

OPEN

Fall Risk Prediction in Multiple Sclerosis Using Postural Sway Measures: A Machine Learning Approach

Ruopeng Sun^{1,2*}, Katherine L. Hsieh¹ & Jacob J. Sosnoff¹

Numerous postural sway metrics have been shown to be sensitive to balance impairment and fall risk in individuals with MS. Yet, there are no guidelines concerning the most appropriate postural sway metrics to monitor impairment. This investigation implemented a machine learning approach to assess the accuracy and feature importance of various postural sway metrics to differentiate individuals with MS from healthy controls as a function of physiological fall risk. 153 participants (50 controls and 103 individuals with MS) underwent a static posturography assessment and a physiological fall risk assessment. Participants were further classified into four subgroups based on fall risk: controls, low-risk MS (n = 34), moderate-risk MS (n = 27), high-risk MS (n = 42). Twenty common sway metrics were derived following standard procedures and subsequently used to train a machine learning algorithm (random forest – RF, with 10-fold cross validation) to predict individuals' fall risk grouping. The sway-metric based RF classifier had high accuracy in discriminating controls from MS individuals (>86%). Sway sample entropy was identified as the strongest feature for classification of low-risk MS individuals from healthy controls. Whereas for all other comparisons, mediolateral sway amplitude was identified as the strongest predictor for fall risk groupings.

Multiple Sclerosis (MS) is a chronic, inflammatory-mediated neurological disorder affecting more than 2.3 million people worldwide¹. MS is characterized by inflammatory demyelination and axonal damage in the central nervous system². The neuronal damage alters a wide range of cognitive, sensory and motor functions, which contribute to impairment in balance². Balance impairment affects over 75% of persons with MS (PwMS) during the disease course³, and it is associated with an elevated risk of falls and declines in quality of life⁴. Given its importance, identifying and treating balance impairment is often a focus of MS rehabilitation and research.

Traditionally, functional assessment and self-report questionnaires have been utilized to evaluate balance impairment in PwMS. Functional tests such as Berg Balance Scale (BBS)⁵ measures static and dynamic balance ability, whereas self-administered questionnaires such as Activity-Specific Balance Confidence Scale (ABC)⁶ and Falls Efficacy Scale - International (FES-I)⁷ measure individuals' balance confidence and fear of falling during daily life. However, these measures rely on subjective scoring and have poor sensitivity due to ceiling or floor effects⁸. On the other hand, instrumented measures through posturography, which utilizes a force platform to quantify Center of Pressure (COP) movement (an indicator for the neuromuscular control of maintaining an upright stance⁹), provides objective and quantitative measures of postural stability and often is considered the gold standard for balance assessment¹⁰. An advantage of posturography is that it provides precise measurement of movement over fast time scales which affords measurement of subtle alterations in the control of balance.

A number of investigations have analyzed postural impairment in PwMS utilizing posturography. Different variables of postural sway are often utilized because they are thought to reflect different underlying physiological control mechanisms^{9,11}. For example, sway velocity has been reported to be reflective on proprioception function¹², whereas sample entropy, a nonlinear sway regularity/complexity measure, indirectly reflects the ability to adapt to the environment¹³, such as postural perturbations¹⁴. However, due to the large number of outcome variables, it is difficult to compare results across investigations. Indeed, a recent systematic review¹⁵ focusing on postural impairment in PwMS identified over 100 different variables as outcome measures of posturography.

¹Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, Champaign, USA.

²Division of Physical Medicine and Rehabilitation, Stanford University, Stanford, USA. *email: rusun@stanford.edu

Furthermore, the choices of measures selected is rarely rationalized and results in a lack of consensus in determine the appropriate measure. Consequently, when measuring balance impairment in PwMS, it is difficult to determine which measure to use in order to provide clinical meaningful insights for treatment planning¹⁵.

