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VIBRATORY THRESHOLDS AND MOBILITY IN OLDER PERSONS

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Abstract

We tested the hypothesis that vibratory thresholds in the elderly are related to mobility. 629 older persons without dementia underwent testing including 11 lower extremity performance measures and modified UPDRS, summarized as composite mobility and global Parkinsonian signs. Vibratory thresholds were measured at the ankle and toes bilaterally using the graduated Rydel-Seiffer tuning fork. In linear regression models adjusted for age, sex and education, vibratory threshold was associated with composite mobility (Estimate, 0.047, S.E. =0.011, P<0.001) and global parkinsonian signs score (Estimate, -0.252, S.E. =0.126, P=0.047). These findings were primarily due to the association of vibratory threshold with gait and balance components of composite mobility and parkinsonian gait. These results were unchanged when we controlled for: body mass index, physical activity, cognition, depression, vascular risk factors, vascular disease burden, joint pain, and falls. Vibratory thresholds are associated with mobility, supporting the link between peripheral sensory nerve function and mobility in the elderly.

Keywords

Vibration; Mobility; Aging; Peripheral Neuropathy

INTRODUCTION

Loss of mobility is among the most common age-related conditions, and its association with significant morbidity and mortality makes it a large and growing public health concern in our aging population.17,40,41 Mobility involves complex integrated movements of the trunk and legs, whose various aspects (e.g. speed, balance) are ultimately controlled by neural systems located in different brain regions (i.e. cortical; subcortical; spinal cord). 3,10,26,34 However, mobility requires high fidelity bidirectional transfer of sensory and motor signals through peripheral nerves to and from the final effectors of all movements, musculoskeletal structures (that is, muscles and joints). Thus while damage to various brain regions can lead to impaired mobility, impaired peripheral nerve function can also contribute to age-related mobility impairment.31

A wide range of physiologic tests available in the laboratory setting have documented age-related changes in peripheral nerve function and have shown that vibratory threshold is related to mobility even in older persons without known peripheral nerve diseases.9,18,29 In

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contrast, in many studies of community-dwelling older persons, assessments of peripheral neuropathy rely on the presence of self-reported neuropathic complaints or the use of standard clinical examination which does not include quantitative measures of vibration.15 Recent clinical studies in patients with peripheral neuropathy have employed graduated tuning forks which provide more objective semiquantitative information about peripheral sensory nerve function. 20,23,27 We are not aware of any studies which have employed graduated tuning forks in community-dwelling older persons to determine the association of vibratory thresholds and mobility in the elderly.

We used data from participants in the Rush Memory and Aging Project, a community-based study of risk factors for common chronic conditions of aging, 4 to test the hypothesis that vibratory thresholds in the elderly are related to level of mobility. We measured vibratory thresholds with the graduated Rydel-Seiffer tuning fork in more than 600 older adults without dementia and examined the association of vibratory thresholds with a composite measure of mobility which was based on eleven lower extremity performance measures and a global score for Parkinsonian signs, including assessment of parkinsonian gait. 1, 6 Next we examined the extent to which these associations between vibratory threshold and global mobility and global score for Parkinsonian signs were affected by several covariates.

METHODS

Participants

All participants were from the Rush Memory and Aging Project, a community-based, longitudinal clinical-pathologic investigation of chronic conditions of old age. Participants were recruited from more than 40 residential facilities across the metropolitan Chicago area, including subsidized senior housing facilities, retirement communities, and retirement homes, in addition to social service agencies and Church groups. Participants agreed to annual detailed clinical evaluations, and all evaluations were performed at the parent facility or the participants' homes to reduce burden and enhance follow-up participation.4 The study was conducted in accordance with the latest version of the Declaration of Helsinki and was approved by the Institutional Review Board of Rush University Medical Center.

The Memory and Aging Project began in 1997 and had enrolled more than 1200 participants at the time of these analyses with an overall follow-up rate of about 95% of survivors. Because of the rolling admission and mortality, the length of follow-up and number of examinations varies across participants. Further, because the collection of data on vibratory threshold was not added until 2006, these data were only available on a subset of Memory and Aging Project participants (N=721). Eligibility for these analyses required the absence of dementia at the time vibratory thresholds were evaluated. Therefore 82 participants (11.4%) with clinical dementia (see below) and 10 (1.4%) with incomplete tuning fork data were excluded, leaving 629 participants for these analyses.

