology. Details of the NILS-LSA have been previously published.[28,29]

Of 2378 men and women aged 40–84 years in the third phase examination, 1017 men and 989 women (84.2% of all participants, Table 1) completed the walking tests and were included in the present analysis. The participants also completed a structured questionnaire dealing with their socioeconomic characteristics, cardiovascular risk factors and medical history.[28,29] Exclusion criteria included a current medical history of arthritis[6,8] and fractures (musculoskeletal disorders),[30] stroke[1] and Parkinson's disease (neurological disorders),[8,31] and ischemic heart disease and chronic bronchitis (Table 1).[32,33] These diseases were checked and excluded as the possible cause of gait disorders or spatiotemporal gait parameter changes by a physician before the walking tests. One participant who was diagnosed with dementia was excluded because she had a limited ability to comprehend or execute the test, which was judged by a physician. The existence of walking difficulty in activities of daily living (ADL)[11,15] was also excluded (Table 1). The participants who met the above-mentioned requirements and could walk 10 m independently without a walking aid were included in the current gait analysis and therefore 372 participants of the third phase examination were totally excluded.

Protocol

All participants wore short-sleeved T-shirts and shorts for testing. Shoes were made from the same material that had a vinylon/polyester and cotton blended upper part and a urethane foam outsole (Moonstar, Fukuoka, Japan), and were selected to exactly fit each participant's feet. Ten 2.5-cm diameter optical markers were placed on the participants' left and right sides on the fifth metatarsal heads, the lateral malleoli, the lateral epicondyles, and one-third of the way along the straight lines from the greater trochanters to the anterior

Table 1 Inclusion/exclusion characteristics of 2378 participants in the third wave examination of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA), 2002–2004

Characteristics	Men	Women
Inclusion (n = 2006)		
Total (n (%))	1017 (50.7)	989 (49.3)
Age group (n (%))†		
40s	250 (12.5)	279 (13.9)
50s	302 (15.1)	265 (13.2)
60s	250 (12.5)	242 (12.1)
≥70	215 (10.7)	203 (10.1)
Exclusion (n = 372)		
Total (n (%))	187 (50.3)	185 (49.7)
Prevalence of disease (n (%))		
Stroke	42 (22.5)	23 (12.4)
Ischemic heart disease	41 (21.9)	41 (22.2)
Chronic bronchitis	7 (3.7)	3 (1.6)
Arthritis	26 (13.9)	56 (30.3)
Fracture	5 (2.7)	6 (3.2)
Dementia	–	1 (0.5)
Parkinson's disease	3 (1.6)	–
Walking difficulties in ADL (n (%))	50 (26.7)	54 (29.2)
Not completed walking test (n (%))	55 (29.4)	53 (28.6)

†χ^2-Test test examines significance among each age group and sex. Values are numbers (% of total at each inclusion/exclusion category) of samples. ADL, activities of daily living.

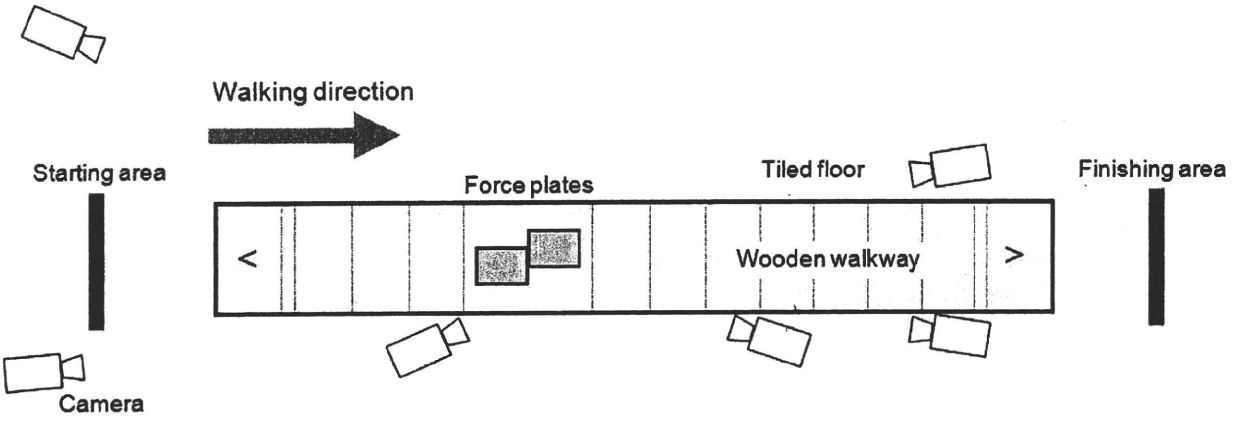

Figure 1 Setup of 3-D gait system: the 10-m walkway consisted of a wooden walkway. Six cameras were placed at various positions and two force platforms were embedded in the center of the walkway. Double support time in pre-swing phase of right foot was measured in this setting.

superior iliac spines and the acromions.[34] The subjects walked on a 10-m walkway at two speeds: (i) at a self-selected pace (comfortable walking); and (ii) as fast as possible without running (brisk walking). Each pace was repeated approximately twice on average. The walkway consisted of a tiled floor and a wooden walkway along the corridor (Fig. 1). The surface of the wooden walkway was covered with gray-colored, thin, stiff rubber, which measured 0.036 m in height from the tile floor surface of the corridor. Force platforms (0.6 m × 0.4 m) (9286; Kistler Instrumente AG, Winterthur, Switzerland), with surface colors similar to those of the walkways, were embedded in the center of the wooden walkway. The starting point for each trial was