In a previous attempt to quantify the diagnostic accuracy of static posturography in fall incidence prediction among PwMS, Prosperini *et al.*¹⁰ utilized various time domain sway measures (i.e. sway velocity, sway path, and sway area) to identify PwMS at risk of falls. They achieved over 70% of classification accuracy using a stepwise logistic regression and identified COP sway path as the only significant predictor of the fall occurrence. However, they provided minimal rationale for choice of COP sway metrics and suggested the need for consensus on which sway measures to use when evaluating balance impairment in PwMS.

One solution to identify appropriate measures to differentiate between PwMS from healthy individuals is through the use of machine learning techniques. Indeed, various machine learning approaches have been recently utilized to classify individuals with clinical pathology from controls, such as support vector machine (SVM), random forest (RF), k-nearest neighbor (KNN) and neural network^{16–19}. Among those approaches, the RF algorithm²⁰ has its unique advantage over others as it can not only construct a prediction rule to classify outcomes such as balance impairment, but it can also assess and rank variables with respect to their ability to predict the classification outcome²¹. The RF variable importance is determined by the Gini Importance, which is defined as the times a feature is used to split a node, normalized by the number of samples it splits²¹. The RF classification algorithm has also shown excellent accuracy in discriminating Parkinson's disease participants based on gait and postural measures¹⁷ and has been used to identify important neuroimaging features for Alzheimer's disease diagnosis²². For more details on random forests approach, see²⁰.

Therefore, the aims of this study were: (1) to identify which postural sway measures differentiate between PwMS and healthy controls, as a function of physiological fall risk; (2) to determine the discriminative ability of postural sway measures for fall risk classification (low, moderate, or high) in PwMS. To achieve these aims, we utilized the random forest algorithm to classify individuals' fall risk based on a comprehensive set of postural sway parameters that contain time-domain, frequency-domain, and non-linear dynamics measures, and calculated the diagnostic accuracy (sensitivity, specificity, and accuracy) and feature importance of the postural sway measures.

Methods

This study is secondary analysis of previously published and unpublished data focusing on mobility in MS^{23–28}. All data were sampled from baseline assessments prior to any interventions.

Participants. Data from 153 participants (50 healthy controls and 103 individuals with MS) were included in the analysis. The inclusion criteria for MS participants included a previously neurologist-confirmed diagnosis of MS and the ability to stand upright for 30 s without aid. Self-reported disability was assessed with the self-reported expanded disability status scale (EDSS_{SR})²⁹, with higher scores indicating higher functional impairment. Inclusion criteria for healthy controls required no history of neurological or orthopedic pathology that might influence balance or mobility, and the ability to stand upright for 30 s without aid. The experimental protocol was approved by and performed in accordance with the relevant guidelines and regulations of the University of Illinois at Urbana-Champaign Institutional Review Board, and all participants provided written informed consent prior to participation.

Procedure. On a single visit, participants were instructed to stand upright for 30 s on a force platform (FP4060-05-PT-1000, Bertec Corp, Columbus, OH) with their feet shoulder-width apart and eyes open, fixating at a target 2 m away. Individual's risk of falls was assessed using the short form of the Physiological Profile Assessment³⁰ (PPA, Neuroscience Research Australia, Sydney), which consists of five validated measures of physiological function (visual contrast sensitivity, proprioception, quadriceps strength, reaction time, and postural sway). The individual fall risk index score was derived from the PPA normative database (Z-scores adjusted) for comparison with population norms, and MS participants were further categorized as low risk (<1), moderate risk (1–2), and high risk (>2)^{30,31}.