Cognitive Testing and Clinical Diagnoses

Subjects underwent a uniform structured clinical evaluation including a medical history, neurologic examination, and cognitive performance testing. Details of the clinical evaluation have been described.4 Cognitive function was assessed at each evaluation via a battery of 21 tests. The Mini-Mental State Examination was used to describe the cohort. Scores on 19 tests were used to create a composite measure of global cognitive function. Psychometric information on this composite measure is contained in previous publications. 42 Participants were evaluated in person by a physician, who used all available cognitive and clinical testing results to diagnose dementia and other common neurologic conditions that affect cognitive function. The diagnosis of dementia followed the criteria of the joint working group of the

National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association. 21

Assessment of Quantitative Vibratory Sensation

Vibration threshold, is a measure of peripheral sensory nerve function, and testing with a graduated tuning fork (Rydel-Seiffer 128 Hz; Martin, Tuttlingen, Germany) has been shown to correlate with the sural sensory nerve action potential amplitude obtained with electrophysiologic testing, an indicator of peripheral neuropathy. 20,23,27 The Rydel-Seiffer tuning fork can be used to assess the ability of subjects to discriminate various vibration intensities. The two arms of this tuning fork bear calibrated weights at their extremities. A triangle and an arbitrary scale from 0 (minimum score) to 8 (maximum score) imprinted on the weights allow assessment of vibration threshold. Once the arms are swinging, the fork vibrates at 128 Hz, and the triangles on the weights appear double. The intersection of these two virtual triangles moves from 0 to 8 in an exponential way with decreasing vibration amplitude of the arms. The vibration extinction threshold is considered to be the nearest value to the apparent point of intersection of the virtual triangles when the subject indicates that vibration is no longer perceived. Vibration threshold was assessed in both legs at the dorsum of the interphalangeal joint of the hallux and at the medial malleolus. The tuning fork was applied as perpendicularly as possible resting on its own weight with the arms of the fork swinging maximally. The participants were asked to indicate the moment when they no longer perceived the decreasing vibration stimulus. The four measures of vibration which were collected (left and right ankle and toes) showed significant (all $p < 0.001$) pairwise correlations ranging from 0.61 to 0.71 [Table 1]. We submitted these four measures to a principal-components analysis, and all four measures loaded on one component with an eigenvalue of 2.93, accounting for 73% of the variance. Because the coefficients of the component were very similar (0.715 to 0.754), this analysis supported summarizing the four measures which were collected in this study into one composite measure of vibratory sensation. The standard deviations of these four components were similar (Table 1) suggesting that these components could be averaged together and did not require transformation to a common scale using z-scores.

Assessment of Mobility

Mobility is a complex movement, and a range of performance measures have been used to capture its different aspects. 6, 16, 33 Composite measures have been used effectively in other longitudinal studies of cognition and motor function. 19,25,36 Composite measures typically have metric properties that are more suited for longitudinal analyses than the results of individual tests. They yield more stable measures of motor function and increase the power to identify risk factors as well as the adverse health consequences of motor decline in aging. Therefore we created a composite measure of mobility based on several standard lower extremity performance measures which have been used to assess gait, balance and lower extremity strength. These performance measures provide important information about mobility and have been used extensively both in this cohort and by other investigators. 6, 11

Several gait and balance performances from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) were tested.11 We asked people to walk eight feet and turn 360° and measured the time and number of steps taken on each task. We asked people to stand on each leg for ten seconds and then to stand on their toes for ten seconds. Finally, we also asked people to walk an eight foot line heel to toe and counted the number of steps off line. Two factors (gait and balance) emerged from a factor analysis of these seven measures as previously described. 6 Gait was based on four measures: time and steps to walk eight feet and turn around. Balance was based on three measures: leg stand, toe stand and tandem

gait. Leg strength was based on measures of strength for four muscle groups in both lower extremities (hip flexion, knee extension, plantar flexion, and ankle dorsiflexion) assessed using hand-held dynamometers (Lafayette Manual Muscle Test System, Model 01163, Lafayette, IN). The mean score for each of the 11 performance measures was converted to a z score using the mean and standard deviation of all study participants at baseline, and the z scores of all 11 z scores were averaged to yield a composite measure of mobility as previously described. 6

Assessment of Parkinsonian Signs

A modified form of the motor section of the Unified Parkinson's Disease Rating Scale was administered. 1, 4, 5 The modifications were intended to make the scale applicable to persons without Parkinson's disease and to facilitate administration by nurse clinicians instead of physicians. There was a total of 17 items from which previously established measures of gait disorder/postural reflex impairment (6 items), bradykinesia (4 items), rigidity (5 items), and tremor (2 items) were derived. The four sign scores were averaged to yield a global parkinsonian signs score. Scores on each measure could range from 0 to 100 and indicated the percent of the total possible item score obtained.

