Decline in Semicircular Canal and Otolith Function With Age

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Objective: To characterize the physiologic nature of the vestibular dysfunction that occurs with the normative aging process.

Study Design: Cross-sectional study.

Setting: Tertiary care academic medical center. **Patients:** Fifty individuals age 70 years and above.

Interventions: Head thrust dynamic visual acuity testing and cervical and ocular vestibular-evoked myogenic potential (VEMP) testing.

Main Outcome Measures: Semicircular canal function measured by head thrust dynamic visual acuity testing in each of the 3 semicircular canal planes, and saccular and utricular function measured by cervical VEMP and ocular VEMP testing, respectively.

Results: We observed significant declines in semicircular canal function in each of the canal planes as well as otolith function associated with aging. We found that individuals with impaired

horizontal and superior semicircular canal function also were likely to have concomitant deficits in utricular but not saccular function. Overall, we noted that the prevalence of semicircular canal dysfunction was highest followed by saccular then utricular impairment, although we did observe individuals with isolated otolith deficits.

Conclusion: These data suggest an overall decline in semicircular canal as well as otolith function associated with aging, although the magnitude of impairment was greater for the semicircular canals than the otoliths in this elderly population. A better understanding of the specific vestibular deficits that occur with aging can inform the development of rational screening, vestibular rehabilitation, and fall risk reduction strategies in older individuals. **Key Words:** Aging—Otolith—Semicircular canal—Vestibular dysfunction.

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Falls are a highly morbid and costly health condition affecting older individuals (1). Studies suggest that the interaction of numerous host and environmental factors leads to a fall event (2,3); increasing evidence suggests that dysfunction of the vestibular system is one such factor that contributes to fall risk (4). A recent analysis showed that vestibular dysfunction is common in the U.S. population and that the prevalence of vestibular dysfunction increases steeply with age (5). However, the physiologic nature of this age-associated decline in vestibular dysfunction is unclear.

The vestibular system consists of 5 organs: 3 semicircular canals (anterior, posterior, and horizontal) and 2 otolith organs—the saccule and the utricle. Vestibular dysfunction

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may reflect pathology within any of these components—in isolation or in combination. Studies of individual vestibular end-organs have observed that both semicircular canal and otolith function seem to decline with age, starting as early as age 40 (6,7). However, given that concurrent assessment of all vestibular end-organs in single individuals has not been performed, it is unclear whether individuals sustain symmetric reductions in semicircular canal and otolith function over time or whether the cumulative toxic, metabolic, infectious, inflammatory, and ischemic exposures associated with the aging process have selective effects within the vestibular apparatus.

The study reported here aims to characterize the physiologic nature of the vestibular dysfunction that occurs with aging and to evaluate whether the normative aging process is predominantly associated with semicircular canal or otolith dysfunction. We used the head thrust dynamic visual acuity (htDVA) test as a measure of semicircular canal function (8), the sound-evoked cervical vestibular-evoked myogenic potential (cVEMP) as a measure of saccular function (9), and the vibration-evoked ocular vestibular-evoked myogenic potential

(oVEMP) as a measure of utricular function (10). We intend to use findings from this study to inform the development and testing of rational screening, vestibular rehabilitation, and fall risk reduction strategies in older individuals.

METHODS

Subjects

Study subjects were recruited from a registry of older individuals interested in participating in clinical studies as well as from outpatient geriatrics clinics. Eligible subjects were age 70 years and above, given the high prevalence of vestibular dysfunction in this age group, and able to provide informed consent to participate in study procedures. Individuals were excluded if they could not participate in study procedures because of blindness, poor neck range of motion, or cervical spine instability (for htDVA testing). Subjects also were excluded if they had a history of diabetes mellitus, given previous data suggesting a significant association between diabetes mellitus and vestibular dysfunction, which could confound the effects of normative aging on the vestibular system (5). Data on patient age, sex, race and educational level were collected based on previous work showing significant associations between these factors and vestibular dysfunction (5). Additional information regarding medical comorbidities also was obtained as a measure of the general health of the population. This study was approved by the Johns Hopkins Medicine institutional review board.

