

Phybrata Digital Biomarkers of Age-Related Balance Impairments, Sensory Reweighting, and Intrinsic Fall Risk

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Objective: To assess the utility of digital biomarkers derived from a head-mounted wearable physiological vibration acceleration (phybrata) sensor to quantify age-related balance impairments, sensory reweighting, and fall risks in older populations.

Methods: Data were collected and analyzed from 516 participants aged 77.7 ± 8.0 yrs (min 51 yrs, max 98 yrs, 334 females, 182 males) in 4 residential senior living communities. Participants first completed a questionnaire that included their fall history in the past 6 months. A 2-minute standing balance test was then carried out for each participant using the phybrata sensor (1 minute with eyes open, followed by 1 minute with eyes closed). Four balance performance biomarkers were derived from the phybrata time series data: eyes open (Eo) and eyes closed (Ec) phybrata powers, average phybrata power $(Eo+Ec)/2$, and Ec/Eo phybrata power ratio. Sensory reweighting biomarkers were derived from phybrata acceleration spectral density (ASD) distributions. Results are compared for participants with no reported fall history (NF) and those reporting one or more falls (FR) in the previous 6 months.

Results: All four phybrata balance performance biomarkers show significantly higher values for FR participants vs NF participants. As a fall risk biomarker, Ec phybrata power was found to have the strongest statistical correlation with the reported retrospective incidence of falls within the previous 6 months. The Ec phybrata biomarker also showed the strongest statistical difference between F and M participants. Phybrata sensory reweighting biomarkers quantify age-related impairments and sensory reweighting across sensory inputs (visual, vestibular, proprioceptive), central nervous system (CNS) processing, and neuromotor control (vestibulocollic reflex), revealing progressive reductions in visual and vestibular balance regulation and vestibulocollic head stabilization that are offset by an increasing reliance on proprioceptive balance control.

Conclusion: Phybrata digital biomarkers enable rapid objective assessment of progressive age-related balance impairments, sensory reweighting, and fall risks in older populations.

Keywords: presbystasis, age-related balance decline, vestibular, phybrata, wearable sensor, biomarker, balance performance, fall risk, sensory reweighting

Introduction

Age-related balance dysfunction, clinically referred to as presbystasis, is a complex condition characterized by a gradual decline in balance and mobility. This condition not only significantly heightens the risk of falls but also makes it increasingly more difficult to continue living actively, independently, and productively. The economic burden of presbystasis exceeds \$280 billion annually in the US, with over \$50 billion in direct medical expenses for falls alone.¹ More than \$230 billion in additional costs result from spending on long-term care, productivity loss, caregiver burden, and diminished quality of life.² Most falls result from a combination of intrinsic/physiological risks (eg impaired postural stability)³ and extrinsic/environmental risks (uneven surfaces or obstacles, poor lighting, inappropriate footwear, challenging physical activities),⁴ but deficits in balance and gait are the most prominent pre-disposing risk factors at the population level.^{5–11} Simple tests of balance have been shown to be a good prognostic indicator for risk of all-cause

mortality in middle-aged and older individuals,^{12,13} highlighting the opportunity to combine more detailed and quantitative balance testing with targeted interventions to mitigate adverse health outcomes.

Human balance relies on three primary sensory inputs that provide critical information to the brain regarding the body's movement and orientation to maintain stable balance control. Visual inputs from the eyes inform the brain about relative movements of the body with respect to objects in the surrounding environment, inputs from the vestibular balance organs in the inner ear provide information on the body's own movement by detecting linear and rotational head motion and deviations from earth-vertical (gravity), and proprioceptive and somatosensory inputs from the skin, tendons, muscles, and joints relay information regarding the body's orientation relative to and contact with objects in the surrounding environment. The central nervous system (CNS), which includes the brain and spinal cord, integrates and processes these sensory inputs, generating motor control outputs that are transmitted to the musculoskeletal system via the peripheral nervous system (PNS), enabling the body to stand and move without losing balance. The vestibular system also works closely with the eyes, muscles, and joints to coordinate balance functions automatically¹⁴ through the vestibulo-ocular reflex (VOR), which regulates the eye muscles to maintain gaze during head movements, the vestibulo-collic reflex (VCR), which controls the neck muscles to support the head during movements, and the vestibulospinal reflex (VSR), which controls the muscles of the body and limbs to maintain posture and balance.

Although presbystasis is a multifaceted disorder, studies of balance aging have identified vestibular dysfunction as the primary cause of balance decline in more than 55% of adults over age 50, or around 70 million people in the U.S.⁵⁻⁸ Furthermore, more than 35% of US adults over 40 years of age already suffer from age-related dysfunction in the vestibular balance system,⁹ often long before symptoms begin to be observed. This dysfunction impacts both the peripheral vestibular organs in the inner ear and central vestibular processing in the brain,¹⁰ significantly increases fall risk,¹¹ and has also been linked to the onset and progression of cognitive decline.¹⁵ Part of the normal aging process is the loss of vestibular hair cells, which weakens the sensory signals generated by the vestibular organs and triggers a cascade of additional atrophy effects in the other components of the vestibular system.^{8,10,16} These atrophy effects include decrease in the gain of the synapses between the motion sensing cells and the vestibular nerve and decreased conductivity along the vestibular nerve, both of which further weaken the signals received by the brain. These weaker signals can lead to atrophy in those parts of the CNS that integrate and process sensory input and motor control output signals.

A key element of balance-related CNS processing is sensory reweighting (SR), the process by which the brain continuously evaluates the reliability and recalibrates the relative importance, or weighting, that it assigns to visual, vestibular, and proprioceptive sensory inputs.^{17,18} SR allows the brain to amplify or attenuate signals from different sensory systems based on their perceived reliability. SR can occur dynamically – in response to changing environmental factors such as poor lighting or uneven surfaces – or it can occur slowly over time – in response to changing physiological factors, such as loss of vestibular hair cells, decline in vision, or peripheral neuropathies that degrade proprioceptive signals. Age-related reductions in the response time or accuracy of the SR process significantly increase fall risks in older people.¹⁹ Evaluation of SR can provide valuable insights into potential underlying causes of balance decline.

Many outcome measures are available for the assessment and treatment of patients with balance and dizziness disorders.²⁰ Balance researchers and clinical specialists quantify age-related balance and mobility decline, vestibular-specific impairments, changes in SR, and related fall risks using specialized laboratory equipment such as computerized dynamic posturography (CDP) systems.^{8,20-25} These systems are costly and require dedicated facilities and trained staff, and they are typically available only in balance and gait research labs or specialized neuromotor clinics that are not widely accessible to most older patients with declining balance and postural control. As a result, most clinicians assessing balance in their older patients day-to-day are limited to visually scored tests or self-reported scales for balance, dizziness, ambulatory performance, and fall risks.²⁶ While low-cost and easy to perform, their reliability and utility are limited²⁷ and more than half of elderly patients with balance disorders report vague, inconsistent, or contradictory descriptions of their symptoms.²⁸ Earlier detection and more effective management of vestibular dysfunction in older adults hinges on the development of more objective and readily available diagnostic methods.

Wearable sensor technologies offer a promising approach to enabling more widely accessible instrumented assessments of balance and mobility decline.^{29,30} However, current technology typically relies on arrays of multiple

synchronized sensors mounted on different parts of the body to match the quantitative performance of traditional balance research lab solutions.²⁹ We have previously demonstrated that this limitation can be overcome using a single head-mounted wearable inertial motion unit (IMU)-based physiological vibration acceleration (phybrata) sensor with a simple two-minute test.^{31,32} The head-mounted design and tiny mass of the device enable the separation of postural control contributions from visual, vestibular, and proprioceptive inputs along with CNS processing and neuromotor control by mapping them to specific vibrational frequency bands in the phybrata data.^{32,33} Previous studies have shown that phybrata-based biomarkers can effectively quantify changes in postural stability, underlying impairments across multiple balance system components, and the resulting sensory reweighting due to head trauma such as concussions,^{31,32,34} diseases like multiple sclerosis,³⁵ and spinal cord injuries.³⁶ The diagnostic performance of the phybrata sensor has been shown to match that of full-body video motion capture and IMUs mounted on multiple parts of the body in assessing standard balance and gait parameters and postural transitions during activities of daily living.^{37,38} The combination of phybrata sensor data and machine learning (ML) has been shown to outperform the diagnostic performance of alternatives such as neurocognitive tests, clinical scales, symptoms checklists, balance and gait testing, MRI, EEG, eye tracking, and blood biomarkers.³⁴ Comparisons of head-mounted and body-mounted IMUs have demonstrated that for the head-mounted sensor, a 60 second test duration is sufficient for both clinical diagnostic applications and research studies.³⁸

The present study investigates the use of digital biomarkers derived from phybrata balance assessments to quantify declining postural stability, underlying impairments across multiple balance system components, the resulting sensory reweighting, and increased fall risks in older adults.

Methods

Participants

Data were collected and analyzed from 516 participants aged 77.7 ± 8.0 yrs (min 51 yrs, max 98 yrs, 334 females, 182 males) during day-long balance clinics held at 4 residential elderly centers in the San Francisco Bay area, California. At check-in and prior to testing, clinical staff at each center measured and recorded each participant's height and weight and recorded their age and the number of falls reported in the past 6 months. Table 1 summarizes participant ages, gender, and fall histories. 329 participants reported no falls (NF) in the previous 6 months (age 76.6 ± 7.9 yrs, min 51 yrs, max 95 yrs, 230 females, 99 males). 187 participants reported falling one or more times (FR) in the previous 6 months (age 79.6 ± 7.7 yrs, min 54 yrs, max 98 yrs, 104 females, 83 males).

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki with research ethics approval under Western IRB Study Number 1188786, and informed consent was obtained for all participants in the study. The participant provided informed consent for publication of the image in Figure 1.

Table 1 Summary of Participants and Reported Fall Histories

	All Participants (516)			Female Participants (334)			Male Participants (182)		
	Total	No Falls Reported	Falls Reported	Total	No Falls Reported	Falls Reported	Total	No Falls Reported	Falls Reported
Number	516	329	187	334	230	104	182	99	83
Mean age (yrs)	77.7	76.6	79.6	77.4	76.5	79.3	78.2	76.7	80
Stnd Dev (yrs)	8.0	7.9	7.3	7.6	7.3	7.7	8.6	9.1	7.8
Min (yrs)	51	51	54	51	51	60	51	51	54
Max (yrs)	98	95	98	98	95	98	98	94	98



Figure 1 Phyrbrata sensor attached to the mastoid using an adhesive patch.