Participants also provided demographic information and completed questionnaires on balance confidence (ABC or FES-I). The ABC and FES are both validated measures for fear of falling, and have been shown to be highly correlated ($r = 0.88$)³². The FES-I contains 16 items scored on a four-point scale (1 = not at all concerned to 4 = very concerned), which assesses the degree of perceived self-efficacy at avoiding a fall during basic activities of daily living (ADL)⁷. The total score of FES-I ranged from 16–64, with lower scores indicating higher perceived self-efficacy at avoiding a fall. The ABC balance scale (a 16-item scale) measures individual's confidence in maintaining balance while performing ADL⁶. The total score of ABC ranges from 0–100%, and higher scores indicate higher confidence in maintaining balance. Due to differences in research procedure across multiple studies, 37 participants only completed the ABC scale, 27 participants only completed the FES-I scale, and 89 participants completed both ABC and FES-I scale. In order to compare the self-reported balance confidence across multiple studies, the FES-I score was converted to a percentage score (0–100%, with higher scores indicating higher confidence) similar to the ABC score using the following formula: $FES_p = 100\% * \text{abs}(FES - 64) / (64 - 16)$.

The self-reported Balance Confidence was derived as the average of ABC and FES_p. If only ABC or FES was available, then that available measure was used.

All participants also completed the Berg Balance Scale assessment⁵, which consists of 14 physical tasks, such as transfer from sitting to standing position, standing with eyes closed, and picking up an object from the floor, all of which are part of normal daily activities. Each task performance is assigned 0–4 points by a trained personnel to give a total score of 0–56.

	Controls	MS _{Low}	MS _{Mod}	MS _{High}
N (M/F)	50 (15/35)	34 (10/24)	27(7/20)	42 (13/29)
Age*	64.94 (4.91)	54.00 (13.12)	58.26 (8.28)	56.76 (9.71)
EDSS* (Median & IQR)	NA	4.0 (3.0)	6.0 (2.0)	6.0 (0.5)
BBS*	55.12 (2.03)	50.68 (4.80)	45.22 (7.82)	40.05 (8.36)
PPA*	-0.08 (0.62)	0.28 (0.51)	1.50 (0.31)	3.01 (0.91)
Balance Confidence*	93.12 (7.05)	74.67 (19.87)	58.90 (25.06)	55.92 (17.19)

Table 1. Participant characteristics. All values were presented with mean and standard deviation, unless otherwise listed. * Significant group difference was observed ($p < 0.05$).

Data processing and feature extraction. COP data were sampled at 1000 Hz and low pass filtered (4th order Butterworth) at 10 Hz for further analysis. A comprehensive set of common postural sway measures that includes time and frequency domain measures and non-linear dynamics were derived from the COP sway data using established procedures^{9,33} and a customized MATLAB program (Mathworks, Inc., Natick, MA): Sway path length (Anterior-Posterior-AP, Medial-Lateral-ML, and Resultant Distance-RD); Mean sway velocity (AP, ML, and RD), 95% confidence ellipse sway area, Sway range (AP, ML direction), Root mean squared sway amplitude (AP, ML); total power, centroidal frequency, frequency dispersion, 95% power frequency; Sample Entropy (AP, ML), and Approximate Entropy (AP, ML). For both Sample Entropy and Approximate Entropy calculation, the input parameter were chosen as $m = 3$, $r = 0.2$, according to Rhea *et al.*³³.

Model training and performance evaluation. To provide clinical meaningful output for MS fall risk diagnosis, Random Forest algorithms were employed to classify individuals' fall risk categories (i.e. low, moderate, high) based on postural sway metrics. The RF algorithm is an ensemble of random decision trees (in our case, 1000 trees, chosen by examining the convergence of classification accuracy as additional trees were added³⁴), in which the final predicted class for a test example is obtained by combining the predictions of all individual trees. This classifier has been shown to improve the generalization performance of individual decision trees²⁰.

Binary classification between healthy controls and MS groups (HC vs MS_{Low}, HC vs MS_{Mod}, HC vs MS_{High}, MS_{Low} vs MS_{Mod}, MS_{Low} vs MS_{High}, MS_{Mod} vs MS_{High}) were performed based on sway measures and on clinical balance measures (BBS and Balance Confidence) separately. All classification algorithms were implemented using the open-source machine learning library Scikit-learn in Python³⁵.