Vestibular Physiologic Testing

All participants underwent comprehensive vestibular physiologic testing, including head thrust DVA testing and cervical and ocular VEMP testing.

Head Thrust DVA Testing

The participant was seated 2 m in front of a high-resolution 18.1-inch monitor. Static visual acuity was measured first, by repeatedly displaying a single optotype (the letter E, randomly rotated each trial by 0, 90, 180, or 270 degrees) on the monitor. Participants viewed 3 optotypes per acuity level, with optotype size then being decremented in steps equivalent to a visual acuity change of 0.1 LogMAR (log10X, where X = 160 degrees). The better one's visual acuity, the lower one's LogMAR score, with LogMAR = -0.3, 0, 0.3, 0.7, 1.0, and 1.3 corresponding to Snellen visual acuity of 20/10, 20/20, 20/40, 20/100, 20/200, and 20/400, respectively.

Static visual acuity was scored when the participant failed to correctly identify all 3 optotypes on an acuity level; the level just larger than this acuity level was set as the static visual acuity. For the dynamic component of the test, a single-axis rate sensor was positioned on the subject's head so that the sensor's axis of maximum sensitivity approximately aligned with that of the semicircular canal of interest. Passive (manually imposed) head thrusts were delivered within a semicircular canal-pair plane in a random direction. One practice trial for a horizontal head thrust was performed, before beginning the htDVA test in the planes of the horizontal, superior, and posterior semicircular canals. During each head thrust, the optotype was displayed when head velocity, sensed by the rate sensor, was between 120 and 180 degrees per second for more than 40 ms, in concordance with parameters used to generate normative values in our laboratory (8). The optotype flashed on the monitor for no longer than

85 ms, equivalent to approximately a 9- to 13.5-degree head rotation. To allow for blinks or transient loss of attention, the subject could view each optotype up to 3 times, after which, they were required to state the perceived orientation. The htDVA test was started at the subject's static visual acuity level, and the optotype size was progressively increased if the optotype orientation was incorrectly identified. The test was terminated once the subject correctly identified all 3 optotype presentations at 1 acuity level; the DVA LogMAR score represented this acuity level. The htDVA test score was calculated by subtracting the static visual acuity LogMAR score from the DVA LogMAR score, to account for possibly poor baseline static visual acuity. Participants did not wear glasses or contact lenses during DVA testing, given difficulties consistently viewing through the corrective lenses during head movement; poor DVA scores were corrected for by poor static visual acuity values (which also were obtained without corrective lenses).

Cervical VEMP Testing

Participants were positioned supine with their upper bodies elevated at a 30-degree angle from horizontal. The neck was actively flexed by the participant during cVEMP stimulation and recording to provide tonic background muscle activity. Airconducted 500-Hz, 125-dB SPL tone bursts of positive polarity, with a linear envelope (1 ms rise/fall time, 2 ms plateau), at a repetition rate of 5 per second were delivered monaurally via intra-auricular speakers. Cervical VEMPs were recorded from an electrode montage consisting of a noninverting electrode placed at the midpoint of the ipsilateral sternocleidomastoid muscle belly, an inverting electrode placed on the sternoclavicular junction, and a ground electrode placed on the manubrium sterni. Recording was only initiated if baseline rectified electromyographic activity, monitored in real time by the experimenter, was approximately 50 µV, to ensure sufficient tonic muscle contraction as well as adequate electrode impedance. The responses to 100 stimuli were averaged. The first positive and negative peaks that occurred between 13 and 23 ms after stimulus onset were designated p13 and n23, respectively. The raw peak-to-peak amplitude was calculated as the sum of the p13 and the n23 amplitudes. The corrected peak-to-peak amplitude was calculated by dividing the raw peak-to-peak amplitude by the rectified background electromyographic activity recorded during the 10-ms interval before stimulus onset. Differences in tone burst-evoked cVEMP peak-to-peak amplitude between subjects age 70 years and over and younger individuals were considered based on previous reports from our laboratory demonstrating a high interrater reliability of this measure (11).