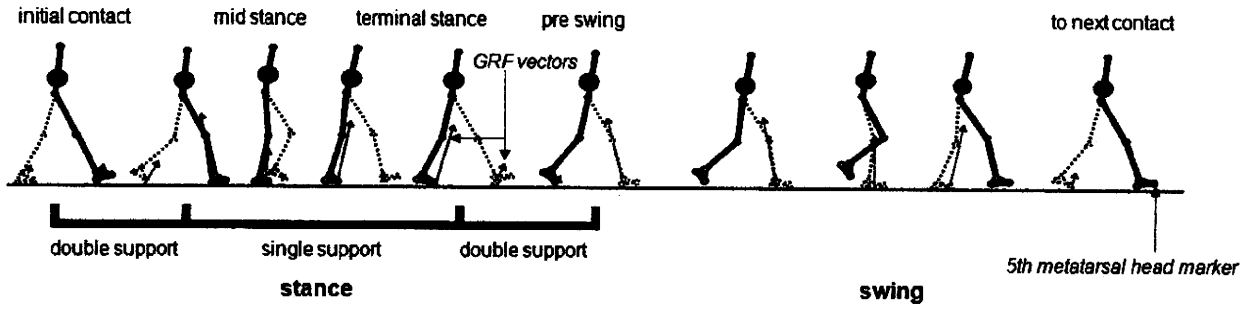

Figure 2 Definition of gait cycle using ground reaction force (GRF) and the fifth metatarsal head marker.

selected in relation to the foot contacts on the force platforms. The distance from each starting and departure point to the force platforms was approximately 3.5–4.5 m. One trial each of comfortable and brisk walking was used in the data analysis. The trials used were those that lacked the least data.

The Vicon 370 system (Oxford Metrics Ltd, Oxford, UK), which consisted of six cameras, was used to obtain the 3-D coordinates of the trunk, thighs, shins and feet. The calibration residual at each camera was set below 1.0 mm. The data were processed using a custom routine that was programmed by the Clinical Gait Analysis Forum of Japan.[34] The raw coordinate data at 60 Hz were digitally filtered with a fourth-order, zero-lag, Butterworth filter[22] with a cut-off at 5 Hz, and the raw ground reaction force data at 1200 Hz were digitally filtered with a cut-off at 10 Hz. The force data were interpolated to correspond with the coordinate data to synchronize the datasets. Smoothed coordinates of the lower extremities were used to construct a rigid link-segment model.[22] Segment masses and inertial properties were determined using previously reports[35] and the participants' mass and height, which were used for calculating COM.

Gait cycle and walking variable calculation

SAS ver. 9.1.3.[36] was used to automatically identify gait event times and each phase of the gait cycle based on kinematic and kinetic gait data. The divisions of the gait cycle are shown in Figure 2.[30] The gait event times for initial contacts and toe off were determined using vertical force data and the vertical motion of the optical marker on the fifth metatarsal head. The period from the first right initial contact to ipsilateral second initial contact was one gait cycle.[30]

Both the right and left leg motions were captured, and primarily the right stride was analyzed. Left leg motion was used for calculating the step length and double support times. The mean COM velocities, step lengths, step frequencies and double support times during a gait cycle were also automatically computed by SAS. The double support time was defined as the duration of time during which each foot was on the ground in the pre-swing phase. The mean COM velocity, step length, and step frequency were normalized as proposed by Hof[37] as follows:

Normalized COM velocity, $\hat{v} = \frac{v}{\sqrt{gl_0}}$,

Normalized step length, $\hat{l} = \frac{l}{l_0}$,

Normalized step frequency, $\hat{f} = \frac{f}{\sqrt{g/l_0}}$,

where v is actual mean COM velocity, l_0 is the leg length of each subject, l is the actual step length, f is the actual step frequency and g is the acceleration due to gravity (9.81 m/s^2). Leg length was measured from the ground to the greater trochanter during quiet standing. Patients with arthritis and fracture were excluded (Table 1), and no case of limited knee extension was observed in the present study. The double support time was also normalized by each subject's cycle duration, from right initial contact to next right initial contact (over one gait cycle).

For the calculation of walking variables, technical difficulties sometimes caused missing data due to the effect of occlusion while capturing motion. Thus, for example, the mean COM velocity over the gait cycle was calculated using data from 1716 men and women (85.5% of the total sample) during comfortable walking and using data from 1614 men and women during brisk walking (80.4%). To demonstrate the lack (or presence) of bias with respect to velocity data loss, the Student's *t*-test was used to compare the velocity between the group with all available data and that with data available only in the velocity category. The results showed that the velocities were not significantly different between the two groups, and this was confirmed for all walking variables.

Statistical analyses

All analyses were performed using SAS ver. 9.1.3. Sex differences were examined using the Student's *t*-test. For analysis of age differences, participants were divided

into eight groups based on sex and age (40–49, 50–59, 60–69 and 70–84 years for each sex). Trends in differences across all age groups in the walking variables were tested using the General Linear Model (GLM), and differences by age group were tested using the Tukey–Kramer method for each sex. $P < 0.05$ was considered statistically significant.

Results

The proportion of the sample drawn from each age group and each sex group was the same (χ^2-test, $P > 0.05$). The mean ± standard deviation age was 58.1 ± 11.4 years in men and 58.7 ± 11.4 years in women, which was not significant ($P > 0.05$).

The results of the GLM and Tukey–Kramer tests revealed age-related changes in each age and sex group. Descriptive statistics for all values are shown in Tables 2 and 3 and Figure 3. Mean COM velocities during comfortable and brisk walking significantly decreased with age in both sexes ($P < 0.001$). Age-related changes in the comfortable COM velocity were marked in the 70–84-year group compared with other age groups. Similar changes were found in the brisk COM velocity. The step lengths and frequencies followed these COM velocity patterns in both sexes during both comfortable and brisk walking.

These age-related changes occurred earlier in the middle-aged group. Earlier patterns involving brisk gait parameters were more apparent in women: for example, the brisk COM velocity decreased at 60–69 years in men and at 50–59 years in women, then the decrease accelerated at 70–84 years (Tables 2,3, Fig. 3). The step length and frequency followed these COM velocity patterns. The double support time during pre-swing was significantly increased with age only at the women's comfortable walking pace; it was significantly longer in the 70–84-year group compared to other age groups (Table 3, Fig. 3). The men's double support times showed no significant age-related differences among age groups (P for trend >0.05, Fig. 3).