Measurements

Participants were tested using the previously reported phyrbrata sensor^{31,32,34–37} attached to the patient's mastoid using a disposable medical adhesive, as shown in [Figure 1](#), while standing still for 60 sec with eyes open (Eo) and then again for 60 sec with eyes closed (Ec). During testing, participants were instructed to stand upright in a relaxed position with their feet together and their arms at their sides while maintaining their gaze in a straight-ahead direction focused on a visual target mounted on the wall 10 feet away at eye level. Patients were also instructed not to talk or move during testing. The test administrator always stood by the subjects: (1) to monitor subjects' postural sway throughout the trial; and (2) so that the subjects had no fear of falling during eyes-closed testing. Testing was repeated if any anomalous patient movement was observed during phyrbrata testing. A smartphone app connects to the phyrbrata sensor via a Bluetooth low-energy (BLE) wireless link to configure and run tests, collect data, and interface with cloud-based data storage, analytics, and reporting services. The phyrbrata IMU includes a 3-axis accelerometer to record x (anterior-posterior (AP), or front-back), y (vertical), and z (medial-lateral (ML), or left-right) acceleration time series data in units of g. During each 60 sec test, data is recorded at a sampling rate of 100 hz, generating a total of 6000 samples for each of the 3 axes (x, y, z). The accelerometer signals are filtered to remove drift, as in our previous studies with the same device.^{31,32} [Figure 2](#) shows sample Eo and Ec x, y, z phyrbrata time series signals for a participant reporting no falls in the previous 6 months ([Figure 2a](#)), a participant reporting one fall in the previous 6 months ([Figure 2b](#)), and a participant reporting multiple falls in the previous 6 months ([Figure 2c](#)). [Figure 3](#) shows sample Eo and Ec AP/ML phyrbrata spatial scatter plots and phyrbrata power bar graphs for the same three participants as in [Figure 2](#).

Data Analysis

For each pair of tests (60 sec Eo followed by 60 sec Ec), four phyrbrata metrics were calculated from the time series data as previously described:^{31,32} Eo and Ec powers (in watts), (Eo+Ec)/2 average power, and Ec/Eo power ratio. Data analyses were carried out using the commercially licensed statistical analysis software package NCSS (NCSS LLC, Kaysville, UT, USA). Data analysis included descriptive statistics, analysis of variance (ANOVA, MANOVA), and receiver operating characteristic (ROC) curves for the 4 phyrbrata metrics and sub-populations of interest (F vs M, NF vs FR). Eo and Ec distributions generally failed 2 or more of 3 normality tests (Shapiro–Wilk, skewness, kurtosis) and were log-transformed prior to ANOVA/MANOVA. Means and 95% confidence intervals (CIs) were calculated using the bootstrap method. Acceleration spectral density (ASD) frequency analyses of Eo and Ec phyrbrata time series data were carried out for each participant and used to calculate sensory reweighting profiles as previously described.^{32,35,36} Benefits

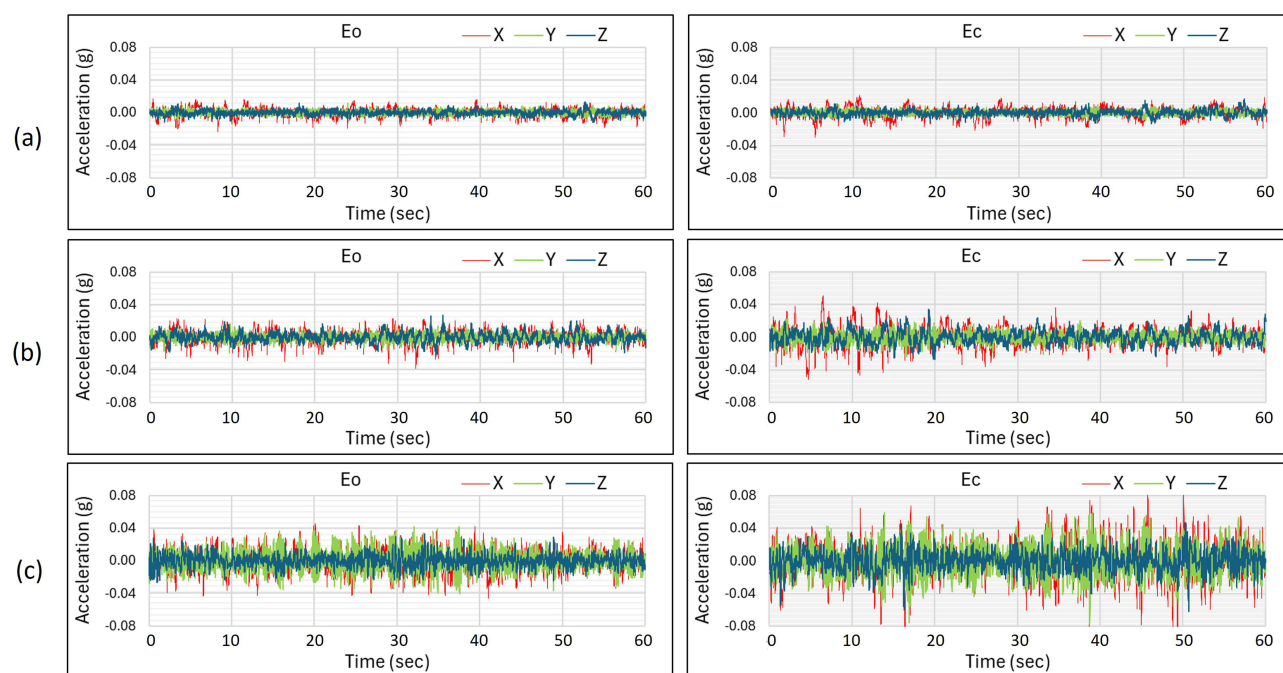


Figure 2 Sample eyes open (Eo) and eyes closed (Ec) x (anterior-posterior, AP), y (vertical), z (medial-lateral, ML) phybrata time series data for participants (a) with no reported fall history (b) reporting a single fall in the past 6 months (c) reporting multiple falls in the past 6 months.

of the direct measurement of acceleration and the use of power-based and frequency-based metrics in the present study include greater sensitivity to differences in Eo vs Ec performance and less sensitivity to sampling duration.³²

Results

Figure 4 presents box plots comparing the distributions of the 4 phybrata metrics for 329 participants with no reported falls and 187 participants with one or more reported falls (Figure 4a); 230 female participants and 99 male participants with no reported falls (Figure 4b); and 104 female participants and 83 male participants with one or more reported falls (Figure 4c). Corresponding means, 95% CIs, and MANOVA results are presented in Table 2.

All four phybrata metrics show significantly higher values for FR participants vs NF participants (Figure 4a): Eo, $F(1,515) = 149.82$, $p < 0.00001$; Ec, $F(1,515) = 294.10$, $p < 0.00001$; (Eo+Ec)/2, $F(1,515) = 269.85$, $p < 0.00001$; Ec/Eo, $F(1,515) = 97.04$, $p < 0.00001$. The Ec metric shows the strongest correlation with falls status. All four phybrata metrics also show significant differences ($p < 0.05$) between F vs M participants in the NF group (Figure 4b): Eo, $F(1,328) = 5.14$, $p = 0.02$; Ec, $F(1,328) = 19.80$, $p = 0.00001$; (Eo+Ec)/2, $F(1,328) = 15.88$, $p = 0.0001$; Ec/Eo, $F(1,328) = 12.20$, $p = 0.0006$. Three of the four phybrata metrics (Ec, (Eo+Ec)/2, Ec/Eo) showed significant differences between F and M participants in the FR group (Figure 4c): Ec, $F(1,186) = 12.14$, $p = 0.006$; (Ec+Eo)/2, $F(1,186) = 10.44$, $p = 0.002$; Ec/Eo, $F(1,186) = 6.91$, $p = 0.009$.

Figure 5 shows receiver operating characteristic (ROC) curves for the classification of falls history for all 516 participants for all possible cutoff values of the 4 phybrata metrics Eo, Ec, (Eo+Ec)/2, Ec/Eo. Key ROC results are summarized in Table 3. As a metric for clinical assessment of fall risk, Ec achieves area under the curve (AUC) = 0.88 (95% CI = 0.84–0.91), and for a cutoff value of Ec = 0.90 watts, the corresponding sensitivity and specificity are 0.76 and 0.85, respectively. The above cutoff value for Ec (0.90 watts) agrees well with the corresponding box plot distributions in Figure 4a, highlighting the utility of this simple and physiologically intuitive phybrata digital biomarker for rapid diagnostic testing of fall risk. As discussed further below, these ROC results compare favorably with more complex, time-consuming, and expensive approaches for instrumented fall risk assessments. Table 3 also includes ROC results for the classification of falls history for the 334 F participants and 182 M participants for all possible cutoff values of the 4 phybrata metrics. The statistically significant differences observed between M vs F participants in the distributions of the