Other Covariates

Gender, age, and years of education were obtained at baseline evaluation. Weight and height were measured and used to calculate body mass index (BMI). We included a term for BMI for linear associations and a quadratic term for BMI (BMI*BMI), because both low and high values of BMI can be associated with adverse health consequences. Physical activity was assessed using questions adapted from the 1985 National Health Interview Survey.22 Activities included walking for exercise, gardening or yard work, calisthenics or general exercise, bicycle riding, and swimming or water exercise. Minutes spent engaged in each activity were summed and expressed as hours of activity per week, as previously described (3.2 hours, SD, 3.94 hours).4 Depressive symptoms were assessed via a 10-item version of the Center for Epidemiologic Studies Depression Scale. 28 The total score reflects the number of depressive symptoms experienced in the past week (mean 1.3, SD, 1.82). We summarized vascular risk factors as the number of the following three risk factors: hypertension (68%), diabetes mellitus (16%), and smoking (40%). Hypertension and diabetes were recorded as present if the participant reported having been diagnosed with the condition or was found to be on medication for the condition.2,37 Vascular disease burden was the number of four vascular diseases: myocardial infarction (14%), congestive heart failure (6%), claudication (15%), and stroke (13%), as previously described. 5 Joint pain (64%) and falls (64%) were based on participant report.

Statistical Analyses

Spearman correlations were used to assess the bivariate associations of vibration measures with demographic variables and other covariates. Wilcoxon rank sum test were used to compare men and women. Linear regression models which controlled for age, sex and education were used to examine the association between vibration and composite mobility, and this model was repeated three times for each of the three components. Similar analyses were performed using the global score of Parkinsonian signs and each of its four components. Next, we repeated each of these core models, controlling for covariates that might affect the association of vibration and mobility. We examined each covariate alone and all covariates together in a single model. When examining the effect of body composition (i.e., BMI), we included both linear and quadratic terms for BMI (BMI and BMI × BMI), because both low and high values of BMI can be associated with adverse health consequences. Statistical significance was taken to be $p<0.05$. Models were examined

graphically and analytically, and assumptions were judged to be adequately met. The data analysis for this paper was generated using SAS/STAT® software, Version 9, for Linix. 35

RESULTS

Descriptive Properties of the Cohort and Vibratory Thresholds

There were 629 participants (76.2% women) in this study. Their mean age was 81.8 years (SD = 7.65); mean years of education were 14.3 years (SD = 3.25); Mini-Mental State Examination score was 27.5 (SD = 2.81); and BMI was 27.0 (SD=5.23). Vibration ranged from 0 to 8 with higher scores indicating better sensation [mean 4.2 (SD= 2.26); median=4.5; (Q1 - Q3, 2.5 - 6.0)]. The distribution was almost uniform with a mild negative skew likely due to an increased number of participants with values equal to 0 (skewness =-0.26). Vibration was inversely related to age (r_S= -0.32. p<0.001) and was not associated with education (r_S =0.050, p=0.208). Men had lower vibration scores, indicating more impaired sensation as compared to women (z = -3.4379, p<0.001). Vibration was modestly related to physical activity (r_S= 0.09. p=0.026), depressive symptoms (r_S= -0.10 p=0.016), cognitive function (r_S= 0.14 p<0.001), and vascular diseases (r_S= -0.16. p<0.001), but it was not associated with BMI; vascular risk factors, or a history of joint pain or falls (all p's > 0.175).

Vibratory Threshold and Mobility

A linear regression model which controlled for age, sex and education was used to examine the association of vibratory threshold with mobility. Vibratory threshold was associated with composite mobility (Table 2). Further analyses showed that this association was primarily due to the association of vibratory threshold with gait and balance since there was only a trend for an association with leg strength (Table 2).