Descriptive statistics and the results of sex differences for gait parameters are depicted in Table 4. The results of mean COM velocity differed according to walking pace: the comfortable COM velocity was significantly faster in women than in men ($P < 0.001$), and the brisk COM velocity was significantly faster in men than in women. Step length pattern was similar to COM velocity pattern: the brisk step length was longer in men than in women ($P < 0.001$), but the comfortable step length was not significantly different. On the other hand, women had a higher step frequency during both walking paces ($P < 0.001$). The results of the pre-swing double support time were equal to the step frequency.

Discussion

Mobility is essential for independence in the elderly. A better understanding of age-related changes in gait provides useful information for appropriate intervention programs targeting specific age groups.[8] The present cross-sectional, descriptive study showed spatiotemporal components of gait over one gait cycle among community-living middle-aged and elderly Japanese subjects. The sample of 1017 men and 989 women was large enough to allow analysis by age group,[17] and, to the best of our knowledge, the sample size is the largest to be published in which gait characteristics have been analyzed using a 3-D gait system. There was no disproportionate lack of gait data caused by difficulties in capturing the 3-D coordinates.

Mean COM velocities decreased with age, which is in almost complete agreement with previous results, despite the use of different measurement equipment and instrumentation.[16–21,25,29] The age-related decreases in the normalized COM velocities accelerated at 70 years and over were noted at a relatively later age compared with the previous reports: they showed the accelerated decline occurred in 50–59- and 60–69-year age groups,[17] at 62 years,[19] between 60- and 70-year age groups,[20] and at 65 years and in the 67–73-year age group.[18] The differences in age of accelerated decline among the previous and the present findings were likely due to the differences in method and data characteristics.

The brisk COM velocity decreases advancing with age were earlier compared with the comfortable walking. Some previous studies showed the age-related decrease was independent of walking pace,[18–20] while another reported that the decrease depended on the pace.[7] In a report by Bohannon on the comfortable and maximum walking speeds of adults aged 20–79 years,[7] walking speed was found to be influenced by the interaction of pace and age. This result matched our present findings that the age-related decrease was clearer during brisk walking than during comfortable walking. Moreover, these earlier age-related declines in the brisk COM velocities were apparent in women. Some studies reported that the critical age for marked velocity decrease did not differ by sex,[16,19] while another found the critical age to be earlier in men.[17] However, Callisaya *et al.*[8] showed women's walking velocity to be an earlier age-related change compared to men's parameters during the preferred speed of walking among the subjects aged 60 years and older. These results are in agreement with our own, though our data was particularly strong in the brisk parameters across middle-aged and elderly persons. The brisk walking task required greater forward momentum and increased demands in muscle activity[24,38–40] and aerobic capacity[33,41] might alter the spatiotemporal gait parameters accompanying aging.

Table 2 Men's normalized mean COM velocities, step lengths and frequencies and double support times during comfortable and brisk walking in each age group

Men: walking parameters by age group	Mean COM velocity				Step length				Step frequency				Double support times (pre-swing)			
	N	Mean	SD	95% CI	N	Mean	SD	95% CI	N	Mean	SD	95% CI	N	Mean	SD	95% CI
Comfortable walking																
40s	211	0.524	0.053	0.517–0.531	240	0.892	0.065	0.884–0.900	207	0.587	0.043	0.582–0.593	208	14.8	1.5	14.6–15.0
50s	266	0.527	0.059	0.520–0.534	289	0.897	0.076	0.888–0.906	259	0.590	0.042	0.585–0.595	249	14.8	1.5	14.6–14.9
60s	218	0.523	0.067	0.514–0.532	240	0.901	0.089	0.890–0.913	215	0.583	0.046	0.577–0.589	205	14.5	1.6	14.3–14.7
70–	186	0.485	0.070	0.475–0.495	213	0.859	0.096	0.846–0.872	185	0.569	0.047	0.562–0.576	177	15.2	2.0	14.9–15.5
P for trend†	<0.001				<0.001				<0.001				NS			
(Tukey–Kramer test)‡	40s, 50s, 60s >70–				40s, 50s, 60s >70–				40s, 50s, 60s >70–				NA			
Brisk walking																
40s	190	0.705	0.078	0.694–0.716	229	0.998	0.074	0.989–1.008	180	0.707	0.070	0.696–0.717	173	13.3	6.0	12.4–14.2
50s	235	0.699	0.082	0.688–0.709	272	0.998	0.088	0.987–1.008	214	0.697	0.064	0.688–0.705	209	13.3	5.6	12.6–14.1
60s	191	0.678	0.079	0.667–0.690	237	1.000	0.094	0.988–1.012	185	0.685	0.066	0.676–0.695	180	13.4	5.0	12.6–14.1
70–	182	0.618	0.092	0.605–0.631	203	0.946	0.100	0.932–0.960	177	0.657	0.066	0.647–0.667	169	14.1	2.1	13.8–14.4
P for trend†	<0.001				<0.001				<0.001				NS			
(Tukey–Kramer test)‡	40s > 60s > 70–., 50s > 70–				40s, 50s, 60s >70–				40s > 60s > 70–., 50s > 70–				NA			

†Trend tests examine main effects of age in each gait parameter. ‡Tukey–Kramer tests examine the significant difference among each age group. '>' indicates the significant difference between the age groups, with *P*-value is less than 0.5. Values are numbers of samples (N), means (Mean), standard deviations (SD) and 95% confidence intervals (95% CI) at each variable. Age group: 40s, 40–49 years age group; 50s, 50–59 years age group; 60s, 60–69 years age group; 70–, 70–84 years age group. COM, center of mass; NS, not significant; NA, not applicable.