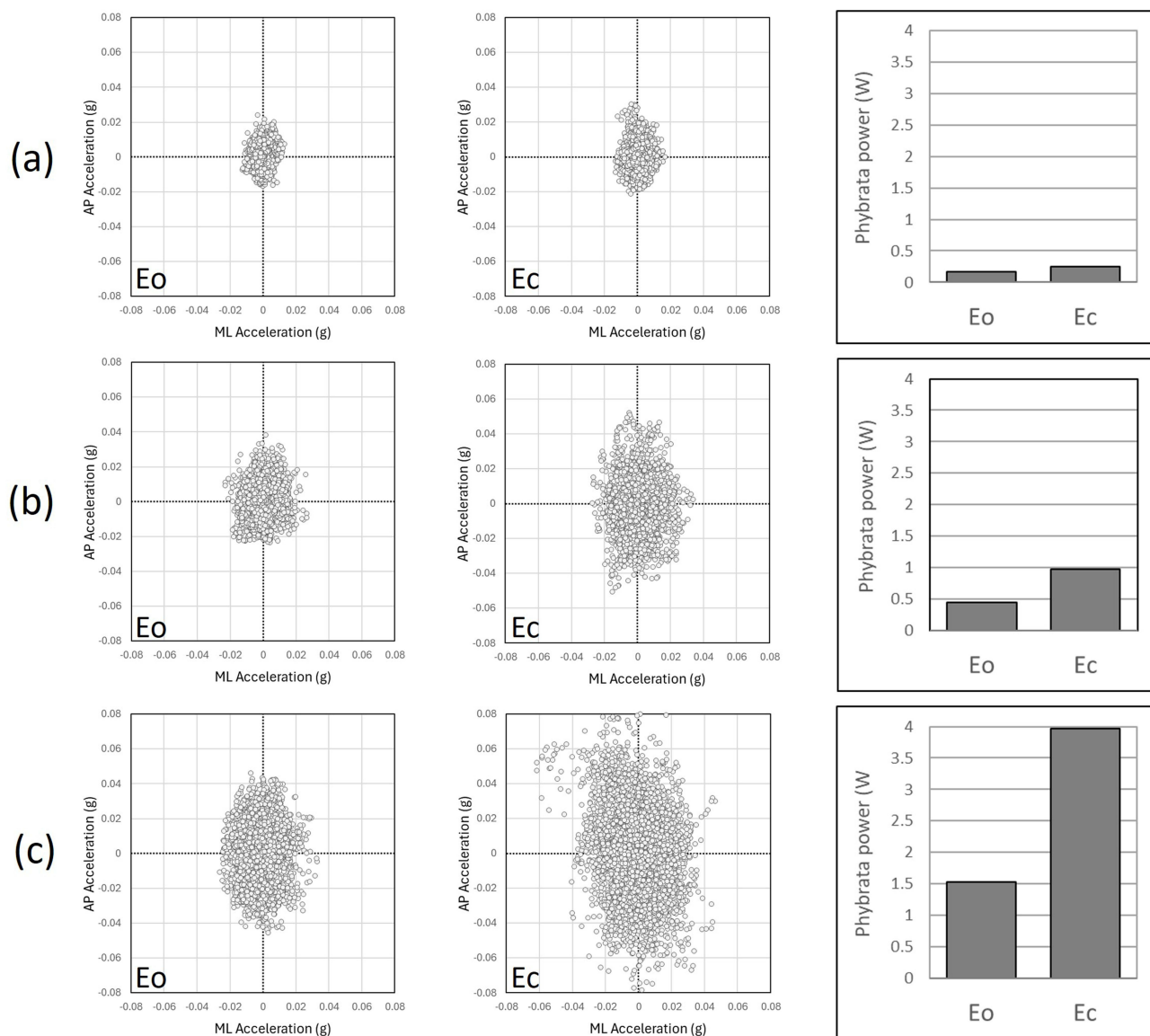


Figure 3 Sample eyes open (Eo) and eyes closed (Ec) AP/ML phybrata spatial scatter plots and phybrata powers for participants (a) with no reported fall history (b) reporting a single fall in the past 6 months (c) reporting multiple falls in the past 6 months.

Abbreviations: Eo, eyes open; Ec, eyes closed; AP, anterior-posterior; ML, medial-lateral.

four phybrata metrics in Figure 4 and Table 2 are reflected in the higher cutoff values for M vs F participants for all four phybrata metrics in Table 3.

Figure 6 presents phybrata sensory reweighting plots for the 20 participants with the lowest values of Ec, the 20 participants with the highest values of Ec, and the 20 participants straddling the Ec = 0.9 falls risk threshold (10 immediately below and 10 immediately above). Separate plots are shown for Eo (Figure 6a) and Ec (Figure 6b). Relative changes in reliance on specific mechanisms of postural control were quantified by calculating relative changes within five frequency bands³² in the normalized phybrata ASD frequency spectra: 0.02–0.1 hz (visual regulation); 0.1–0.5 hz (vestibular regulation); 0.5–1 hz (CNS participation, both cerebellar and cortical); 1–10Hz (spinal reflexive loops, proprioception, multi-joint and muscle activity); 10–25 hz (vestibulocollic head stabilization). The normalized sensory reweighting plots in Figure 6 are calculated by integrating over time and frequency in each of the five ASD frequency bands for each individual and then averaging each band over the 20 individuals in each of the three groups. Figure 6

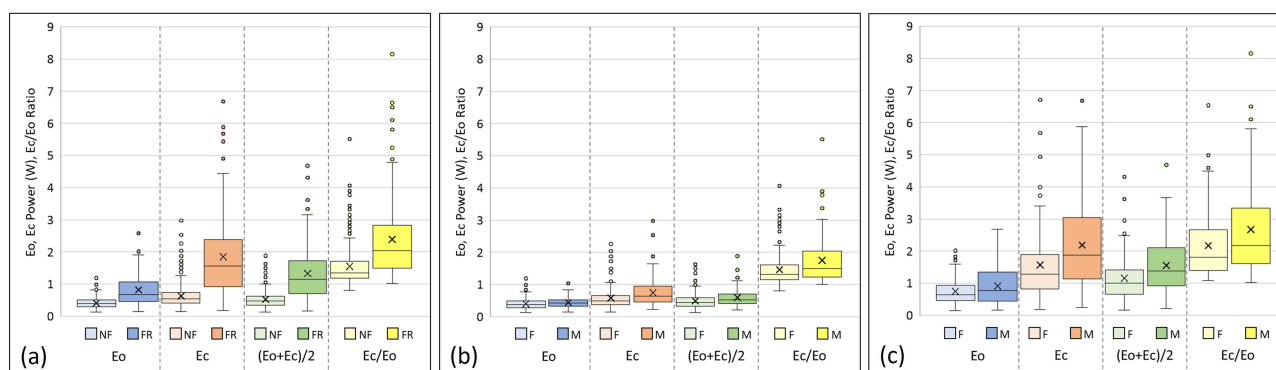


Figure 4 Box plots showing distributions of 4 phybrata metrics for (a) 329 participants with no reported falls and 187 participants with one or more reported falls (b) 230 female participants and 99 male participants with no reported falls (c) 104 female participants and 83 male participants with one or more reported falls.

Abbreviations: F, female; M, male; NF, no falls; FR, falls reported; Eo, eyes open; Ec, eyes closed.

reveals a significant redistribution across the five spectral bands with increasing postural instability and fall risk, with progressive reductions in visual and vestibular balance regulation and vestibulocollic head stabilization that are offset by an increasing reliance on proprioceptive balance control. This observed sensory reweighting is consistent with

Table 2 MANOVA Summary of 4 Phybrata Metrics for 329 Participants with No Reported Falls in the Previous 6 months (NF) and 187 Participants with One or More Reported Falls in the Previous 6 months (FR)

All Participants (516)	Falls Status	Mean	95% CI	F-Ratio	P
Eo power	NF	0.413	0.394–0.432	$F(1,515) = 149.82$	<0.00001****
	FR	0.82	0.749–0.894		
Ec power	NF	0.63	0.587–0.666	$F(1,515) = 294.10$	<0.00001****
	FR	1.845	1.666–2.029		
(Eo + Ec)/2	NF	0.521	0.492–0.548	$F(1,515) = 269.85$	<0.00001****
	FR	1.336	1.210–1.450		
Ec/Eo	NF	1.55	1.483–1.614	$F(1,515) = 97.04$	<0.00001****
	FR	2.389	2.205–2.571		
No falls reported (329 participants)	Gender	Mean	95% CI	F-ratio	P
Eo power	F	0.4	0.377–0.423	$F(1,328) = 5.14$	0.024*
	M	0.442	0.407–0.475		
Ec power	F	0.579	0.533–0.620	$F(1,328) = 19.80$	0.00001****
	M	0.749	0.655–0.826		
(Eo + Ec)/2	F	0.49	0.458–0.519	$F(1,328) = 15.88$	0.0001***
	M	0.595	0.540–0.647		
Ec/Eo	F	1.466	1.397–1.528	$F(1,328) = 12.20$	0.0006***
	M	1.749	1.579–1.895		

(Continued)

Table 2 (Continued).

Falls reported (187 participants)	Gender	Mean	95% CI	F-ratio	P
Eo power	F	0.748	0.664–0.826	F(1,186) = 3.46	0.065 [#]
	M	0.913	0.791–1.028		
Ec power	F	1.571	1.343–1.772	F(1,186) = 12.14	0.0062 ^{**}
	M	2.189	1.899–2.474		
(Eo + Ec)/2	F	1.159	1.015–1.295	F(1,186) = 10.44	0.0015 ^{**}
	M	1.552	1.356–1.739		
Ec/Eo	F	2.166	1.946–2.362	F(1,186) = 6.91	0.0094 ^{**}
	M	2.673	2.348–2.964		

Note: [#]p≥0.05; *p≤0.05; **p≤0.01; ***p≤0.001; ****p≤0.0001.

Abbreviations: F, female; M, male; NF, no falls; FR, falls reported; Eo, eyes open; Ec, eyes closed.

a progressively greater degree of age-related vestibular functional decline in individuals with progressively increasing postural instability and fall risk. A significant increase in the CNS band ($P < 0.05$) is observed for Eo but not for Ec.

Discussion

The present study demonstrates that digital biomarkers derived from a single head-mounted phybrata sensor are sufficiently consistent, reproducible and sensitive to provide objective assessments of progressive age-related balance impairments and sensory reweighting, underlying physiological contributions, and related intrinsic fall risks in older populations. Many previous studies have demonstrated that simple measures of postural sway derived from instruments

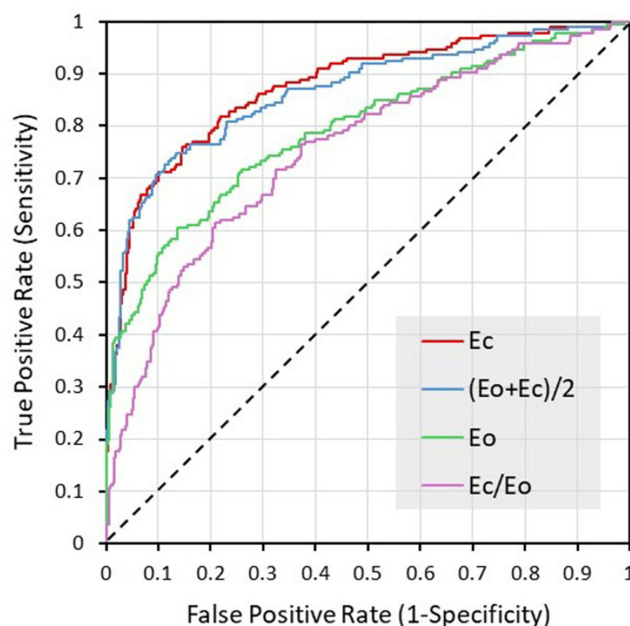


Figure 5 ROC curves for 4 phybrata metrics used for the classification of falls history for all 516 participants.