Next, we repeated the models shown in Table 2 eight times, each time adding a term for a different covariate that might affect the association of vibratory thresholds with global mobility and its components. The estimates of the association of vibratory thresholds with global mobility, gait and balance were unaffected by the addition of terms for body composition, self-report physical activity, global cognition, depression, vascular risk factors, vascular disease burden, joint pain and history of falls (results not shown). Because of its association with peripheral neuropathy, we also examined diabetes mellitus as a covariate alone and this did not affect the association of vibratory thresholds and global mobility and its components (results not shown). In a final model, we included terms to control for age, sex, education and all eight covariates together. While the association of vibratory thresholds with gait was attenuated, with only a trend for an association, the associations of vibratory thresholds with global mobility, balance and leg strength were unchanged (results not shown).

Vibratory Threshold and Parkinsonian Signs

A linear regression model which controlled for age, sex and education was used to examine the association of vibratory threshold with global parkinsonian signs score. Vibratory threshold was associated with global parkinsonian signs score (Table 3). Further analyses showed that this association was primarily due to the association of vibratory threshold with parkinsonian gait (Table 3).

Next, we repeated the models shown in Table 3 eight times, each time adding a term for a different covariate that might affect the association of vibratory thresholds with parkinsonian signs and its components. Adding terms for body composition, self-reported physical activity, global cognition, depression, vascular risk factors and vascular disease burden,

diabetes, joint pain, or history of falls did not affect the association of vibratory thresholds with global parkinsonian score or parkinsonian gait (results not shown). Similarly, including a term for diabetes mellitus did not affect the association of vibratory thresholds with global parkinsonian score or parkinsonian gait (results not shown). In a final model, we included terms to control for age, sex, education and all eight covariates together. The association of vibratory thresholds with global parkinsonian score was attenuated and no longer significant. In contrast, the association of vibratory thresholds with parkinsonian gait remained significant (p=0.002).

DISCUSSION

In a group of more than 600 older persons, vibratory thresholds were related to gait and balance components of a composite mobility measure and parkinsonian gait. These associations was unchanged after controlling for covariates that included: body composition, physical activity, cognition, depression, vascular risk factors, disease burden, diabetes, joint pain, and falls. These findings support studies that link peripheral nerve function with mobility in older persons and underscore that objective measures of peripheral sensory nerve function based on vibratory thresholds can be obtained in community studies.

Quantitative measurements of peripheral nerve function usually involve electronic devices which involve prolonged examination times and high cost. Until recently most have lacked the portability essential for studies conducted in the community setting. The assessment of peripheral nerve function in the community setting varies widely due in part to the wide range of clinical assessments and tests that have been employed. While there have been some exceptions, many community studies rely on self-reported neuropathic complaints to identify participants with peripheral neuropathy. To complement self-reported data, some studies also employ clinical examination for signs of neuropathy,15 which traditionally includes a non-graduated tuning fork to measure the presence or absence of vibration sensation and thus does not provide information about vibratory threshold. This gap led to the development of graduated tuning forks, which are inexpensive and portable and expand the standard clinical exam by providing semiquantitative information about peripheral sensory nerve function. 13،20،27 A study of more than 2000 diabetics compared neuropathic findings using the Rydel-Seiffer tuning fork, 10 gm monofilaments and an electronic neurothesiometer.38 Monofilimant testing was abnormal in almost 70% of those patients with an abnormal Rydel-Seiffer vibratory threshold as compared to 7% with a normal vibratory threshold. Vibratory thresholds measured by the neurothesiometer were 2.5 times higher in patients with an abnormal Rydel-Seiffer vibratory threshold.38 Additional studies have shown that the Rydel-Seiffer vibratory thresholds not only correlate with peripheral sensory nerve function measured with other electronic devices but also with amplitudes of the standard sensory nerve action potentials which reflect function of large heavily myelinated nerve fibers. 13،20،27 In recent years graduated tuning forks have gained wider acceptance and have been used to monitor nerve function in clinical trials for the treatment of polyneuropathy.14 The current study extends prior clinical studies that, show graduated tuning forks can also be used in community-dwelling older persons to provide objective measures of peripheral sensory nerve function which are related to clinical gait and balance measures.