All algorithms were trained and tested through a 10-fold cross validation (CV) scheme³⁶, and the classification performance was evaluated using standard classification metrics (accuracy, sensitivity, and specificity) derived from the confusion matrix. Briefly, sensitivity was calculated as true-positive/(true-positive + false-negative), specificity as true-negative/(true-negative + false-positive), and accuracy as true-positive + true negative/(true-positive + false-negative + true-negative + false-positive). Since no hyper-parameter tuning was performed in this work (as a proof-of-concept, all algorithms are used in their default settings) and with a limited sample size, data split into training and testing sets was not performed.

In order to identify the importance of each variable in detecting altered balance control in PwMS, a feature selection algorithm was subsequently performed based on the RF classification model. The RF classifier identifies the importance of each input features by calculating the Mean Decrease Impurity (MDI), defined as the number of times a feature is used to split a node, weighted by the number of sample it splits³⁷. In other word, if a feature is used multiple times to split a large amount of data, it is identified as a substantial feature.

Ethical approval. All procedures were approved by the University of Illinois at Urbana-Champaign Institutional Review Board

Preprint. A pre-print of this publication has been deposited in bioRxiv: <https://doi.org/10.1101/410704>.

Results

Table 1 summarizes the characteristics of the 153 participants (108 Female, 45 Male) in this study. All 50 healthy controls had low fall risk (PPA < 1). Participants with MS were further categorized to low risk ($n = 34$, PPA < 1), moderate risk ($n = 27$, PPA 1–2), and high risk ($n = 42$, PPA > 2) of falls based on PPA. Overall, significant group difference ($p < 0.05$) in age, EDSS, BBS, PPA, and self-reported balance confidence scale were observed within the MS group. MS individuals with increased fall risk also exhibited higher disability (EDSS_{SR}), lower balance confidence, and lower functional performance (BBS).

Table 2 provides a summary of the RF classification performance based on sway measures. Sway-based classifier can consistently differentiate healthy controls and MS individuals with high classification accuracy (86.3–92.3%), sensitivity (76.5–85.7%) and specificity (92.0–96.0%). However, sway-based classifier achieved relatively low accuracy in differentiating MS subgroups (Accuracy: 49.5–71.2%, Sensitivity: 48.1–71.4%, Specificity: 22.2–73.5%).

Table 3 provides a summary of the RF classification performance based on the BBS and self-reported balance confidence scale. Good classification performance for differentiating controls and MS individuals were observed (Accuracy: 73.5–95.6%, Sensitivity: 66.7–95.0%, Specificity: 78.0–96.0%). With moderate classification performance observed in differentiating MS subgroups (Accuracy: 61.4–76.7%, Sensitivity: 51.9–87.5%, Specificity: 59.3–72.7%). It is worth noting that this clinical measure-based classifier achieved lower accuracy (73.5%) than the sway-based classifier (86.3%) in differentiating healthy controls and low risk PwMS, but improved the

	MS _{Low}			MS _{Mod}			MS _{High}		
	ACC	SEN	SPC	ACC	SEN	SPC	ACC	SEN	SPC
Controls	86.3	76.5	92.0	92.3	85.2	96.0	89.3	85.7	92.0
MS _{Low}				50.0	48.1	52.9	71.2	71.4	73.5
MS _{Mod}							49.5	66.7	22.2

Table 2. Diagnostic performance of RF algorithm using posturography measures. ACC-accuracy, SEN - sensitivity, SPC – Specificity.

	MS _{Low}			MS _{Mod}			MS _{High}		
	ACC	SEN	SPC	ACC	SEN	SPC	ACC	SEN	SPC
Controls	73.5	66.7	78.0	92.1	88.9	94.0	95.6	95.0	96.0
MS _{Low}				61.4	51.9	69.7	75.9	80.0	72.7
MS _{Mod}							76.7	87.5	59.3

Table 3. Diagnostic performance of RF algorithm using BBS and balance confidence measures. ACC-accuracy, SEN - sensitivity, SPC – Specificity.