Abbreviations: Eo, eyes open; Ec, eyes closed.

Table 3 Summary of ROC Results for 4 Phybrata Metrics Used to Classify Falls History for All 516 Participants, for 334 Female Participants, and for 182 Male Participants. Grey Shading Indicates AUC and Cutoff Values for the Ec Metric for Each of the 3 Participant Groups

Phybrata Metric	AUC	95% CI	Cutoff	TP	FP	FN	TN	Sensitivity (TP/TP+FN)	Specificity (TN/TN+FP)	Precision (TP/TP+FP)	Accuracy (TP+TN)/(TP+FP+FN+TN)	Youden Index	Distance to Corner
All participants (516)													
Eo	0.792	0.745–0.831	0.58	113	45	74	284	0.604	0.863	0.715	0.769	0.468	0.419
Ec	0.876	0.838–0.905	0.90	142	48	45	281	0.759	0.854	0.747	0.82	0.614	0.281
(Eo+Ec)/2	0.865	0.825–0.896	0.74	140	44	47	285	0.749	0.866	0.761	0.824	0.615	0.285
Ec/Eo	0.752	0.704–0.793	1.78	115	69	72	260	0.615	0.79	0.625	0.727	0.405	0.438
Female participants (334)													
Eo	0.793	0.730–0.843	0.58	61	26	43	204	0.587	0.887	0.701	0.793	0.474	0.429
Ec	0.868	0.817–0.906	0.90	75	22	29	208	0.721	0.904	0.773	0.847	0.626	0.295
(Eo+Ec)/2	0.854	0.799–0.895	0.74	74	24	30	206	0.712	0.896	0.755	0.838	0.607	0.307
Ec/Eo	0.753	0.691–0.804	1.78	56	35	48	195	0.539	0.848	0.615	0.752	0.386	0.486
Male participants (182)													
Eo	0.781	0.701–0.841	0.7	46	9	37	90	0.554	0.909	0.836	0.747	0.463	0.455
Ec	0.879	0.816–0.921	1.18	62	8	21	91	0.747	0.919	0.886	0.841	0.666	0.266
(Eo+Ec)/2	0.872	0.806–0.917	0.92	63	9	20	90	0.759	0.909	0.875	0.841	0.668	0.258
Ec/Eo	0.731	0.647–0.797	1.9	56	28	27	71	0.675	0.717	0.667	0.698	0.392	0.431

Abbreviations: Eo, eyes open; Ec, eyes closed; AUC, area under the curve; TP, true positive; FP, false positive; FN, false negative; TN true negative.

such as force plates³⁹ or wearable IMUs^{29,30} are more reproducible and reliable than subjective balance tests^{20,26} for the assessment of balance disruptions in older populations. In addition to static balance, head movement kinematics have been shown to enable functional assessments of gait impairments^{40–42} and activities of daily living.^{43,44} The present study, however, demonstrates the unique ability of the phybrata sensor to map the systematic sensory reweighting across multiple physiological systems that accompanies age-related balance decline and increased fall risk.

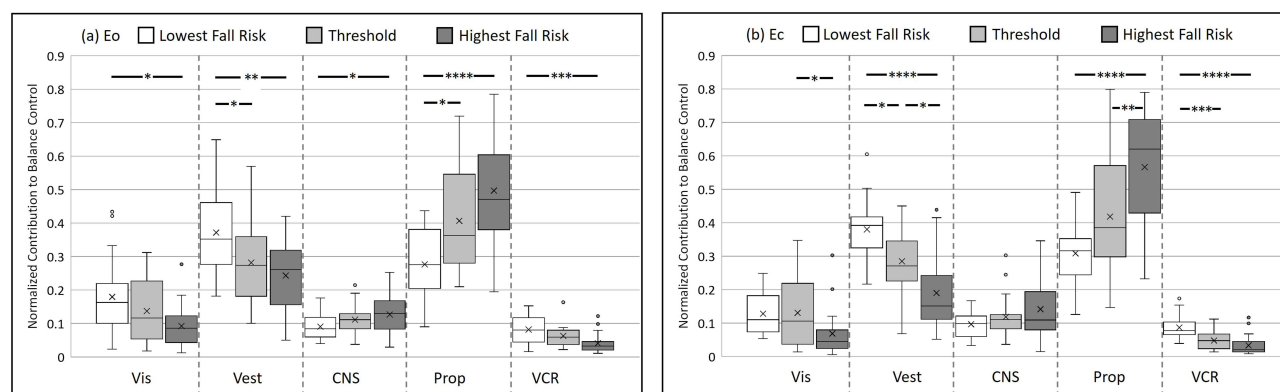


Figure 6 Phybrata sensory reweighting plots for 20 lowest fall risk participants, 20 threshold low/high fall risk participants, and 20 highest fall risk participants (a) Eo (b) Ec. **Note:** * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$.

Abbreviations: Eo, eyes open; Ec, eyes closed; Vis, vision; Vest, Vestibular; CNS, central nervous system; Prop, proprioception; VCR, vestibulocollic reflex.

The specific phybrata biomarkers discussed here are:

- (i) Four balance performance biomarkers derived from the phybrata time series data: eyes open (Eo) and eyes closed (Ec) phybrata powers, average phybrata power $(Eo+Ec)/2$, and Ec/Eo phybrata power ratio.
- (ii) Fall risk biomarker derived from the phybrata time series data: Ec.
- (iii) Five SR biomarkers derived from phybrata ASD data to quantify age-related impairments and sensory reweighting across sensory inputs (visual, vestibular, proprioceptive), CNS sensorimotor integration, and neuromotor control (vestibulocollic reflex).

These phybrata biomarkers can serve as:

- (i) Physiological biomarkers that assess critical sensory and neuromotor functions related to aging.
- (ii) Systems aging biomarkers that identify patterns and pathways in the systemic aging and dysfunctions of the body's integrated neuromotor system.
- (iii) Longitudinal and clinical biomarkers of aging that provide insights into the progression of neuromotor aging processes by monitoring individuals over extended periods, allowing researchers to predict health outcomes, understand the dynamics of aging, and develop targeted and personalized interventions to promote healthy neuromotor aging.

Phybrata Balance and Fall Risk Biomarkers

As illustrated in [Figure 4a](#), all four phybrata metrics show significant statistical correlations with reported fall history (FR vs NF). ROC analysis ([Figure 5](#) and [Table 3](#)) gives AUC values ranging from 0.75–0.88, which are all higher than the typical AUC range of 0.5–0.7 that have been reported for many other common fall risk assessments.²⁶ The Ec metric shows the strongest correlation with falls status (AUC = 0.88), although the $(Eo+Ec)/2$ metric is very close in classification performance (AUC = 0.87). This result is consistent with the observation that, compared to young adults, older adults experience relatively greater difficulty maintaining their balance during sensory feedback perturbations such as standing with the eyes closed or on foam,^{45,46} and this behavior has also been correlated with loss of vestibular function.⁴⁶ These same four phybrata metrics have previously shown similar significant statistical correlations with the diagnosis of concussion in a study population of 175 individuals aged 7–66 yrs.³² The $(Ec+Eo)/2$ metric showed the strongest correlation with concussion diagnosis, although the Ec metric was very close in classification performance. ROC curves demonstrated that Eo and Ec/Eo may be utilized as independent measures to confirm accompanying neurological and vestibular impairments. Phybrata testing and sensory reweighting analysis revealed the significant contribution of vestibular impairment to balance disruption following concussion injuries and allowed subsequent monitoring of improvements throughout treatment and rehabilitation.^{31,32} For the diagnosis of concussion, the combination of phybrata sensor data and machine learning models has been shown to enable both binary classification of concussion patients and multiclass predictions of specific concussion-related neurophysiological impairments, outperforming the diagnostic performance of alternatives such as neurocognitive tests, clinical scales, symptoms checklists, balance and gait testing, MRI, EEG, eye tracking, and blood biomarkers.³⁴ The above similarities in phybrata results highlight the degree to which concussions and other repetitive head impact injuries can lead to “accelerated aging”,⁴⁷ with impairment profiles that mirror “normal aging”, including significant impairments to vestibular function.⁴⁸

As illustrated in [Figure 4b](#), all four phybrata metrics also show significant differences ($p < 0.05$) between F vs M participants in the NF group. As illustrated in [Figure 4c](#), three of the four phybrata metrics (Ec, $(Eo+Ec)/2$, Ec/Eo, but not Eo) showed significant differences between F and M participants in the FR group. The ROC results in [Table 3](#) also indicate lower thresholds in F vs M for the emergence of fall risk (NF vs FR) for all four phybrata metrics. These results are in contrast to a previous study of the balance performance of 347 healthy college students aged 18–21 years,³¹ in which statistically significant differences as a function of gender were observed for Eo and Ec but not for Ec/Eo. In the concussion study discussed above,³² significant differences in phybrata performance were observed as a function of age in the healthy control participants. Taken together, these results indicate that phybrata testing is sufficiently sensitive to

detect gender-based differences in overall postural control regardless of age (Eo, Ec), the progression of balance decline and fall risk with age (Ec), and the important contribution of vestibular disruptions (increasing Ec/Eo). The observed higher Eo for FR vs NF with no significant difference between M and F may indicate that CNS contributions to age-related balance decline are less dependent on gender in the current study population. Similar trends in age- and gender-related balance performance have also been reported using much more expensive CDP equipment and much more time-consuming test protocols.⁴⁹

Phybrata Sensory Reweighting Biomarkers

The most widely accepted method to quantitatively assess an individual's ability to use visual, proprioceptive and vestibular cues to maintain postural stability during standing balance is the sensory organization test (SOT).^{50–52} The SOT uses a sophisticated six-degree-of-freedom CDP motion platform with dual force plates and a wrap-around visual screen to measure changes in a person's balance ability when different combinations of visual, vestibular, and proprioceptive sensory systems are either available or disrupted. Test results include separate scores averaged over three trials of six different SOT conditions, along with an overall equilibrium index score. Multiple studies have used SOT to quantify overall balance decline, underlying sensory system impairments, and fall risk in older population.^{21–25} SOT results from a cohort of 34 older adults comparing those with and without elevated fall risks²¹ demonstrate qualitative trends similar to those reported here, with elevated fall risk participants recording lower overall equilibrium index scores, lower sensory analysis scores for vestibular and visual function, and higher sensory analysis score for proprioception. ROC curves using the SOT composite score to predict fall risk had an AUC of 0.65,²¹ typical of the values ranging from 0.5 to 0.7 that have been reported for many other common fall risk assessments,²⁶ and much lower than the phybrata Ec results reported here, with AUC = 0.88 (Figure 5). Other SOT studies of balance in older populations consistently report lower overall equilibrium index scores and lower sensory analysis scores for vestibular function.^{22–24} The present results are the first to demonstrate clear progressive trends in declining balance performance and sensory reweighting, with decreased vestibular function offset by greater reliance on proprioception, across a large cross-sectional study cohort (N = 516) spanning a wide range of age and balance performance. Compared with SOT, phybrata testing can be completed with much shorter test times and far less complex and expensive apparatus. The portability and ease of use of the phybrata sensor eliminates the need for participants to come to a dedicated balance testing facility.