Table 3 Women's normalized mean COM velocities, step lengths and frequencies and double support times during comfortable and brisk walking in each age group

Women: walking parameters by age group	Mean COM velocity				Step length				Step frequency				Double support times (pre-swing)			
	N	Mean	SD	95% CI	N	Mean	SD	95% CI	N	Mean	SD	95% CI	N	Mean	SD	95% CI
Comfortable walking																
40s	228	0.542	0.060	0.535–0.550	267	0.905	0.072	0.896–0.913	223	0.602	0.044	0.596–0.608	212	14.9	1.7	14.7–15.2
50s	224	0.547	0.066	0.538–0.556	252	0.902	0.082	0.891–0.912	219	0.607	0.051	0.600–0.614	214	14.9	1.7	14.7–15.1
60s	210	0.536	0.064	0.527–0.544	236	0.890	0.079	0.880–0.900	207	0.602	0.045	0.596–0.608	189	15.0	1.9	14.8–15.3
70–	173	0.472	0.071	0.461–0.483	189	0.833	0.093	0.820–0.847	169	0.570	0.051	0.562–0.578	148	15.8	1.9	15.5–16.1
P for trend†	<0.001				<0.001				<0.001				<0.001			
(Tukey–Kramer test)‡	40s, 50s, 60s >70–				40s, 50s, 60s >70–				40s, 50s, 60s >70–				70– > 60s, 50s, 40s			
Brisk walking																
40s	216	0.702	0.072	0.692–0.711	269	0.972	0.070	0.963–0.980	210	0.728	0.071	0.719–0.738	201	13.9	1.6	13.7–14.2
50s	215	0.675	0.080	0.665–0.686	252	0.960	0.087	0.950–0.971	212	0.706	0.073	0.696–0.715	209	14.2	1.7	13.9–14.4
60s	212	0.653	0.072	0.643–0.662	230	0.941	0.085	0.929–0.952	209	0.696	0.072	0.687–0.706	199	14.2	1.8	14.0–14.5
70–	173	0.577	0.084	0.565–0.590	187	0.890	0.109	0.875–0.906	163	0.651	0.064	0.562–0.578	157	14.3	8.8	12.9–15.7
P for trend†	<0.001				<0.001				<0.001				NS			
(Tukey–Kramer test)‡	40s > 50s > 60s > 70–				40s > 60s > 70–., 50s > 70–				40s > 50s, 60s > 70–				NA			

†Trend tests examine main effects of age in each gait parameter. ‡Tukey–Kramer tests examine the significant difference among each age group. '>' indicates the significant difference between the age groups, with $P < 0.05$. Values are numbers of samples (N), means, standard deviations (SD) and 95% confidence intervals (95% CI) at each variable. Age group: 40s, 40–49 years age group; 50s, 50–59 years age group; 60s, 60–69 years age group; 70–, 70–84 years age group. COM, center of mass; NS, not significant; NA, not applicable.

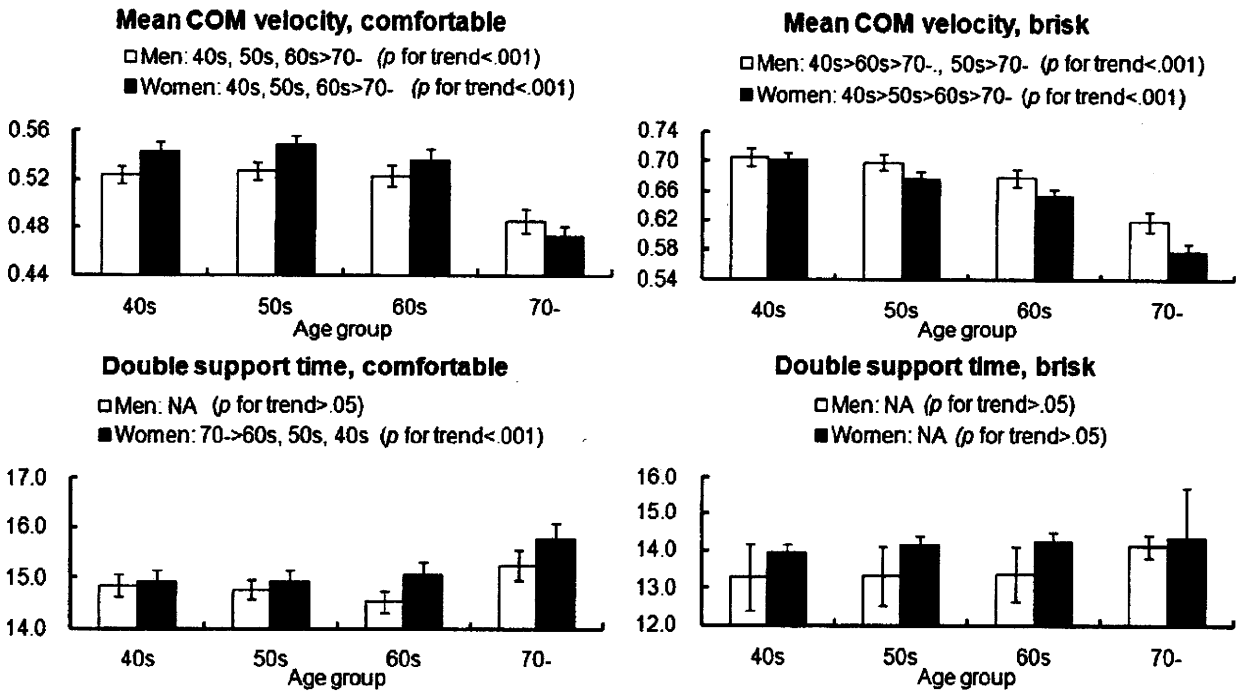

Figure 3 Age-related differences (trend tests and Tukey–Kramer tests); means and 95% confidence intervals of normalized mean center of mass (COM) velocities ($(m/sec)/\sqrt{((m/sec^2)\times m)}$) and double support times (s/s) during comfortable and brisk walking in men and women. Significant differences by age group in men and women are noted on the upper side of each figure. '>' indicates the significant difference between the age groups, with *P*-values of ≤0.05.