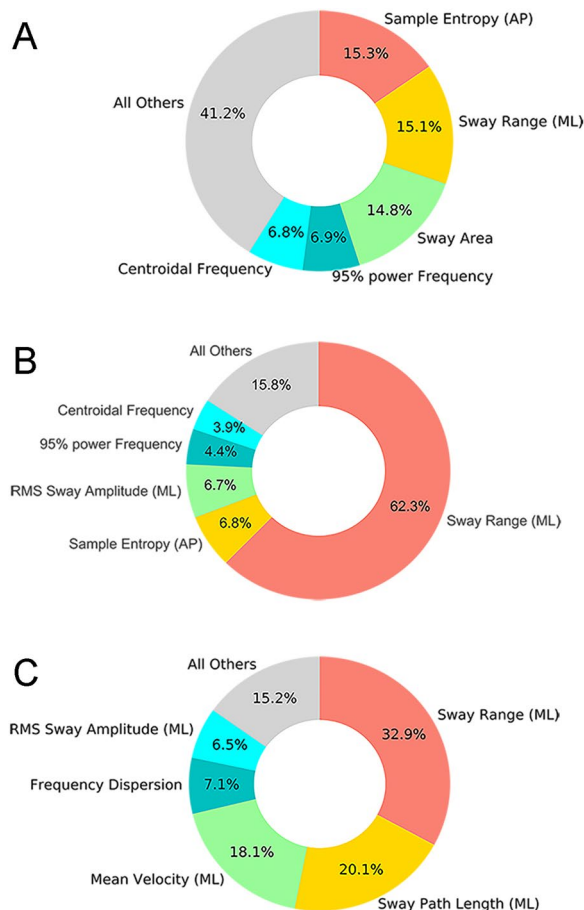


Figure 1. Sway metrics importance as measure by the Mean Decrease Impurity (MDI) of each RF classifier. (A) Controls vs MS_{Low}; (B) Controls vs MS_{Mod}; (C) Controls vs MS_{High}.

accuracy in differentiating MS subgroups (61.4–76.7%), especially in differentiating PwMS with high fall risk among other subgroups (75.9–76.7% in comparison to 49.5–71.2% using only sway measures).

The importance of sway measures for differentiating the fall risk categories in PwMS and controls were extracted using the weighted percentage (MDI) of each RF classifier. Figure 1A shows the top-five sway measures for differentiating Low-risk MS individuals from Controls, with Sample Entropy (AP), Sway Range (ML), and Sway Area identified as the top predictors from this model with similar weight (~15%). Figure 1B shows the top

sway measures for differentiating Mod-risk MS individuals from Controls. Sway Range (ML) was identified as the governing predictor from this model (62.3% of total importance measure). Figure 1C shows the top sway measures for differentiating High-risk MS individuals from Controls, in which Sway Range (ML), Sway Path Length (ML), and Mean Velocity (ML) were identified as the top predictors from the model (ML sway amplitude account for 71.1% of total importance).

Discussion

This work aimed to identify postural sway parameters that best differentiate between PwMS and healthy controls, as a function of physiological fall risk utilizing a machine learning approach. This work also investigated the discriminative ability of using postural sway measures for fall risk classification in PwMS. Utilizing a machine learning approach (random forest classifier), we demonstrated that postural sway measures can discriminate low-risk PwMS from healthy controls, with over 86% of classification accuracy. In contrast, clinical balance measures (BBS) and self-report balance confidence measures achieved equal to superior discriminative ability in separating MS individuals with moderate and high risk of falls. These findings suggest that posturography measures are sensitive to subtle change in the balance control among MS individuals with minimal fall risk, whereas the balance impairment in moderate and high-risk MS individuals can be assessed with traditional clinical measures with high accuracy.