The phybrata sensor exploits the fact that the head serves as an egocentric reference for balance, walking, and most other voluntary motor activities⁵³ and centralizes the integrated sensing of physiological signals. Maintaining the biomechanical stability of the head and eyes is thus a fundamental goal of human balance and postural stability control. During quiet stance, body motion increases in order of lower limbs, pelvis, trunk, and head, exhibiting frequency components up to 30 Hz at the head due to head-neck stabilization via vestibulocollic reflexes.⁵⁴ Direct measurement of head acceleration has been shown to provide much more sensitive detection of body motion across this entire frequency range than is possible using center of pressure (COP) measurements with force plates and CDP systems.³² ASD is a widely used engineering tool for analyzing random vibrations in complex industrial systems,⁵⁵ including the design of robots that can mimic human bipedal motion.^{56–58} Physiological vibration has been shown to be inherent to human postural and motor control,^{59,60} including components described as tremor,^{59,61} rambling and trembling,⁶⁰ and head micro-movements.⁶² Ensemble-average ASD analyses have been utilized to capture the significant time varying spectral changes that result from intermittent balance control processes that utilize multiple physiological system inputs and outputs,^{63,64} and to identify statistically significant spectral features that can distinguish patients vs control groups.⁶³ In clinical medicine, head-mounted accelerometers have been used to compare normal and pathological passive head acceleration spectra for healthy individuals and those with essential tremor,⁶⁵ to compare head and eye tremors for the assessment of vestibulo-ocular impairments,⁶⁶ to detect changes in intercranial pulsatility⁶⁷ associated with diffuse brain tissue atrophy and white matter degeneration following stroke, and to measure the mechanocardiographic motion of the body⁶⁸ resulting from cardiovascular blood flow. Analysis of head micro-movements in MRI image data has been used to classify different neurodevelopmental disorder phenotypes.⁶² Acceleration spectral analysis of body center of mass data

has also been utilized to study differences in the complex multi-system postural control process between young children and adults.⁶⁹

Changes in the spectral characteristics of postural control have been observed for many different postural challenges and medical conditions.^{17,18,32–36,63,70–85} Age-related changes in specific frequency bands have been observed,^{76,77} and it has been proposed as early as 1997 that the analysis of these spectral characteristics during quiet stance may be a clinically useful tool in identifying biomarkers associated with age-related loss of functional balance capacity and increasing fall risk.⁷⁷ Spectral analysis of postural sway, sensory impairments, and sensory reweighting due to a wide range of postural challenges and medical conditions reveals that specific frequency bands correspond to distinct postural regulation strategies.^{17,18,32–36,71–75,82,84} The present study validates the clinical utility of digital biomarkers derived from phybrata ASD analyses to enable rapid objective assessment of progressive age-related balance impairments, sensory reweighting, and the underlying physiological contributions.

The results presented in Figure 6 are consistent with other studies reporting a general trend toward age-related decline in peripheral and central vestibular function^{6–11,15,16,86–89} that is compensated for by a greater reliance on proprioceptive balance control.^{89,90} The observed increase in the CNS band for Eo may reflect central vestibular compensation for declining peripheral vestibular function, as has been previously reported in older populations.⁹¹ Recent studies comparing SOT results for sensory-specific changes in balance and MRI results for changes in brain structure⁸⁹ have demonstrated the same combination of poorer vestibular function and greater proprioceptive reliance with declining overall balance performance, and shown that these changes are correlated with thinner vestibular cortex, greater gyrification within sensorimotor, parietal, and frontal cortices, and lower free water-corrected axial diffusivity across the corona radiata and corpus callosum. These structural changes are also linked to changes in higher order neurological processes and cognition that play a key role in the regulation of gait and balance in older adults via movement planning, multi-task attention, and response to environmental changes.⁹² Another important contribution to higher-frequency proprioceptive postural sway fluctuations in elderly adults is the increased physiological tremor that results from reduced lower extremity muscle strength.^{25,93,94} The combination of vestibular deficits and proprioceptive compensation strategies in elderly balance thus reflects multiple disruptions in motor control feedback and correlates well with the observed decline in overall postural stability as individuals are forced to rely more on proprioception.^{89,90}

Limitations and Future Developments

The present study is limited to correlating phybrata biomarkers with cross-sectional data from the study population and self-reported retrospective fall histories. Future studies could include longitudinal data collection to directly measure changes in balance performance, vestibular function, and sensory reweighting over time and to track prospective falls incidence, as have been reported in previous longitudinal studies of age-related changes in fall risk and vestibular function.^{95,96} The phybrata sensor has also previously been used in longitudinal studies of balance performance in athletes.³¹ The lack of direct comparison with other balance assessment tools is another limitation of the present study, which can be overcome by adding more comprehensive vestibular clinical exams and motor, sensory, coordination, and balance testing as in our previous phybrata studies of concussion.³² A further improvement could be gained by combining phybrata balance testing with instrumented gait analyses to examine the correlation between impairments and sensory reweighting in static balance vs dynamic gait and their relative impacts on fall risk, for a more complete evaluation of age-related decline. The present study does not include direct assessments of specific peripheral vestibular impairments (otoliths vs semicircular canals),^{6,10,44,97} the relative contributions of peripheral vs central vestibular impairments,^{6,98} or related cognitive impairments.^{15,92} These limitations could be addressed in future collaborations with related clinical specialists, as in our previous phybrata studies of motor and cognitive impairments in multiple sclerosis.³⁵ The frequency band assignments used in the present sensory reweighting analysis rely on previously reported studies. Although the results are consistent with widely reported trends in sensory, CNS, and neuromotor contributions to postural stabilization, future studies should investigate in more detail the potential overlap between these frequency bands, variations across study populations, and individual variations as a function of time, impairments, and interventions.

The results presented here highlight many potential applications of phybrata biomarkers for aging biology research, clinical trials, and clinical practice. Current studies of aging focus heavily on molecular and omic biomarkers to quantify the accumulation of age-related molecular damage and other mechanisms of aging, with the goal of identifying interventions that can reduce the consequences.^{99,100} A key challenge that remains to be addressed is connecting many of these biomarkers with actionable insights regarding functional decline in healthcare and preventative settings.¹⁰¹ Phybrata digital biomarkers can address this challenge by directly quantifying the decline in functional mobility that is one of the most profound and directly observable indicators of aging. In addition to sharing the same traditional biomarker clinical goals, digital biomarkers such as those described here contribute new capabilities for continuous longitudinal measurements of more complex physiological systems such as balance.¹⁰²

Phybrata balance assessments can also be extended to IMU-based analysis of gait impairments, which has been shown in multiple studies to enable assessment of age-related decline in balance, mobility, and cognition and the corresponding increase in fall risk.^{29,30,95,103} Head movement kinematics derived from IMUs have been shown to enable functional assessments of gait impairments,^{40–42} and fall risk predictions using head and neck kinematics during gait testing have been reported to outperform those derived from foot-mounted sensors (AUC = 0.75 vs AUC = 0.68).⁴⁰ The combined use of IMUs and camera-based motion capture features has been shown to enhance fall-risk classification, with AUC = 0.88.¹⁰⁴ The fall risk classification performance of standard balance and gait testing approaches can also be improved using machine learning,^{105–107} and we have demonstrated that this is also the case for phybrata testing.³⁴ Decreases in head sway measured using accelerometers in a head-mounted display have been shown to monitor the response to vestibular rehabilitation,⁷⁵ highlighting the potential to use phybrata sensors to monitor sensory reweighting during such interventions. Adding postural sway frequency analysis has been shown to improve the sensitivity of SOT for the detection of vestibular dysfunction,¹⁰⁸ and SOT assessments have been combined with gait analysis in a locomotor sensory organization test (LSOT) to study sensory reweighting during ambulatory tasks,¹⁰⁹ highlighting additional potential extensions of phybrata testing.

At the other end of the aging spectrum, CDP has been used to study balance development in children, revealing that the proprioceptive system is fully developed in the first 3–4 years and the visual system by the age of 15, while the vestibular system continues to develop until the age of 16 or later.¹¹⁰ The role of the vestibular system in early childhood development has also begun to receive significant attention,¹¹¹ based on studies revealing that unidentified or untreated vestibular issues in childhood can lead to a number of poor outcomes. In particular, peripheral and central vestibular dysfunction have been identified in children with neurodevelopmental disorders that impact motor coordination, fine motor skills, postural instability, cognitive development and educational performance, and emotional and social behavior.^{111,112} Involuntary head micro-movements such as those detected using the phybrata sensor have recently been shown to reflect age-dependent development and decline in human motor stability across a very wide age range.⁶² It has been proposed that these head micro-movements may serve as an important biomarker in diagnosing and treating children with developmental disorders.¹¹³

The above results and discussion highlight the crucial role played by the vestibular system in human development, normal functioning, and aging. The vestibular system provides absolute information about the body's orientation and movement, regardless of external visual cues or the position of other body parts, while vision and proprioception primarily offer relative information based on objects in the surrounding environment and body parts' positions relative to each other. In everyday life, these objects are often moving, forcing us to rely on vestibular inputs as the veridical reference against which other sensory inputs are evaluated when conflicts among multiple sensory inputs occur.¹¹⁴ The phybrata sensor and biomarkers described here provide a powerful new tool to enable much more frequent and accessible objective assessments of vestibular function at all ages.