Table 4 Normalized mean COM velocities, step lengths and frequencies and double support times during comfortable and brisk walking among men and women

Walking parameters	Men				Women				*P*-value†
	N	Mean	SD	95% CI	N	Mean	SD	95% CI	
Comfortable walking									
Mean COM velocity	881	0.516	0.064	0.512–0.521	835	0.527	0.071	0.523–0.532	<0.001
Step length	982	0.889	0.083	0.883–0.894	944	0.886	0.085	0.881–0.891	NS
Step frequency	866	0.583	0.069	0.580–0.586	818	0.597	0.045	0.593–0.600	<0.001
Double support time (pre-swing)	839	14.8	1.7	14.7–14.9	763	15.1	1.8	15.0–15.2	<0.001
Brisk walking									
Mean COM velocity	798	0.677	0.089	0.671–0.683	816	0.656	0.089	0.650–0.662	<0.001
Step length	941	0.987	0.092	0.981–0.993	938	0.945	0.092	0.939–0.951	<0.001
Step frequency	756	0.687	0.075	0.682–0.692	794	0.698	0.049	0.693–0.703	<0.001
Double support time (pre-swing)	731	13.5	5.0	13.2–13.9	766	14.2	4.3	13.9–14.5	<0.01

†Student *t*-tests examine the sex differences. Values are numbers of samples (N), means, standard deviations (SD) and 95% confidence intervals (95% CI) at each variable. COM, center of mass; NS, not significant.

Further investigation should have discussed the difference between comfortable and brisk walking parameters.[38,42,43]

Age-related step length decreases during comfortable and brisk walking were almost concomitant with the COM velocity decreases, which was similar to the previous findings.[16,20] In brisk walking, however, age-related reduction in the step length seemed to be smaller than that in the step frequency compared with comfortable walking. For example, women's brisk step length decrease was 8.4% across middle-aged and elderly groups compared with their step frequency decrease of 10.7% (Table 3). This was observed also in men's. This may suggest that ambulatory ability observed in the COM velocity may be caused more by the step length during comfortable walking and the step frequency

during brisk walking in the elderly. This was also apparent in middle-aged women. The interpretation was limited qualitatively and should be further explored.

Step frequencies also decreased with age and this decrease was found even in middle-aged women during brisk walking. Previous studies in step frequency reported no age-related changes,[16,17,21] age-related decrease[8,18–20,25] and age-related increase.[26] Moreover, the current age- and sex-related decrease depending on required walking pace was not previously reported.[16,17] One explanation of these conflicts was that degree of the age-related reduction in step frequency was relatively less than that in other gait parameters such as velocity or step length.[8,17,19,20] Therefore, sample size, subject characteristics and measuring instruments may affect the age-related decrease in the step frequency.[16,25] Double support times in the present study did not increase with age, with the exception of women's comfortable data. On the other hand, exploratory analyses of actual values of double support times showed age-related increases in both sexes during both walking paces (data not shown, P for trend <0.001, <0.022). This shows that the double support as a percentage of one gait cycle remained almost constant in middle-aged and elderly subjects. Ferrandez *et al.*[32] found that double support time increased as velocity decreased, and that prolonged double support time was affected more by walking velocity than age.

The present study found brisk COM velocity and step length to be greater in men than in women. By contrast, step frequencies and double support times were greater in women than in men. This is characteristic of sex differences and is supported by previous findings.[8,17,21] Although the comfortable COM velocity was faster in women than in men, this is believed to be a result of the difference in body size as the actual comfortable COM velocity was significantly faster in men than in women (men, 1.46 ± 0.18 m/s; women, 1.43 ± 0.20 m/s; $P < 0.001$). The comfortable step length did not differ significantly between either sex group, perhaps because of the slower men's COM velocity.

The present gait data may give some insight into gait assessment and preventive walking exercise programs for older persons as previously reported.[42,44,45] The values for the gait parameters during one gait cycle may be useful to clinicians judging the ambulatory ability of patients from a short indoor walk.[7,42] Patients whose gait parameters are lower than that of their appropriate age group are at increased risk of ADL difficulties.[8,11] Comfortable and brisk walking velocities are predictive of adverse outcomes such as loss of physical function, requirement of caregivers, hospitalization and increased mortality in elderly persons.[8,10–12] Decreased step length and prolonged double support time are correlated with fear of falling and/or future fall risk.[4,5,9] Also, the other gait parameters such as gait velocity,[9,11] stride-to-stride variability[4] and lateral sway[3,5,6,46] are associated with the falling events. We did not directly ascertain whether the participants had a history of falls and/or a fear of falling in our gait parameters. Further work should confirm which gait measure is the best independent predictor for future fall risk in a large sample.

A moderate workload prescription in walking exercise programs should be given by controlling both step length and step frequency during comfortable walking in the elderly. Brisk walking, which is recommended for moderately vigorous endurance training and has a high impact compared to comfortable pace walking, might be considered for middle-aged women and the elderly to improve physical functions such as muscle strength[7,40,43] and/or cardiovascular fitness.[33,41]

This study has some limitations. Some previous gait investigations used the results of several trials or mean values of gait, while we used gait data from one trial of each participant. This was done because of technical difficulties in the automatically computed 3-D gait parameters. Next, the conjunction of our excluding criteria with the potential diseases might overestimate gait disorders: the elderly subjects were more likely to be healthy and physically fit. Moreover, patients with dementia were considered to be less in the present sample. The general comparability of the present gait variables with previously reported data is limited because of the lack of data for young adults in their 20s and 30s. Furthermore, our cross-sectional analysis approach could not demonstrate a cause-and-effect relationship from aging. We are planning longitudinal studies to further determine the effects of aging on gait. The present study included regional limitations such as race, culture, lifestyle, genetics and socioeconomic status which also may be important. However, the findings did permit age- and sex-related differences in gait to be clarified in the elderly.