Overall, the observations further confirm that individuals with MS across the disability spectrum have postural control deficits¹⁵. The novel contribution of this investigation is identifying distinct COP parameters that are sensitive to balance impairment in MS as a function of fall risk. Indeed, ML sway amplitude parameters including sway range, sway path length, mean sway velocity were the strongest predictors for discriminating moderate and high-risk PwMS from healthy controls. This observation is consistent with Morrison and colleagues³⁸ who demonstrated that a sample of 22 persons with MS had greater fall risk which coincided with deficits in medio-lateral postural control. On the other hand, Sample Entropy, a measure of movement complexity (lower value indicating reduced signal complexity) and potential reduced adaptability to small perturbations^{13,14}, was further identified as a key predictor for discriminating low-risk PwMS from healthy controls. This finding is consistent with previous research by Roeing *et al.*²⁶ and Huisinga *et al.*³⁹ that proposed reduced complexity in postural control as a biomarker for balance impairment in individuals with MS.

Several previous reports have attempted to predict fall risk in PwMS using postural sway measures. For example, Prosperini *et al.*¹⁰ used time-domain sway measures and logistic regression that achieved over 70% accuracy in discriminating faller from non-faller in PwMS. Furthermore, Kasser *et al.*⁴⁰ utilized a logistic regression to achieve 81% accuracy in discriminating faller and non-faller with differences in the amount of body sway under different sensory conditions (i.e., eyes open to eyes closed). Hoang *et al.*³¹ also utilized logistic regression and achieved 71.2% accuracy (area under the Receiving Operating Characteristic curve) in discriminating faller from non-faller with sway range during eyes closed balance task. It is important to note that these previous reports predicted future falls while the current investigation is based on physiological fall risk. Consequently, direct comparisons between investigations may not be appropriate.

One limitation of the present study is that only a single postural control condition was included. Altered sensory test conditions which are common in balance assessments (i.e., eyes closed, standing on compliance surface) were not included in the data analysis. It has been reported that static posturography under altered sensory condition may yield better discriminative ability between PwMS and healthy controls⁴¹, and thus could further improve the classification performance. Another limitation of this work is the relative small sample size ($n = 30\text{--}50$ per group), which may limit generalization. It is also important to note that the current observations relate to postural assessment at one point in time. Further research is needed to determine which posturography metrics are most sensitive to rehabilitation. Lastly, the present work did not measure the fall occurrence, thus how the results relate to prediction of future falls is not clear. However, findings from this work may set the foundation for the development of guidelines for accurate reporting of balance impairment in PwMS.

Conclusion

The current findings highlight the benefits of posturography for balance impairment and fall risk assessment among PwMS, and provide insights on the standardization of metrics. Specifically, static posturography is sensitive for discriminating PwMS with minimal fall risk from healthy controls, with sample entropy measure identified as a core predictor. Whereas for quantification of balance impairment in high-risk MS individuals, medio-lateral sway amplitude is the strongest predictor. Furthermore, clinical balance measures also achieved high discriminative ability in separating MS individuals with moderate and high risk of falls. Therefore, the assessment technique and sway metrics should be based on the target populations, i.e. utilizing posturography (sway entropy) to identify individuals with subtle balance impairment and using clinical balance measures to assess individuals with high fall risk. These findings from this work may set the foundation for the development of guidelines for accurate reporting of balance impairment in PwMS.

Received: 18 February 2019; Accepted: 21 October 2019;

Published online: 06 November 2019

References

1. Browne, P. *et al.* Atlas of multiple sclerosis 2013: a growing global problem with widespread inequity. *Neurology* **83**, 1022–1024 (2014).
2. Cameron, M. H. & Lord, S. Postural control in multiple sclerosis: implications for fall prevention. *Curr Neurol Neurosci Rep* **10**, 407–412 (2010).
3. Kister, I. *et al.* Disability in multiple sclerosis A reference for patients and clinicians. *Neurology* **80**, 1018–1024 (2013).
4. Sosnoff, J. J. *et al.* Mobility, balance and falls in persons with multiple sclerosis. *Plos One* **6**, e28021 (2011).