Progressive mobility disability is commonly thought to result from changes in the musculoskeletal system that interact with non-specific age-related changes in the central and peripheral nervous system.24 Mobility reflects the output of an integrated set of motor systems in the brain which are distributed throughout the central nervous system and are linked through peripheral nerves to muscle, the final effector of all movement. Thus, intact heavily myelinated peripheral nerves which mediate the transfer of proprioception and

vibratory sensation are crucial for the perception of joint position and movements of body segments essential for the maintenance of balance and posture. Thus loss of distal sensation in peripheral neuropathy is associated with increased vibratory thresholds as well as impaired posture and balance.7,8,39 In addition, peripheral neuropathy can also be associated with distal leg weakness and mediolateral leg instability which degrades compensatory responses to external perturbations resulting in poor balance and postural instability.12 Thus both peripheral sensory and motor deficits in patients with peripheral neuropathy are likely to contribute to impaired ambulation and increased risk of falling.30,32 Therefore without quantitative measures of peripheral sensory nerve function as part of the assessment of mobility in community-dwelling elderly, it will be difficult to tease apart the relative contribution of various central and peripheral CNS structures to the different aspects of impaired mobility and the development of mobility disability. In the current study vibratory thresholds were most strongly related to gait and balance measures and parkinsonian gait signs but only marginally related to leg strength and were not related other parkinsonian signs (i.e. rigidity; tremor; bradykinesia). The ongoing demands of continuous high-fidelity joint position information for maintenance of posture and locomotion is likely to explain in part why vibratory thresholds are more strongly related to gait and balance measures.31 While the findings in the current study were robust, these findings were cross sectional; longitudinal data will be needed to verify these findings, since the individual clinical components which contribute to mobility may change at different rates over time.

The current study has several limitations. We used a volunteer cohort of community-dwelling adults who may not be representative of the general population, so the results need to be replicated in a more diverse cohort. Although we controlled for a number of important possible confounding clinical variables, we cannot exclude the possibility that subclinical disease also contributed to our findings. Vibratory thresholds employed in the current study assess peripheral sensory nerve function; further studies which also examine peripheral motor function are needed to fully characterize the contribution of the peripheral nerve to mobility. The strengths of the present study include the use of multiple performance measures which are known to contribute to mobility and the control for a number of important potential confounding variables in a large number of men and women without clinical dementia.

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ABBREVIATIONS

BMI	Body Mass Index
Q1-Q3	interquartile range
UPDRS	United Parkinson's Disease Rating Scale

Table 1

Descriptive Properties of Vibrations Measures and Principal Components Analysis

	Vibratory Threshold*	Correlations**				Principal Component ***
		Right Toe	Right Ankle	Left Toe	Left Ankle	
Right Toe	4.02 (2.74)	-	0.66	0.71	0.61	0.732
Right Ankle	4.36 (2.56)		-	0.61	0.68	0.715
Left Toe	4.03 (2.69)			-	0.69	0.754
Left Ankle	4.27 (2.58)				-	0.727

* Mean (SD);

** Pearson Correlation Coefficients (all $p < 0.001$)

*** Principal components analysis yielded one component with eigenvalue = 2.927.

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Table 2

Vibratory Threshold and Mobility Measures*

Outcome	Estimate (S.E.) p-value
** Global Mobility	0.047 (0.011, p<0.001)
Balance	0.067 (0.015, p<0.001)
Gait	0.045 (0.016, p=0.005)
Leg Strength	0.022 (0.012, p=0.061)

* Unstandardized regression coefficients estimated from separate linear regression models adjusted for age, sex, years of education and a term for vibratory threshold. This model was repeated with each of the four outcomes in the table.

** **Global mobility** is a composite measure based on subcomponents balance, gait and leg strength which summarize 11 lower extremity performance measures.

Table 3

Vibratory Threshold and Parkinsonian Signs*

Outcome	Estimate (SE) p-value
** Global Parkinsonian Score	-0.252 (0.126, p= 0.047)
Parkinsonian Gait	-1.251 (0.311, p<0.001)
Bradykinesia	-0.063 (0.198, p=0.751)
Rigidity	0.041 (0.110, p=0.708)
Tremor	-0.059 (0.078, p=0.449)

* Unstandardized regression coefficients estimated from separate linear regression models adjusted for age, sex, years of education and a term for vibratory threshold. This model was repeated with each of the five outcomes in the table.

** Global parkinsonian score is a composite measure based on subcomponents: parkinsonian gait, bradykinesia, rigidity and tremor which summarize the motor section of the UPDRS rating scale.