Ocular VEMP Testing

Participants were positioned supine with their upper bodies elevated at a 30-degree angle from horizontal. Maximum upgaze was maintained during oVEMP stimulation and recording. "Mini taps," as described by Iwasaki et al. (12), were delivered by a reflex hammer at the Fz cranial site (in the midline at the hairline, 30% of the distance between the inion and nasion). Fz taps have been shown to provide an acceleration wave that propagates through the cranium to the mastoid on either side, predominantly causing an outward linear acceleration of the utricles bilaterally (13). Ocular VEMPs were recorded from an electrode montage consisting of a noninverting electrode placed over the contralateral inferior oblique muscle approximately 3 mm below the eye and centered beneath the pupil, an inverting electrode centered 2 cm below the noninverting electrode, and a ground electrode placed on the manubrium sterni. The responses to

100 stimuli were averaged. Before testing with tap stimulation, 20-degree vertical saccades were performed to ensure that symmetrical signals were recorded from both eyes. If these saccadic responses showed greater than 25% asymmetry, the electrodes were removed, and new ones were applied. The first negative and positive peaks of the oVEMP response that occurred between 10 and 20 ms after stimulus onset were designated n1 and p1, respectively. Differences in oVEMP n1 amplitudes between subjects age 70 years and older and younger individuals were evaluated, given that this is the portion of the response that is most clearly vestibular and previous data from our laboratory demonstrating a high interrater reliability of this measure (11,14).

Statistical Analysis

Vestibular physiologic testing results were compared between the study subjects age 70 years and older and normative data generated in our laboratory for individuals age 50 years and younger, given previous studies that show consistent declines in vestibular function beginning at about 50 years of age (6,7). The Student's t test was used for comparisons of continuous variables, and the χ^2 test was used to compare proportions. A power analysis demonstrated that a sample size of 50 subjects would provide a power of 0.9 at an alpha level of 0.05 to detect clinically significant differences in vestibular testing results between individuals age 70 years and older and younger individuals. Based on our data and published references, we defined a clinically significant difference as a difference in LogMAR score of 0.16 for htDVA testing (8), a 3- μ V change in peak-to-peak amplitude for cervical VEMP testing (15), and a 3- μ V change

TABLE 1. Descriptive characteristics of study population

	N = 50			
	Mean (standard deviation)			
Characteristics	n (%)			
Demographic characteristics				
Age	77 (5.6)			
Sex				
Male	24 (48)			
Female	26 (52)			
Race				
White	44 (88)			
Black	6 (12)			
Education	` /			
Less than high school	4 (8)			
High school diploma (including GED)	13 (26)			
More than high school	33 (66)			
Medical comorbidities	` ′			
Smoking (number of pack-years smoked)				
Nonsmoker	24 (48)			
<20	12 (24)			
≥20	14 (28)			
History of hypertension	` ′			
No	18 (36)			
Yes	32 (64)			
History of myocardial infarction	` ′			
No	45 (90)			
Yes	5 (10)			
History of stroke	, í			
No	43 (86)			
Yes	7 (14)			
Use of ≥4 prescription medications	` /			
No	18 (36)			
Yes	32 (64)			

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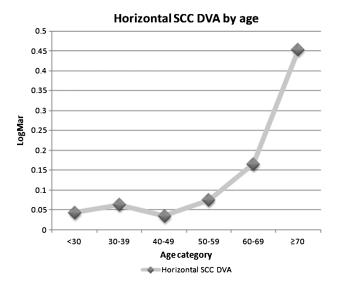


FIG. 1. htDVA in the horizontal semicircular canal plane by age. Overall differences are statistically significant (p < 0.0001). The better one's visual acuity, the lower one's LogMAR score.

in n1 amplitude for ocular VEMP testing (10). SAS 9.2 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