5. Berg, K. O., Wood-Dauphinee, S. L., Williams, J. I. & Maki, B. Measuring balance in the elderly: validation of an instrument. *Canadian journal of public health = Revue canadienne de sante publique* **83**, 57–11 (1992).
6. Powell, L. E. & Myers, A. M. The activities-specific balance confidence (ABC) scale. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **50**, M28–M34 (1995).
7. Yardley, L. *et al.* Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age and ageing* **34**, 614–619 (2005).
8. Edginton Bigelow, K. & Berme, N. Development of a protocol for improving the clinical utility of posturography as a fall-risk screening tool. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences* **66**, 228–233 (2010).
9. Prieto, T. E., Myklebust, J., Hoffmann, R., Lovett, E. & Myklebust, B. Measures of postural steadiness: differences between healthy young and elderly adults. *IEEE Transactions on biomedical engineering* **43**, 956–966 (1996).
10. Prosperini, L., Fortuna, D., Gianni, C., Leonardi, L. & Pozzilli, C. The diagnostic accuracy of static posturography in predicting accidental falls in people with multiple sclerosis. *Neurorehabilitation and neural repair* **27**, 45–52 (2013).
11. Chiari, L., Rocchi, L. & Cappello, A. Stabilometric parameters are affected by anthropometry and foot placement. *Clinical biomechanics* **17**, 666–677 (2002).
12. Masani, K., Popovic, M. R., Nakazawa, K., Kouzaki, M. & Nozaki, D. Importance of body sway velocity information in controlling ankle extensor activities during quiet stance. *Journal of Neurophysiology* **90**, 3774–3782 (2003).
13. Lipsitz, L. A. & Goldberger, A. L. Loss of complexity and aging. *Jama* **267**, 1806–1809 (1992).
14. Busa, M. A. & van Emmerik, R. E. Multiscale entropy: A tool for understanding the complexity of postural control. *Journal of Sport and Health Science* **5**, 44–51 (2016).
15. Comber, L., Sosnoff, J. J., Galvin, R., & Coote, S. Postural control deficits in people with Multiple Sclerosis: A systematic review and meta-analysis. *Gait & posture*, **61**, 445–452 (2018).
16. Tahir, N. M. & Manap, H. H. Parkinson Disease Gait Classification based on Machine Learning Approach. *Journal of Applied Sciences* **12**, 180–185 (2012).
17. Arora, S., Venkataraman, V., Donohue, S., Biglan, K. M., Dorsey, E. R., & Little, M. A. (2014, May). High accuracy discrimination of Parkinson's disease participants from healthy controls using smartphones. In 2014 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) (pp. 3641–3644). IEEE.
18. Howcroft, J., Kofman, J. & Lemaire, E. D. Feature selection for elderly faller classification based on wearable sensors. *Journal of neuroengineering and rehabilitation* **14**, 47 (2017).
19. Sun, R. & Sosnoff, J. J. Novel sensing technology in fall risk assessment in older adults: a systematic review. *BMC geriatrics* **18**, 14 (2018).
20. Breiman, L. Random forests. *Machine learning* **45**, 5–32 (2001).
21. Boulesteix, A. L., Janitza, S., Kruppa, J. & König, I. R. Overview of random forest methodology and practical guidance with emphasis on computational biology and bioinformatics. *Wiley Interdisciplinary Reviews: Data Mining and Knowledge Discovery* **2**, 493–507 (2012).
22. Gray, K. R. *et al.* Random forest-based similarity measures for multi-modal classification of Alzheimer's disease. *NeuroImage* **65**, 167–175 (2013).
23. Moon, Y., Wajda, D. A., Motl, R. W. & Sosnoff, J. J. Stride-time variability and fall risk in persons with multiple sclerosis. *Multiple sclerosis international* **2015** (2015).
24. Roeing, K. L., Wajda, D. A., Motl, R. W. & Sosnoff, J. J. Gait termination in individuals with multiple sclerosis. *Gait & posture* **42**, 335–339 (2015).
25. Sosnoff, J. J. *et al.* Fall risk and incidence reduction in high risk individuals with multiple sclerosis: a pilot randomized control trial. *Clinical rehabilitation* **29**, 952–960 (2015).