In conclusion, age- and sex-related gait alterations were apparent in one gait cycle of walking in a large sample of community-dwelling, middle-aged and elderly Japanese men and women, when analyzed by a 3-D gait system. There were marked age-related gait differences in subjects aged 70 years and over compared to subjects aged 40–69 years during comfortable walking, and subtle differences were also observed in subjects aged 40–69 years during brisk walking. The earlier age-related changes were clearer in women than in men. These results may guide the assessment of gait patterns attributed to usual aging and to develop moderate exercise programs for the elderly.

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Diabetes reduces auditory sensitivity in middle-aged listeners more than in elderly listeners: A population-based study of age-related hearing loss

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
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Summary

Background: Diabetes mellitus (DM) and hearing impairment are both highly prevalent in older adult populations, but how the impact of diabetes on hearing varies by age is not well-studied.

Material/Methods: The subjects were 2306 adults aged 40 to 86 years who participated in a population-based study of aging, and were divided into 2 age groups, 40–64 years and 65–86 years, for cross-sectional analysis. Air-conduction pure-tone thresholds at octave intervals from 125 to 8000 Hz were obtained. Outcomes were categorized in relation to presence or absence of DM. Hearing levels at 7 frequencies were set in the general linear model as objective variables with adjustment for confounders. Explanatory variables were age (<65 years vs. >65 years), DM (absence vs. presence), and interaction between age and DM.

Results: A statistically-significant adverse effect of DM on hearing was observed. This effect varied by age at the higher frequencies. The DM-age interaction was not synergistic at any test frequencies. No significant effects of the DM-age interaction were observed below 4000 Hz. In contrast, significant reciprocal effects of the DM-by-age interaction were found at 4000 Hz and 8000 Hz. Diabetes may accordingly affect higher-frequency hearing more strongly in the younger age-bracket.

Conclusions: This study demonstrated that diabetes detrimentally affected hearing in community-dwelling middle-aged and elderly people, and that the effect of diabetes on higher-frequency hearing might be stronger in middle age. Screening for hearing impairment in diabetic patients may provide benefits for intervention or prevention of early presbycusis, particularly in this age group.

key words: diabetes • aging • hearing • interaction • population-based study

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BACKGROUND

Diabetes mellitus (DM) is a prevalent disease in older people. DM in older adults has become a major public health problem, affecting an increasing number of individuals worldwide. According to a 2006 national nutrition survey in Japan, the rates of likely DM (HbA1c >6.1% or in treatment) were 3.2%, 10.2%, 13.6%, and 18.0% for people in their 40s, 50s, 60s, and 70s or over, respectively. The rates of subclinical DM (HbA1c 5.6–6.1%) were 14.2%, 19.0%, 23.1%, and 24.7% for people in their 40s, 50s, 60s, and 70s or over, respectively [1].

Hearing loss is also highly prevalent in older adult populations [2,3]. Research has shown that presbycusis affects about 30% of people aged 65 and over [4,5], and that about half of the population aged over 75 years has significant hearing loss [6].

A relationship between DM and hearing loss was first proposed in a case report by Jordao in 1857 [7]. Although this potential association has been investigated ever since then [8–13], it has not been as firmly established as the association between DM and its known complications affecting the renal, visual, and peripheral nervous systems. Several factors, such as noise exposure, presbycusis, and syndromic hearing loss, might confound the association between DM and hearing impairment. Although aging is thought to be a key factor in both glucose metabolism and cochlear function, it is difficult to demonstrate the interrelated contribution of DM and aging to hearing impairment.

We aimed to investigate the impact of DM on hearing, and the relationship between this and age, in middle-aged and elderly community-dwelling individuals.

MATERIAL AND METHODS

Subjects

The present study was conducted as part of the comprehensive 'Longitudinal Study of Aging (NILS-LSA)' conducted by the National Institute for Longevity Sciences of the National Center for Geriatrics and Gerontology. The NILS-LSA is a population-based biennial survey of a cohort of approximately 2200 people, which started in November 1997. The subjects of the NILS-LSA were randomly selected from resident registrations, stratified by both age and sex. Details of the methodology used in the NILS-LSA have been reported elsewhere [14]. The study protocol was reviewed by the Ethical Committee of the National Center for Geriatrics and Gerontology, and written informed consent was obtained from all participants.

Data obtained from the 4th wave examination of NILS-LSA were analyzed cross-sectionally in the present study. Participants were 2383 adults aged 40 to 86 years who took part in the NILS-LSA between May 2004 and July 2006. Demographic characteristics, personal history, family history, lifestyle habits, and medical history were obtained from detailed questionnaires filled out before the examination visit. Venous blood was collected early in the morning after at least 12 hours' fasting.

The definition of DM was based on medical history obtained from questionnaires, or defined as a fasting plasma glucose concentration greater than 126 mg/dl and an HbA1c of more than 6.5%, or the taking of medication to lower the blood glucose level. In this way, participants were classified into a DM (+) group and a DM (–) group. Histories of ear disease and occupational noise exposure were obtained from the 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. History of ear disease and history of occupational noise exposure were treated as binary variables (presence =1, absence =0).

Those who did not undergo blood testing, had incomplete hearing measurements, or provided invalid questionnaire responses were eliminated from the analysis. Accordingly, 2306 participants with complete data were selected for the present analysis. The subjects were divided into 2 groups for analysis: 40–64 and 65–86 years (Table 1).