Pilot deployments of the above phybrata balance testing, together with a variety of balance rehab solutions, are now underway in multiple healthcare settings, including senior living communities, at-home care delivery, and physical therapy clinics. These pilot deployments include assessments of user training and support requirements, integration into clinical workflows, accompanying enhancements to balance treatment technologies and protocols, benefits to patients across multiple dimensions, and the overall healthcare cost/benefit economics of advanced balance testing and rehab solutions.

Conclusions

Using a head-mounted phybrata wearable sensor, we have developed digital biomarkers that enable rapid objective assessment of progressive age-related balance decline, increasing fall risk, underlying physiological contributions, and sensory reweighting in older populations. The ease of use and simple two-minute test protocol allow the device to be used in any senior care location, including clinical settings, independent and assisted senior living communities, and at home. Phybrata digital biomarkers enable frequent and widely accessible preventive screening to promote healthy neuromotor aging and clinical assessments to develop targeted treatment and rehabilitation strategies that can extend the human healthspan.

Abbreviations

IMU, inertial motion unit; Phybrata, physiological vibration acceleration; Eo eyes open; Ec, eyes closed; ASD, acceleration spectral density; NF, no falls reported; FR, fall(s) reported; ROC, receiver operating characteristic; AUC, area under the curve; CNS, central nervous system; PNS, peripheral nervous system; VOR, vestibulo-ocular reflex; VCR, vestibulocollic reflex; VSR, vestibulospinal reflex; SR, sensory reweighting; CDP, computerized dynamic posturography; ML, machine learning; MRI, magnetic resonance imaging; EEG, electroencephalography; BLE, Bluetooth low energy; AP, anterior posterior; ML, medial lateral; ANOVA, analysis of variance; MANOVA, multiple analysis of variance; CI, confidence interval; SOT, sensory organization test; COP, center of pressure.

Acknowledgments

The authors wish to thank: the staff at Sun City Lincoln Hills (Lincoln Hills, CA), Sun City Roseville (Roseville, CA), Quarry Oaks Rocklin (Rocklin, CA), and the Forum at Rancho San Antonio (Cupertino, CA) senior living communities for their support in scheduling and coordinating on-site phybrata testing; Dr. Biljinder Chima and the team members at Rocklin Family Practice and Sports Medicine (Rocklin, CA), Caring Hands Caregivers (Cupertino, CA), and Neursantys Inc. (Menlo Park, CA) who supported data collection; and Andreas Hauenstein for support in developing and maintaining the mobile app and cloud data platform used in this study. PROTX, Inc. provided the sensors, mobile app, and cloud data platform used in this study. Quarry Oaks is sponsored by the Department of Housing and Urban Development and managed by Volunteers of America.

Disclosure

John D Ralston is the co-founder and CEO of Neursantys, Inc., and has a financial interest in the company. In addition, he reports a US provisional patent application 63/741,968 pending to Neursantys Inc. Josh Roper is the co-founder and Vice President of Operations of Neursantys, Inc., and has a financial interest in the company. Scott Stanley is the CEO of Caring Hands Caregivers, and a member of the Neursantys Advisory Board. The authors report no other conflicts of interest in this work.

References

1. Florence CS, Bergen G, Atherly A, Burns E, Stevens J, Drake C. The medical costs of fatal falls and fall injuries in older adults. *J Am Geriatr Soc*. 2018;66(4):693–698. doi:10.1111/jgs.15304
2. Agrawal Y, Pineault KG, Semenov YR. Health-related quality of life and economic burden of vestibular loss in older adults. *Laryngoscope Investig Otolaryngol*. 2017;3(1):8–15. doi:10.1002/lio2.129
3. Roman-Liu D. Age-related changes in the range and velocity of postural sway. *Arch Gerontol Geriatr*. 2018;77:68–80. doi:10.1016/j.archger.2018.04.007
4. Hignett S, Masud T. A review of environmental hazards associated with inpatient falls. *Ergonomics*. 2006;49(5–6):605–616. doi:10.1080/00140130600568949
5. Davis LE. Dizziness in elderly men. *J Am Geriatr Soc*. 1994;42(11):1184–1188. doi:10.1111/j.1532-5415.1994.tb06986.x
6. Iwasaki S, Yamasoba T. Dizziness and imbalance in the elderly: age-related decline in the vestibular system. *Aging Dis*. 2014;6(1):38–47. doi:10.14336/AD.2014.0128
7. Agrawal Y, Merfeld DM, Horak FB, et al. Aging, vestibular function, and balance: proceedings of a national institute on aging/national institute on deafness and other communication disorders workshop. *J Gerontol a Biol Sci Med Sci*. 2020;75(12):2471–2480. doi:10.1093/gerona/glaa097
8. Wagner AR, Akinsola O, Chaudhari AMW, Bigelow KE, Merfeld DM. Measuring vestibular contributions to age-related balance impairment: a review. *Front Neurol*. 2021;12:635305. doi:10.3389/fneur.2021.635305

9. Agrawal Y, Ward BK, Minor LB. Vestibular dysfunction: prevalence, impact and need for targeted treatment. *J Vestib Res.* **2013**;23(3):113–117. doi:10.3233/VES-130498
10. Agrawal Y, Smith PF, Merfeld DM. 6.36 - dizziness, imbalance and age-related vestibular loss. In: Fritzsche B, editor. *The Senses: A Comprehensive Reference (Second Edition)*. Elsevier; **2020**: 567–580. ISBN 9780128054093.
11. Liston MB, Bamio DE, Martin F, et al. Peripheral vestibular dysfunction is prevalent in older adults experiencing multiple non-syncopal falls versus age-matched non-fallers: a pilot study. *Age Ageing.* **2014**;43(1):38–43. doi:10.1093/ageing/aft129
12. Cao C, Cade WT, Li S, McMillan J, Friedenreich C, Yang L. Association of balance function with all-cause and cause-specific mortality among US adults. *JAMA Otolaryngol Head Neck Surg.* **2021**;147(5):460–468. doi:10.1001/jamaoto.2021.0057
13. Araujo CG, de Souza E, Silva CG, et al. Successful 10-second one-legged stance performance predicts survival in middle-aged and older individuals. *Br J Sports Med.* **2022**;56(17):975–980. doi:10.1136/bjsports-2021-105360
14. Peusner KD, Shao M, Reddaway R, Hirsch JC. Basic concepts in understanding recovery of function in vestibular reflex networks during vestibular compensation. *Front Neurol.* **2012**;3:17. doi:10.3389/fneur.2012.00017
15. Smith PF. Aging of the vestibular system and its relationship to dementia. *Curr Opin Neurol.* **2024**;37(1):83–87. doi:10.1097/WCO.0000000000001231
16. Coto J, Alvarez CL, Cejas I, et al. Peripheral vestibular system: age-related vestibular loss and associated deficits. *J Otol.* **2021**;16(4):258–265. doi:10.1016/j.joto.2021.06.001
17. Peterka RJ. Sensorimotor integration in human postural control. *J Neurophysiol.* **2002**;88(3):1097–1118. doi:10.1152/jn.2002.88.3.1097
18. Assländer L, Peterka RJ. Sensory reweighting dynamics in human postural control. *J Neurophysiol.* **2014**;111(9):1852–1864. doi:10.1152/jn.00669.2013
19. Zhang S, Xu W, Zhu Y, Tian E, Kong W. Impaired multisensory integration predisposes the elderly people to fall: a systematic review. *Front Neurosci.* **2020**;14:411. doi:10.3389/fnins.2020.00411
20. Clendaniel RA. Outcome measures for assessment of treatment of the dizzy and balance disorder patient. *Otolaryngol Clin North Am.* **2000**;33(3):519–533. doi:10.1016/S0030-6665(05)70225-5
21. Sung P, Rowland P. Impact of sensory reweighting strategies on postural control using the sensory organization test in older adults with and without fall risks. *Physiother Res Int.* **2024**;29(2):e2075. doi:10.1002/pri.2075
22. Mújdecí B, Aksoy S, Atas A. Evaluation of balance in fallers and non-fallers elderly. *Braz J Otorhinolaryngol.* **2012**;78(5):104–109. doi:10.5935/1808-8694.20120016
23. Whitney SL, Marchetti GF, Schade AI. The relationship between falls history and computerized dynamic posturography in persons with balance and vestibular disorders. *Arch Phys Med Rehabil.* **2006**;87(3):402–407. doi:10.1016/j.apmr.2005.11.002
24. Leopoldo CMS, Nishino LK, Santos MAO. Use of posturography to identify the risk of falling in elderly people with dizziness. *Audiol Commun Res.* **2022**;27:e2684.
25. Judge JO, King MB, Whipple R, Clive J, Wolfson LI. Dynamic balance in older persons: effects of reduced visual and proprioceptive input. *J Gerontol a Biol Sci Med Sci.* **1995**;50(5):M263–270. doi:10.1093/gerona/50A.5.M263
26. Meekes WM, Korevaar JC, Leemrijse CJ, van de Goor IA. Practical and validated tool to assess falls risk in the primary care setting: a systematic review. *BMJ Open.* **2021**;11(9):e045431. doi:10.1136/bmjopen-2020-045431
27. Pardasany PK, Slavin MD, Wagenaar RC, Latham NK, Ni P, Jette AM. Conceptual limitations of balance measures for community-dwelling older adults. *Physical Therapy.* **2013**;93(10):1351–1368. doi:10.2522/ptj.20130028
28. Newman-Toker DE, Cannon LM, Stofferahn ME, Rothman RE, Hsieh YH, Zee DS. Imprecision in patient reports of dizziness symptom quality: a cross-sectional study conducted in an acute care setting. *Mayo Clin Proc.* **2007**;82:1329–1340. doi:10.4065/82.11.1329
29. Subramaniam S, Faisal AI, Deen MJ. Wearable sensor systems for fall risk assessment: a review. *Front Digit Health.* **2022**;4:921506. doi:10.3389/fdgh.2022.921506
30. Ferreira RN, Ribeiro NF, Santos CP. Fall risk assessment using wearable sensors: a narrative review. *Sensors.* **2022**;22(3):984. doi:10.3390/s22030984
31. Grafton ST, Ralston AB, Ralston JD. Monitoring of postural sway with a head-mounted wearable device: effects of gender, participant state, and concussion. *Medical Devices.* **2019**;12:151–164. doi:10.2147/MDER.S205357
32. Ralston JD, Raina A, Benson BW, Peters RM, Roper JM, Ralston AB. Physiological vibration acceleration (Phybrata) sensor assessment of multi-system physiological impairments and sensory reweighting following concussion. *Med Devices.* **2020**;13:411–438. doi:10.2147/MDER.S279521
33. Lin IS, Lai DM, Ding JJ, et al. Reweighting of the sensory inputs for postural control in patients with cervical spondylotic myelopathy after surgery. *J Neuroeng Rehabil.* **2019**;16(1):96. doi:10.1186/s12984-019-0564-2
34. Hope A, Vashisth U, Parker M, Ralston AB, Roper JM, Ralston JD. Phybrata sensors and machine learning for enhanced neurophysiological diagnosis and treatment. *Sensors.* **2021**;21:7417. doi:10.3390/s21217417
35. Heydari S, Lacey C, Stewart-Good K, Mayo C, Ralston JD, Gawryluk JR. The relationship between phybrata wearable sensor data and white matter microstructure in people with multiple sclerosis. Consortium of Multiple Sclerosis Centers Annual Meeting, CMSC 2023. Aurora, Colorado, USA; May 31–June 3, 2023.
36. Lei Y, Rios V, Ji J, Duhon B, Boyd H, Xu Y. Quantifying unsupported sitting posture impairments in humans with cervical spinal cord injury using a head-mounted IMU sensor. *Spinal Cord.* **2024**;62(2):65–70. doi:10.1038/s41393-023-00951-w
37. Abdollah V, Dief TN, Ralston JD, Ho C, Rouhani H. Investigating the validity of a single tri-axial accelerometer mounted on the head for monitoring the activities of daily living and the timed-up and go test. *Gait Posture.* **2021**;90:137–140. doi:10.1016/j.gaitpost.2021.08.020
38. Abdollah V, Noamani A, Ralston JD, Ho C, Rouhani H. Effect of test duration and sensor location on the reliability of standing balance parameters derived using body-mounted accelerometers. *BioMed Eng OnLine.* **2024**;23:2. doi:10.1186/s12938-023-01196-7
39. Quijoux F, Vienne-Jumeau A, Bertin-Hugault F, et al. Center of pressure displacement characteristics differentiate fall risk in older people: a systematic review with meta-analysis. *Ageing Res Rev.* **2020**;62:101117. doi:10.1016/j.arr.2020.101117
40. Roshdibenam V, Jogerst GJ, Butler NR, Baek S. Machine learning prediction of fall risk in older adults using timed up and go test kinematics. *Sensors.* **2021**;21(10):3481. doi:10.3390/s21103481