26. Roeing, K. L., Wajda, D. A. & Sosnoff, J. J. Time dependent structure of postural sway in individuals with multiple sclerosis. *Gait & posture* **48**, 19–23 (2016).
27. Sosnoff, J. J. *et al.* Dual task training in persons with Multiple Sclerosis: a feasibility randomized controlled trial. *Clinical rehabilitation* **31**, 1322–1331 (2017).
28. Sun, R. *et al.* Assessment of Postural Sway in Individuals with Multiple Sclerosis Using a Novel Wearable Inertial Sensor. *Digital Biomarkers* **2**, 1–10 (2018).
29. Kurtzke, J. F. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* **33**, 1444–1444 (1983).
30. Lord, S. R., Menz, H. B. & Tiedemann, A. A physiological profile approach to falls risk assessment and prevention. *Physical therapy* **83**, 237–252 (2003).
31. Hoang, P. D., Cameron, M. H., Gandevia, S. C. & Lord, S. R. Neuropsychological, balance, and mobility risk factors for falls in people with multiple sclerosis: a prospective cohort study. *Archives of physical medicine and rehabilitation* **95**, 480–486 (2014).
32. Huang, T.-T. & Wang, W.-S. Comparison of three established measures of fear of falling in community-dwelling older adults: psychometric testing. *International journal of nursing studies* **46**, 1313–1319 (2009).
33. Rhea, C. K. *et al.* Noise and complexity in human postural control: interpreting the different estimations of entropy. *Plos One* **6**, e17696 (2011).
34. Schwartz, M. H., Rozumalski, A., Truong, W. & Novacheck, T. F. Predicting the outcome of intramuscular psoas lengthening in children with cerebral palsy using preoperative gait data and the random forest algorithm. *Gait & posture* **37**, 473–479 (2013).
35. Pedregosa, F. *et al.* Scikit-learn: Machine learning in Python. *Journal of machine learning research* **12**, 2825–2830 (2011).
36. Kohavi, R. (1995, August). A study of cross-validation and bootstrap for accuracy estimation and model selection. In *Ijcai* (Vol. 14, No. 2, pp. 1137–1145).
37. Archer, K. J. & Kimes, R. V. Empirical characterization of random forest variable importance measures. *Computational Statistics & Data Analysis* **52**, 2249–2260 (2008).
38. Morrison, S., Rynders, C. & Sosnoff, J. Deficits in medio-lateral balance control and the implications for falls in individuals with multiple sclerosis. *Gait & posture* **49**, 148–154 (2016).
39. Huisinga, J. M., Yentes, J. M., Filipi, M. L. & Stergiou, N. Postural control strategy during standing is altered in patients with multiple sclerosis. *Neuroscience letters* **524**, 124–128 (2012).
40. Kasser, S. L., Jacobs, J. V., Foley, J. T., Cardinal, B. J. & Maddalozzo, G. F. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. *Archives of physical medicine and rehabilitation* **92**, 1840–1846 (2011).
41. Spain, R. *et al.* Body-worn motion sensors detect balance and gait deficits in people with multiple sclerosis who have normal walking speed. *Gait & posture* **35**, 573–578 (2012).

Acknowledgements

The authors would like to thank Dr. Salma Musaad at the Illinois Biostatistics Core of the Interdisciplinary Health Sciences Institute at Illinois for the assistance and feedback in the preparation of this manuscript. Data from this work was collected in previous studies that were funded in part by the National Multiple Sclerosis Society, Consortium of MS Centers, and MC10, Inc.

Author contributions

J.S. and R.S. conceived of the study. R.S. performed the data analysis. R.S., K.H. and J.S. co-wrote the manuscript text. All authors reviewed the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information is available for this paper at <https://doi.org/10.1038/s41598-019-52697-2>.

Correspondence and requests for materials should be addressed to R.S.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2019