RESULTS

Fifty subjects age 70 years and older were enrolled in the study. The mean age of the subjects was 77 years (standard deviation, 5.6; range, 70–93 yr). Male subjects comprised 48% of subjects and female subjects 52%; 88% of the subjects were white, and 12% were black, and a majority of subjects had greater than a high school education (Table 1). In terms of medical comorbidities,

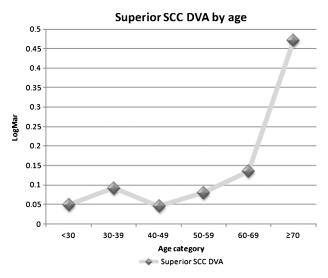


FIG. 2. htDVA in the superior semicircular canal plane by age. Overall differences are statistically significant (p < 0.0001). The better one's visual acuity, the lower one's LogMAR score.

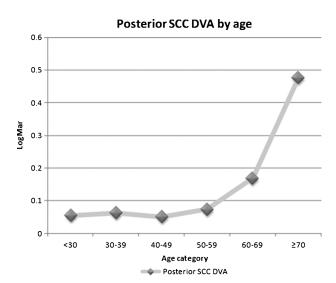


FIG. 3. htDVA in the posterior semicircular canal plane by age. Overall differences are statistically significant (p < 0.0001). The better one's visual acuity, the lower one's LogMAR score.

28% of subjects were heavy smokers, 64% had a history of hypertension, 5% had a history of myocardial infarction, 14% had a history of stroke, and 64% reported using 4 prescription medications or more (Table 1).

We observed a significant decline with age in htDVA when comparing individuals age 70 years and older to data in younger individuals generated in our laboratory. LogMAR scores increased significantly with age (indicative of declining dynamic visual acuity) for the horizontal (p < 0.0001), superior (p < 0.0001), and posterior (p < 0.0001) htDVA tests (Figs. 1–3), suggesting a decline in semicircular canal function in each of the canal planes associated with aging. Peak-to-peak corrected cVEMP amplitudes also decreased significantly with age

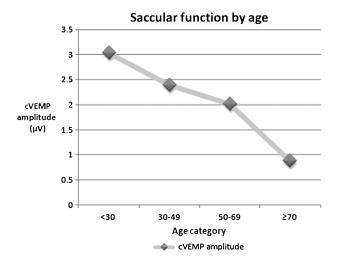


FIG. 4. Cervical VEMP amplitudes (as a measure of saccular function) by age. Overall differences are statistically significant (p < 0.0001). The higher one's cVEMP amplitude, the better one's saccular function.

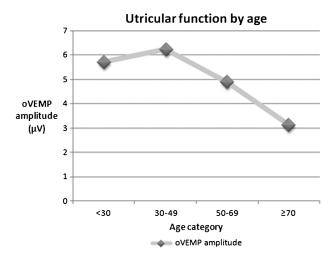


FIG. 5. Ocular VEMP amplitudes (as a measure of utricular function) by age. Overall differences are statistically significant (p< 0.0271). The higher one's oVEMP amplitude, the better one's utricular function.

(p < 0.0001; Fig. 4), suggesting a decline in the saccular function associated with aging. The n1 amplitude of the oVEMP response also decreased significantly with age (p = 0.0271; Fig. 5), indicating an age-related decline in utricular function. We used the mean of right- and left-sided htDVA and VEMP scores for these analyses, given the significant correlation observed between right- and left-sided test scores (Table 2); performing analyses separately by side yielded similar results (data not shown).