Audiometric measurements

Audiometric measurements were examined in a soundproof compartment by laboratory technicians on the same day of the blood draw. Air-conduction pure-tone thresholds at octave intervals from 125 to 8000 Hz were obtained using diagnostic audiometers (AA-73A and AA-78; Rion, Tokyo, Japan). The thresholds over the predetermined output level, according to the Japanese Industrial Standards T 1201 calibration, were treated as that level plus an additional 5 dB; that is to say, over 70 dB at 125 Hz was treated as 75 dB. For analyses of supraliminal levels we used 90 dB at 250 Hz, 105 dB at 500 to 4000 Hz, and 100 dB at 8000 Hz. Pure-tone averages (PTAs) were calculated for the better ear (BE) and the worse ear (WE) in order not to overlook subjects with at least 1 affected ear. The low-frequency PTA was calculated as the average threshold across the 125-, 250- and 500-Hz thresholds. The high-frequency PTA was calculated as the average across the 2000-, 4000- and 8000-Hz thresholds. The mid-frequency PTA was calculated as the average across the 500-, 1000-, 2000- and 4000-Hz thresholds. Hearing impairment was defined as PTAs greater than 25 dB.

Statistical analyses

Statistical analyses were conducted using the Statistical Analysis System (SAS) version 9.13 (SAS Institute, Cary, NC, USA). All values are expressed as mean ± standard error if not specified otherwise. Comparisons of hearing impairment rates between the DM (–) group and DM (+) group by age were performed using the chi-square test. In multivariable analyses, general linear model (GLM) analyses were performed to assess both the individual and the interactive impacts of age and DM on hearing of the BE and WE, based on the mid-frequency PTA. Hearing levels at 7 frequencies were set in the GLM as objective variables. Explanatory variables were age (binary variable; <65 years vs. >65 years), DM (binary variable; absence vs. presence), and interaction between age and DM. Moderator variables were sex, history of ear disease, and history of occupational noise exposure.

RESULTS

Table 1 shows the clinicodemographic profile of the subjects by age group and DM status. A total of 2306 participants

Table 1. Clinicodemographic profile of the subjects by DM status and age group.

(mean ± SE)	40–64 years			65–86 years		
	DM (–)	DM (+)	*p*	DM (–)	DM (+)	*p*
N	1349	67		806	84	
Male (%)	50.1	64.2	0.0246	48.4	56.0	NS
Fasting blood glucose (mg/dl)	96.3±0.4	159.7±1.6	<.0001	98.9±0.6	146.2±1.8	<.0001
HbA1c (%)	5.2±0.01	7.4±0.06	<.0001	5.3±0.02	7.2±0.06	<.0001
History of ear disease (%)	41.4	34.3	NS	33.3	33.3	NS
History of occupational noise exposure (%)	19.4	16.4	NS	18.9	25.0	NS

DM – diabetes mellitus.

Table 2. The prevalence of hearing impairment based on the low-frequency, high-frequency and mid-frequency PTA.

Hearing impairment (%)		40–64 years			65–86 years		
		DM (–)	DM (+)	p	DM (–)	DM (+)	p
Better ear	Low-frequency $PTA_{125,250,500}$ >25 dB	5.6	13.4	0.0087	37.0	44.1	NS
	High-frequency $PTA_{2000,4000,8000}$ >25 dB	16.8	44.8	<.0001	75.1	79.8	NS
	Mid-frequency $PTA_{500,1000,2000,4000}$ >25 dB	7.3	13.4	NS	52.0	59.5	NS
Worse ear	Low-frequency $PTA_{125,250,500}$ >25 dB	19.2	31.3	0.0149	60.3	66.7	NS
	High-frequency $PTA_{2000,4000,8000}$ >25 dB	29.0	59.7	<.0001	87.3	88.1	NS
	Mid-frequency $PTA_{500,1000,2000,4000}$ >25 dB	15.7	40.3	<.0001	66.4	75.0	NS

PTA pure tone averages; DM – diabetes mellitus; NS – not significant.

ages 40 through 86 years were analyzed in 4 subject groups: in the younger age bracket (40-64 years), 67 had diabetes and 1349 did not; in the older age-bracket (65–86 years) 84 had diabetes and 806 did not. The prevalence of DM was 4.7% in the younger participants, and 9.4% in the older participants.

Table 2 provides the results from chi-square analysis regarding the prevalence of hearing impairments (based on low-frequency, high-frequency and mid-frequency PTAs) according to age group and DM status. In the younger group, participants with DM had a significantly higher prevalence of hearing impairment than those without DM, for all frequency criteria except mid-frequency in the BE. In contrast, in the older age bracket, no significant differences were observed in the prevalence rates of any defined hearing impairments according to DM status.

The individual and interactive effects of age and DM on the hearing levels at 7 frequencies, from the GLM analysis, are shown in Table 3. The statistically significant main effect of DM was more moderate than that of age, but it was observed from low to high frequencies in both the BE and WE. The direction of each main effect was confirmed for the BE and WE in the lower sections of Table 3, which provide the mean hearing levels in the 4 groups: DM (–) and DM (+) in the younger and the older age-brackets. The main effect of DM was to impair hearing levels at all frequencies except 125 Hz in the BE and 500Hz in the WE. Moreover, the interactive effect of age and DM was statistically significant at 4000 Hz and 8000 Hz in both the BE and WE. The adverse effect of DM on hearing varied according to age.

For the purpose of visual comparison, the interactive effect of age and DM in the BE at 8000 Hz are graphically presented in the Figure 1. The solitary main effect of DM on hearing level was strong in the younger age bracket but less obvious in the older age bracket.

Discussion

We found a statistically significant harmful effect of DM on hearing and noted that this effect varied by age in the high frequencies. The effects of the DM-age interaction were not synergistic at any of the test frequencies; in other words, aging did not intensify the deleterious effects of DM on hearing. The DM-age interaction was additive at below 4000 Hz, but reciprocal at 4000 Hz and 8000 Hz. The impact of DM on hearing at 4000 Hz and 8000 Hz was more severe in the younger than the older participants. Hearing sensitivity at the higher frequencies is particularly vulnerable to ototoxic insults such as aging [4, 6], hazardous noise exposure [14], and ototoxic agents. Accordingly the present results can be explained by the fact that the effect of DM on

Table 3. Relationship between hearing level, age, and DM status as assessed by general linear model analyses.