41. Hwang TH, Effenberg AO. Head trajectory diagrams for gait symmetry analysis using a single head-worn IMU. *Sensors*. 2021;21(19):6621. doi:10.3390/s21196621
42. Millar JL, Zobeiri OA, Souza WH, Schubert MC, Cullen KE. Head movement kinematics are differentially altered for extended versus short duration gait exercises in individuals with vestibular loss. *Sci Rep*. 2023;13(1):16213. doi:10.1038/s41598-023-42441-2
43. Mijovic T, Carriot J, Zeitouni A, Cullen KE. Head movements in patients with vestibular lesion: a novel approach to functional assessment in daily life setting. *Otol Neurotol*. 2014;35(10):e348–357. doi:10.1097/MAO.0000000000000608
44. Zobeiri OA, Ostrander B, Roat J, Agrawal Y, Cullen KE. Loss of peripheral vestibular input alters the statistics of head movement experienced during natural self-motion. *J Physiol*. 2021;599(8):2239–2254. doi:10.1113/JP281183
45. Bohannon RW, Larkin PA, Cook AC, Gear J, Singer J. Decrease in timed balance test scores with aging. *Phys Ther*. 1984;64(7):1067–1070. doi:10.1093/ptj/64.7.1067
46. Anson E, Bigelow RT, Studenski S, Deshpande N, Agrawal Y. Failure on the foam eyes closed test of standing balance associated with reduced semicircular canal function in healthy older adults. *Ear Hear*. 2019;40(2):340–344. doi:10.1097/AUD.0000000000000619
47. Dennis EL, Vervoorde S, Adamson MM, et al. Accelerated aging after traumatic brain injury: an ENIGMA multi-cohort mega-analysis. *Ann Neurol*. 2024;96(2):365–377. doi:10.1002/ana.26952
48. Banman CJ, Schneider KJ, Cluff T, Peters RM. Altered vestibular balance function in combat sport athletes. *J Neurotrauma*. 2021;38:2291–2300. doi:10.1089/neu.2020.7432
49. Eriksen ND, Hougaard DD. Age- and gender-specific normative data on computerized dynamic posturography in a cohort of Danish adults. *Eur Arch Otorhinolaryngol*. 2023;280(5):2191–2200. doi:10.1007/s00405-022-07706-y
50. Nashner LM, Black FO, Wall C. Adaptation to altered support and visual conditions during stance: patients with vestibular deficits. *J Neurosci*. 1982;2(5):536–544. doi:10.1523/JNEUROSCI.02-05-00536.1982
51. Monsell EM, Furman JM, Herdman SJ, Konrad HR, Shepard NT. Computerized dynamic platform posturography. *Otolaryngol Head Neck Surg*. 1997;117(4):394–398. doi:10.1016/S0194-5998(97)70132-3
52. Chaudhry H, Findley T, Quigley KS, et al. Measures of postural stability. *J Rehabil Res Dev*. 2004;41(5):713–720. doi:10.1682/JRRD.2003.09.0140
53. Amblard B, Assaiante C, Fabre JC, Mouchino L, Massion J. Voluntary head stabilization in space during oscillatory trunk movements in the frontal plane performed in weightlessness. *Exp Brain Res*. 1997;114(2):214–225. doi:10.1007/PL00005630
54. Forbes PA, Siegmund GP, Schouten AC, Blouin JS. Task, muscle and frequency dependent vestibular control of posture. *Front Integr Neurosci*. 2015;8:94. doi:10.3389/fnint.2014.00094
55. Broch JT. *Mechanical vibration and shock measurements*. Available from: <https://www.bksv.com/media/doc/bn1330.pdf>. Accessed June 06, 2025.
56. Mergner T, Schweigart G, Fennell L. Vestibular humanoid postural control. *J Physiol Paris*. 2009;103(3–5):178–194. doi:10.1016/j.jphysparis.2009.08.002
57. Mergner T, Lippi V. Posture control—human-inspired approaches for humanoid robot benchmarking: conceptualizing tests, protocols, and analyses. *Front Neurobot*. 2018;12:21. doi:10.3389/fnbot.2018.00021
58. Tanabe H, Fujii K, Suzuki Y, Kouzaki M. Effect of intermittent feedback control on robustness of human like postural control system. *Sci Rep*. 2017;6(1):22446. doi:10.1038/srep22446
59. Kouzaki M, Masani K. Postural sway during quiet standing is related to physiological tremor and muscle volume in young and elderly adults. *Gait Posture*. 2011;35(1):11–17. doi:10.1016/j.gaitpost.2011.03.028
60. Zatsiorsky VM, Duarte M. Rambling and trembling in quiet standing. *Motor Control*. 2000;2(2):185–200. doi:10.1123/mcj.4.2.185
61. Vial F, Kassavetis P, Merchant S, Haubenberger D, Hallett M. How to do an electrophysiological study of tremor. *Clin Neurophysiol Pract*. 2019;4:134–142. doi:10.1016/j.cnp.2019.06.002
62. Torres EB, Mistry S, Caballero C, Whyatt CP. Stochastic signatures of involuntary head micro-movements can be used to classify females of ABIDE into different subtypes of neurodevelopmental disorders. *Front Integr Neurosci*. 2017;11:10. doi:10.3389/fnint.2017.00010
63. El-Jaroudi A, Redfern MS, Chaparro LF, Furman JM. The application of time-frequency methods to the analysis of postural sway. *Proc IEEE*. 1996;84(9):1312–1318. doi:10.1109/5.535249
64. Ferdjallah M, Harris GF, Wertsch JJ. Instantaneous spectral characteristics of postural stability using time-frequency analysis. Proc 19th Internat Conf - IEEE/EMBS. Chicago, IL. USA; October 30–November 2, 1997.
65. MacDonald MC. *Simultaneous Recordings of Head and Hand Tremor in Subjects with Essential Tremor: An Investigation of Coherence* [Thesis]. Kingston, Ontario, Canada: Centre for Neuroscience Studies, Queen's University; 2008.
66. Spauschus A, Marsden J, Halliday DM, Rosenberg JR, Brown P. The origin of ocular microtremor in man. *Exp Brain Res*. 1999;126(4):556–562. doi:10.1007/s002210050764
67. Wagshul ME, Eide PK, Madsen JR. The pulsating brain: a review of experimental and clinical studies of intracranial pulsatility. *Fluids Barriers CNS*. 2011;8(1):5. doi:10.1186/2045-8118-8-5
68. He DD, Winokur ES, Sodini CG. An ear-worn vital signs monitor. *IEEE Trans Biomed Eng*. 2015;62(11):2547–2552. doi:10.1109/TBME.2015.2459061
69. Oba N, Sasagawa S, Yamamoto A, Nakazawa K. Difference in postural control during quiet standing between young children and adults: assessment with center of mass acceleration. *PLoS One*. 2015;10(10):e0140235. doi:10.1371/journal.pone.0140235
70. Diener HC, Dichgans J, Bacher M, Gompf B. Quantification of postural sway in normals and patients with cerebellar diseases. *Electroencephalogr Clin Neurophysiol*. 1984;57(2):134–142. doi:10.1016/0013-4694(84)90172-X
71. Kanekar N, Lee Y-J, Aruin AS. Frequency analysis approach to study balance control in individuals with multiple sclerosis. *J Neurosci Methods*. 2014;222:91–96. doi:10.1016/j.jneumeth.2013.10.020
72. Sim T, Yoo H, Lee D. Analysis of sensory system aspects of postural stability during quiet standing in adolescent idiopathic scoliosis patients. *J Neuroeng Rehabil*. 2018;15(1):54. doi:10.1186/s12984-018-0395-6
73. Chagdes JR, Rietdyk S, Haddad JM, et al. Multiple timescales in postural dynamics associated with vision and a secondary task are revealed by wavelet analysis. *Exp Brain Res*. 2009;197(3):297–310. doi:10.1007/s00221-009-1915-1