We next considered the extent to which semicircular canal and otolith dysfunction occurred concurrently within single individuals. We examined how performance on each of the vestibular physiologic tests correlated with performance on all the other tests (Table 3). We observed that htDVA scores were highly correlated within the 3 semicircular canal planes, such that LogMAR values for the horizontal htDVA test were significantly correlated with LogMAR values for the superior and posterior htDVA tests (Table 3). We also found that performance on the semicircular canal tests did not correlate with performance on the otolith tests; moreover, we noted that saccular function was not significantly correlated with utricular function (Table 3). We further evaluated the question of concurrent vestibular deficits graphically by plotting cVEMP and oVEMP amplitudes as a function of quartiles of htDVA for each of the canal planes. We observed that as horizontal semicircular canal function

TABLE 2. Correlation between right- and left-sided vestibular physiologic test scores

Test	Horizontal	Superior	Posterior	Cervical	Ocular
	DVA	DVA	DVA	VEMP	VEMP
r value	e ^a 0.70	0.59	0.58	0.66	0.48
	e <0.0001	<0.0001	<0.0001	<0.0001	0.0005

DVA indicates dynamic visual acuity; VEMP, vestibular-evoked myogenic potential.

^aPearson's correlation coefficient.

TABLE 3. Correlation between scores of individual vestibular physiologic tests^a

Horizontal DVA	1				
Superior DVA	$r = 0.69^b$				
	p < 0.0001	1			
Posterior DVA	r = 0.64	r = 0.70			
	p < 0.0001	p < 0.0001	1		
Cervical VEMP	r = 0.20	r = 0.12	r = 0.06		
	p = 0.18	p = 0.41	p = 0.70	1	
Ocular VEMP	r = -0.20	r = -0.11	r = -0.11	r = 0.10	
	p = 0.18	p = 0.47	p = 0.43	p = 0.47	1
	Horizontal DVA	Superior DVA	Posterior DVA	Cervical VEMP	Ocular VEMP

Significant correlations are highlighted.

declined, utricular function declined concomitantly, whereas saccular function remained unchanged (Fig. 6). Similar observations were made for superior semicircular canal function (Fig. 7), although no clear trends were seen for posterior semicircular canal function (Fig. 8). It should be noted that these analyses were performed in subjects age 70 years and older only (without individuals from younger age groups). As such, differences in cVEMP and oVEMP amplitudes were small, and the analyses did not achieve statistical significance and are thus considered exploratory.

Finally, we evaluated the relative prevalence of semicircular canal versus otolith dysfunction in the study population. For each of the vestibular physiologic tests (horizontal, superior, and posterior canal htDVA and cervical and ocular VEMP), we used the 95th percentile score from individuals younger than 50 years (previously obtained in our laboratory) to define abnormal values (8,11). We examined the distribution of vestibular deficits within each of the 50 subjects, for the right and left sides (Fig. 9). We observed that most individuals had evidence of semicircular dysfunction bilaterally, although the presence of otolith deficits was less consistent. For the most part, individuals did not exhibit isolated vestibular deficits, although we did find, for example, in subject 21 evidence of only right- and left-sided saccular dysfunction

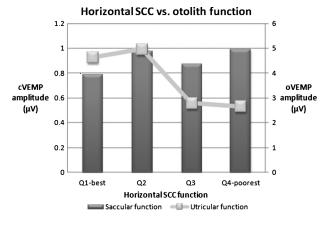


FIG. 6. Cervical and ocular VEMP amplitudes as a function of quartiles of htDVA in the horizontal semicircular canal plane in individuals age \geq 70 years.

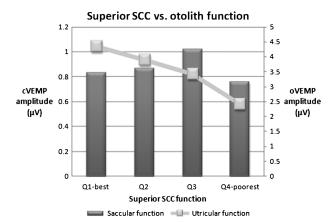


FIG. 7. Cervical and ocular VEMP amplitudes as a function of quartiles of htDVA in the superior semicircular canal plane in individuals age 70 years or older.

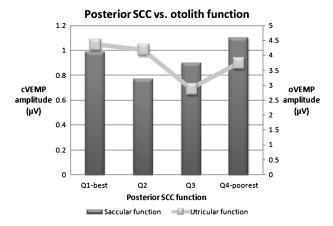


FIG. 8. Cervical and ocular VEMP amplitudes as a function of quartiles of htDVA in the posterior semicircular canal plane in individuals age 70 years or older.

^aThe mean of right- and left-sided scores are used.

 $^{{}^{}b}r$ is the Pearson's correlation coefficient.