		Hearing level at 125 Hz		Hearing level at 250 Hz		Hearing level at 500 Hz		Hearing level at 1000 Hz		Hearing level at 2000 Hz		Hearing level at 4000 Hz		Hearing level at 8000 Hz	
Better ear based on the mid-frequency		**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**
	DM	3.13	NS	4.41	0.0359	6.41	0.0114	6.98	0.0083	5.35	0.0208	11.68	0.0006	18.96	<0.0001
	Age	496.5	<0.0001	445.3	<0.0001	509.1	<0.0001	648.4	<0.0001	907.7	<0.0001	1094	<0.0001	1536	<0.0001
	DM × age	1.49	NS	1.21	NS	1.39	NS	1.04	NS	0.89	NS	5.62	0.0179	8.39	0.0038
		Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
40–64 years	DM (–)	20.5	19.9–21.1	18.3	17.7–18.9	14.3	13.7–14.9	10.9	10.3–11.6	15.3	14.5–16.0	18.0	17.1–19.0	23.2	22.0–24.3
	DM (+)	22.9	20.7–25.0	20.9	18.6–23.2	17.4	15.1–19.8	14.3	11.7–16.8	18.6	15.7–21.6	25.7	22.0–29.3	34.7	30.3–39.2
65–86 years	DM (–)	29.3	28.6–30.0	26.9	26.2–27.7	23.8	23.1–24.6	22.6	21.8–23.4	30.9	30.0–31.9	39.8	38.7–41.0	54.5	53.1–55.9
	DM (+)	29.8	27.8–31.7	27.8	25.8–29.8	25.0	22.9–27.1	24.1	21.8–26.3	32.4	29.8–35.0	41.4	38.2–44.7	57.1	53.2–61.0
Worse ear based on the mid-frequency		**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**	**F value**	**p value**
	DM	6.93	0.0085	9.74	0.0018	3.56	NS	4.26	0.039	9.14	0.0025	11.88	0.0006	16.49	<0.0001
	Age	460.6	<0.0001	408.8	<0.0001	411.9	<0.0001	523.6	<0.0001	753	<0.0001	926.32	<0.0001	1364	<0.0001
	DM × age	0.21	NS	0.18	NS	1.29	NS	1.01	NS	2.47	NS	6.61	0.0102	10.47	0.0012
		Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
40–64 years	DM (–)	22.8	22.1–23.6	21.1	20.3–22.0	18.4	17.5–19.3	15.6	14.7–16.6	20.4	19.5–21.4	24.2	23.1–25.3	23.2	26.3–28.8
	DM (+)	26.0	23.1–28.9	25.2	21.9–28.4	22.2	18.7–25.8	19.6	16.0–23.3	26.6	22.8–30.3	33.6	29.3–37.9	34.7	35.7–45.5
65–86 years	DM (–)	34.0	33.1–34.9	32.7	31.7–33.8	31.3	30.2–32.4	30.5	29.4–31.7	38.8	37.7–40.0	48.1	46.7–49.4	54.5	59.1–62.2
	DM (+)	36.3	33.7–38.8	35.8	33.0–38.7	32.3	29.2–35.5	32.0	28.7–35.2	40.9	37.6–44.2	49.7	45.9–53.5	57.1	58.1–66.9

Objective variables: Hearing level at respective frequencies; Explanatory variables: DM, age, DM × age; Moderator variables: sex, history of ear disease (presence=1), history of occupational noise-exposure (presence=1).
The degrees of freedom were 1 for all F values. DM – diabetes mellitus; presence vs. absence; age: <65 years vs. ≥65 years;
CI – confidence interval; NS – not significant.

hearing in the higher frequencies might be more emphatic in the younger age bracket because this type of hearing is generally better preserved in younger than in older people.

Regarding the association of diabetes with hearing, Bainbridge et al. reported the risk for hearing loss in people with self-reported DM in a recent study examining a large sample of 5140 non-institutionalized adults in the US National Health and Nutrition Examination Surveys [15]. They found that people with DM were at increased risk for hearing loss. The literature also contains some discussion about the cross-contribution of DM and aging to hearing impairment [9,15–17]. Although Bainbridge et al. mentioned that the relative contribution of DM to hearing impairment might have been stronger among their study group (age 20 to 69 years) than in a previously reported older group, they did not analyze the DM-by-age interaction as it relates to hearing in a straightforward manner. They demonstrated that the prevalence of hearing impairment among people with diagnosed DM statistically exceeded the prevalence among those without DM in all groups except people aged 60 to 69 years. They therefore speculated that hearing of younger people, before the cumulative effects of aging, noise exposure, and other factors have made substantial contributions to hearing impairment, is potentially affected by DM more than in older people. Vaughan et al. tested audiometric measures including ultra-high-frequency range in 342 veterans with DM and 352 without DM. They concluded that patients aged 60 or younger with DM may show early high-frequency hearing loss similar to early presbycusis, while there was less difference in hearing loss between patients with and without DM after age 60 [17]. They found a significant effect of DM in both ears after adjusting for age, but only in the ultra-high-frequency range (10–16 kHz), and the DM-age interaction was significant in the right ear but not in the left at this frequency range. They also demonstrated that differences between patients with and without DM diminished or disappeared at 10, 12.5, 14 and 16 kHz in the right ear as age increased. Vasilyeva et al. prospectively assessed hearing abilities in middle-aged mice with Type 1 DM or Type 2 DM, and found that induction of diabetes in middle-aged CBA/CaJ mice promoted amplification of age-related peripheral hearing loss [18].