74. Quek J, Brauer SG, Clark R, Treleaven J. New insights into neck-pain-related postural control using measures of signal frequency and complexity in older adults. *Gait Posture*. 2014;39(4):1069–1073. doi:10.1016/j.gaitpost.2014.01.009
75. Lubetzky AV, Harel D, Krishnamoorthy S, et al. Decrease in head sway as a measure of sensory integration following vestibular rehabilitation: a randomized controlled trial. *J Vestib Res*. 2023;33(3):213–226. doi:10.3233/VES-220107
76. Singh NB, Taylor WR, Madigan ML, Nussbaum MA. The spectral content of postural sway during quiet stance: influences of age, vision and somatosensory inputs. *J Electromyogr Kinesiol*. 2012;22(1):131–136. doi:10.1016/j.jelekin.2011.10.007
77. Williams HG, McClenaghan BA, Dickerson J. Spectral characteristics of postural control in elderly individuals. *Arch Phys Med Rehabil*. 1997;78(7):737–744. doi:10.1016/S0003-9993(97)90082-4
78. Fujimoto C, Kamogashira T, Kinoshita M, et al. Power spectral analysis of postural sway during foam posturography in patients with peripheral vestibular dysfunction. *Otol Neurotol*. 2014;35(10):e317–e323. doi:10.1097/MAO.0000000000000554
79. Baloh RW, Jacobson KM, Beykirch K, Honrubia V. Static and dynamic posturography in patients with vestibular and cerebellar lesions. *Arch Neurol*. 1998;55(5):649–654. doi:10.1001/archneur.55.5.649
80. Anagnostou E, Stavropoulou G, Zachou A, Kararizou E. Spectral Composition of Body Sway in Persistent Postural-Perceptual Dizziness. *Otol Neurotol*. 2021;42(9):e1318–e1326. doi:10.1097/MAO.0000000000003252
81. Tanaka S, Ando K, Kobayashi K, et al. Locomotive syndrome and the power spectral characteristics of body sway. *Geriatr Gerontol Int*. 2020;20(7):691–696. doi:10.1111/ggi.13937
82. Micarelli A, Viziano A, Micarelli B, Di Fulvio G, Alessandrini M. Usefulness of postural sway spectral analysis in the diagnostic route and clinical integration of cervicogenic and vestibular sources of dizziness: a cross-sectional preliminary study. *J Vestib Res*. 2021;31(5):353–364. doi:10.3233/VES-190729
83. Laboissière R, Letievant JC, Ionescu E, Barraud PA, Mazzuca M, Cian C. Relationship between spectral characteristics of spontaneous postural sway and motion sickness susceptibility. *PLoS One*. 2015;10(12):e0144466. doi:10.1371/journal.pone.0144466
84. Salsabili H, Bahrpeyma F, Esteki A, Karimzadeh M, Ghomashchi H. Spectral characteristics of postural sway in diabetic neuropathy patients participating in balance training. *J Diabetes Metab Disord*. 2013;12:29. doi:10.1186/2251-6581-12-29
85. Palmerini L, Rocchi L, Mellone S, Valzania F, Chiari L. Feature selection for accelerometer-based posture analysis in Parkinson's disease. *IEEE Trans Inf Technol Biomed*. 2011;15(3):481–490. doi:10.1109/TITB.2011.2107916
86. Agrawal Y, Zuniga MG, Davalos-Bichara M, et al. Decline in semicircular canal and otolith function with age. *Otol Neurotol*. 2012;33(5):832–839. doi:10.1097/MAO.0b013e3182545061
87. Cyran CA, Boegle R, Stephan T, Dieterich M, Glasauer S. Age-related decline in functional connectivity of the vestibular cortical network. *Brain Struct Funct*. 2016;221(3):1443–1463. doi:10.1007/s00429-014-0983-6
88. Noohi F, Kinnaird C, De Dios Y, et al. Deactivation of somatosensory and visual cortices during vestibular stimulation is associated with older age and poorer balance. *PLoS One*. 2019;14(9):e0221954. doi:10.1371/journal.pone.0221954
89. Hupfeld KE, McGregor HR, Hass CJ, Pasternak O, Seidler RD. Sensory system-specific associations between brain structure and balance. *Neurobiol Aging*. 2022;119:102–116. doi:10.1016/j.neurobiolaging.2022.07.013
90. Wiesmeier IK, Dalin D, Maurer C. Elderly use proprioception rather than visual and vestibular cues for postural motor control. *Front Aging Neurosci*. 2015;7:97. doi:10.3389/fnagi.2015.00097
91. Peters RM, Blouin JS, Dalton BH, Inglis JT. Older adults demonstrate superior vestibular perception for virtual rotations. *Exp Gerontol*. 2016;82:50–57. doi:10.1016/j.exger.2016.05.014
92. Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. *Age Ageing*. 2012;41(3):299–308. doi:10.1093/ageing/afs012
93. Kouzaki M, Masani K. Postural sway during quiet standing is related to physiological tremor and muscle volume in young and elderly adults. *Gait Posture*. 2012;35(1):11–17.
94. Muehlbauer T, Gollhofer A, Granacher U. Associations between measures of balance and lower-extremity muscle strength/power in healthy individuals across the lifespan: a systematic review and meta-analysis. *Sports Med*. 2015;45(12):1671–1692. doi:10.1007/s40279-015-0390-z
95. Lockhart TE, Soangra R, Yoon H, et al. Prediction of fall risk among community-dwelling older adults using a wearable system. *Sci Rep*. 2021;11(1):1–4. doi:10.1038/s41598-021-00458-5
96. Baloh RW, Enrietto J, Jacobson KM, Lin A. Age-related changes in vestibular function: a longitudinal study. *Ann N Y Acad Sci*. 2001;942:210–219. doi:10.1111/j.1749-6632.2001.tb03747.x
97. Nashner LM, Shupert CL, Horak FB, Black FO. Chapter 33, organization of posture controls: an analysis of sensory and mechanical constraints. In: Allum JHH, Hülliger M, editors. *Progress in Brain Research*. Vol. 80. Elsevier; 1989:411–418.
98. Thompson TL, Amedee R. Vertigo: a review of common peripheral and central vestibular disorders. *Ochsner J*. 2009;9(1):20–26.
99. Tao X, Zhu Z, Wang L, et al. Biomarkers of aging and relevant evaluation techniques: a comprehensive review. *Aging Dis*. 2024;15(3):977–1005. doi:10.14336/AD.2023.00808-1
100. Moqri M, Herzog C, Poganik JR, et al. Biomarkers of aging for the identification and evaluation of longevity interventions. *Cell*. 2023;186(18):3758–3775. doi:10.1016/j.cell.2023.08.003
101. Herzog CMS, Goeminne LJE, Poganik JR, et al; Biomarkers of Aging Consortium. Challenges and recommendations for the translation of biomarkers of aging. *Nat Aging*. 2024;4(10):1372–1383. doi:10.1038/s43587-024-00683-3
102. Babrak LM, Menetski J, Rebhan M, et al. Traditional and digital biomarkers: two worlds apart? *Digit Biomark*. 2019;3(2):92–102. doi:10.1159/000502000
103. Lamoth CJ, van Deudekom FJ, van Campen JP, Appels BA, de Vries OJ, Pijnappels M. Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people. *J Neuroeng Rehabil*. 2011;8:2. doi:10.1186/1743-0003-8-2
104. Wang X, Cao J, Zhao Q, et al. Identifying sensors-based parameters associated with fall risk in community-dwelling older adults: an investigation and interpretation of discriminatory parameters. *BMC Geriatr*. 2024;24(1):125. doi:10.1186/s12877-024-04723-w
105. Song W, Latham NK, Liu L, et al. Improved accuracy and efficiency of primary care fall risk screening of older adults using a machine learning approach. *J Am Geriatr Soc*. 2024;72(4):1145–1154. doi:10.1111/jgs.18776

106. Soylemez E, Tokgoz-Yilmaz S. Predicting fall risk in elderly individuals: a comparative analysis of machine learning models using patient characteristics, functional balance tests, and computerized dynamic posturography. *J Laryngology Otol.* 2024;2024:1–31. doi:10.1017/S0022215124002160
107. Usmani S, Saboor A, Haris M, Khan MA, Park H. Latest research trends in fall detection and prevention using machine learning: a systematic review. *Sensors.* 2021;21(15):5134. doi:10.3390/s21155134
108. Yeh JR, Hsu LC, Lin C, Chang FL, Lo MT. Nonlinear analysis of sensory organization test for subjects with unilateral vestibular dysfunction. *PLoS One.* 2014;9(3):e91230. doi:10.1371/journal.pone.0091230
109. Chien JH, Eikema DJ, Mukherjee M, Stergiou N. Locomotor sensory organization test: a novel paradigm for the assessment of sensory contributions in gait. *Ann Biomed Eng.* 2014;42(12):2512–2523. doi:10.1007/s10439-014-1112-7
110. Steindl R, Kunz K, Schrott-Fischer A, Scholtz AW. Effect of age and sex on maturation of sensory systems and balance control. *Dev Med Child Neurol.* 2006;48(6):477–482. doi:10.1017/S0012162206001022
111. Wiener-Vacher SR, Hamilton DA, Wiener SI. Vestibular activity and cognitive development in children: perspectives. *Front Integr Neurosci.* 2013;7:92. doi:10.3389/fnint.2013.00092
112. Van Hecke R, Danneels M, Dhooge I, et al. Vestibular function in children with neurodevelopmental disorders: a systematic review. *J Autism Dev Disord.* 2019;49(8):3328–3350. doi:10.1007/s10803-019-04059-0
113. Mansour Y, Burchell A, Kulesza RJ. Central auditory and vestibular dysfunction are key features of autism spectrum disorder. *Front Integr Neurosci.* 2021;15:743561. doi:10.3389/fnint.2021.743561
114. Hwang S, Agada P, Kiemel T, Jeka JJ. Dynamic reweighting of three modalities for sensor fusion. *PLoS One.* 2014;9(1):e88132. doi:10.1371/journal.pone.0088132

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