Subject			Right					Left		
	Hor SCC	Sup SCC	Post SCC	Saccule	Utricle	Hor SCC	Sup SCC	Post SCC	Saccule	Utricle
1						40.000	2000	100000		
2						(***********	PO 25 (12)	15.791713		
3						10000		(35.00)		
4						3-19635	53.63			
5				92111		200	3 5 6 7 3	167577	- 12 34	
6								F 15 - 67 18 1		
7							369-77-73	257.573		
8			1 5 m				1872.253	V 312 33	3476 63	27,23 %
9			7 11 1			25000		2000		
10										
11							10000			
12						19. 11. 14 hr	1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -			
13						13-13-6	1000			
14									23333	
15			114/10/10			7 1797		1-1-21		
16										
17	1000					516 100			179-417	
18						57733		100000		
19				1.000				10.20		10000
20						1977 316	11,000,000	100000		1000000
21										
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23						1000		0.0000000000000000000000000000000000000		
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41						1000	10 3000			
42						100000		2000		
43								10 100		
44						100000				
45						7.7.000	10000			
46						VALUE OF		7 - 1		
47										
48							100,000	10000		
49			10000					1000		27,27
50						0-1915	11000			

FIG. 9. Right- and left-sided vestibular abnormalities by end-organ in each of the 50 subjects. A colored box indicates dysfunction of that end-organ.

(Fig. 9). When these data were aggregated for the overall study population, we observed that the prevalence of vestibular abnormalities was highest for the semicircular canals (82%–94%), followed by the saccule (54%–62%) and then the utricle (18%–24%; Fig. 10).

DISCUSSION

To our knowledge, this study is the first to comprehensively assay the human peripheral vestibular system to

determine the relative and concurrent presence of specific vestibular deficits in older individuals. We observed a global decline in vestibular function associated with aging: each of the 5 vestibular end-organs demonstrated reduced responses in older compared with younger individuals. However, these data suggest that the magnitude of the decline was asymmetric throughout the vestibular apparatus: the vast majority of individuals age 70 years and older had evidence of semicircular canal dysfunction, whereas only half of participants had abnormal saccular

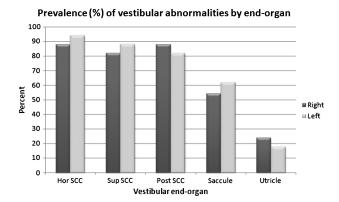


FIG. 10. Prevalence (%) of vestibular abnormalities by end-organ.

function and 1 in 5 had utricular impairment. Histopathologic analyses of age-related changes in the temporal bone corroborate these findings, demonstrating declines in vestibular hair cell populations and otoconial degeneration particularly above age 70 years (16). Moreover, the predominance of semicircular canal abnormalities also has been noted in pathologic studies: a loss of sensory hair cells was found to be significantly more prevalent in the cristae ampullares of the semicircular canals relative to the otolithic maculae (17). Hair cell populations have been found to be equally depleted in all 3 semicircular canal ampullae, concordant with this study (18). The relative sparing of utricular function also may have a histologic correlate: several studies have observed greater reductions with age in otoconial counts in the saccule compared with the utricle (19,20).

Previous vestibular physiologic data also support the current findings. Age-related declines in semicircular canal function, as measured by the angular vestibuloocular reflex, caloric response, and htDVA, have been demonstrated (21-23). Reductions in saccular and utricular function with age also have been observed based on cervical and ocular VEMP testing, respectively (11,15). One study in patients with bilateral vestibular hypofunction noted a significantly higher prevalence of horizontal semicircular canal impairment (based on caloric abnormalities) compared with saccular impairment (measured by cervical VEMP testing) (24). The reason behind a predominance of semicircular canal dysfunction relative to otolith dysfunction with aging is unclear; whether intrinsic anatomic and physiologic differences in the neuroepithelia play a role remains to be elucidated.

We also noted trends suggesting that impaired horizontal and superior semicircular canal function was associated with concomitant utricular but not saccular dysfunction. A previous report similarly described a case of a 77-year-old man who had an atrophic utricular macula and obliteration of the horizontal and superior canal ampullae with sparing of the saccular macula and posterior canal ampulla on postmortem histologic examination (18). The shared susceptibility of these structures may reflect the common embryologic origin and vascular supply of

the pars superior of the labyrinth. Additionally, vestibular neuritis has a known predilection for the superior vestibular nerve (25). Repeated mild viral insults to the superior vestibular nerve and its associated end-organs may underlie the concurrent decline of the pars superior structures.

For the most part, older individuals exhibited widespread vestibular deficits involving the semicircular canals, although we did see occasional cases of isolated otolith deficits. Whether specific vestibular deficits have greater significance with respect to clinically significant outcomes, such as fall risk, is unclear. Falls are an important clinical consequence of vestibular dysfunction; however, the evidence regarding a differential risk of falls with semicircular canal versus otolith dysfunction is scant and equivocal. One study observed no difference in fall history between individuals with semicircular canal dysfunction alone and individuals with both semicircular canal and otolith dysfunction (26). In contrast, another report in patients with progressive supranuclear palsy found that only otolith dysfunction increased fall risk (27). Moreover, it should be noted that even if certain types of vestibular dysfunction were known to confer increased fall risk, vestibular rehabilitation techniques that are targeted to specific subsets of deficits are just being developed (28) and are not in standard clinical use at present. We are currently investigating the clinical significance of specific subtypes of vestibular dysfunction in these subjects and, in the future, plan to consider the benefits of targeted intervention in achieving demonstrable fall risk reduction.

Limitations of this study include the study size, as well as the potential methodologic limitations of the vestibular physiologic tests. It should be noted that the function of the vestibular apparatus cannot be directly probed; therefore, any vestibular reflex test necessarily reflects the function of an afferent and efferent limb and any central processing. As such, it is difficult to determine the function of a vestibular end-organ in isolation from the function of other organ systems. For example, htDVA testing may not only capture semicircular function but may also reflect oculomotor function as well as cognitive processing. This may be particularly true in older individuals who are more likely to have concomitant deficits. In this study, 6 participants had evidence of abnormal oculomotor function (a saccade or smooth pursuit abnormality), and excluding these patients from the analyses did not significantly change our findings. Numerous other studies also have documented progressive age-related declines in dynamic visual acuity; these studies suggest that DVA scores are significantly associated with angular vestibuloocular reflex gain (based on search-coil data) throughout the age range (including in elderly individuals) (21,29,30). Similarly, otolith function is estimated based on an oligosynaptic reflex involving the sternocleidomastoid or inferior oblique muscles; therefore, VEMP responses may be biased in older individuals because of decreased function of the efferent limb. One study found significant age-related declines in cVEMP amplitudes but no significant differences in tonic muscle activity between age groups (31). Moreover,

several studies have reported significant age-related changes in VEMP latencies and thresholds as well as in amplitudes; the authors suggested that the latency and threshold parameters may be less affected by tonic muscle activity compared with amplitude (31,32). Given these considerations, we submit that our findings are suggestive, although not conclusive, of declines in semicircular canal and otolith function with aging. Another potential methodologic limitation relates to the differential sensitivity of the various vestibular tests. The tap-evoked oVEMP test, for example, has been reported to deliver a suprathreshold stimulus to the utricle, thereby possibly limiting the detection of abnormal values (33).

These findings provide evidence that there is an overall decline in semicircular canal, as well as otolith function associated with aging, and that the magnitude of impairment seems to be greater for the semicircular canals than for the otoliths. We also conclude that declines in function may occur concurrently for the structures that comprise the pars superior of the labyrinth—the horizontal and superior semicircular canals and the utricle, and that older individuals generally sustain bilateral semicircular canal impairment, although isolated otolith dysfunction also can be observed. A better understanding of the specific vestibular deficits that occur with aging can inform the development of rational screening, vestibular rehabilitation, and fall risk reduction strategies in older individuals.

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