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Next Steps in Wearable Technology and Community Ambulation in Multiple Sclerosis

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Abstract

Purpose of Review Walking impairments are highly prevalent in persons with multiple sclerosis (PwMS) and are associated with reduced quality of life. Walking is traditionally quantified with various measures, including patient self-reports, clinical rating scales, performance measures, and advanced lab-based movement analysis techniques. Yet, the majority of these measures do not fully characterize walking (i.e., gait quality) nor adequately reflect walking in the real world (i.e., community ambulation) and have limited timescale (only measure walking at a single point in time). We discuss the potential of wearable sensors to provide sensitive, objective, and easy-to-use assessment of community ambulation in PwMS.

Recent Findings Wearable technology has the ability to measure all aspects of gait in PwMS yet is under-studied in comparison with other populations (e.g., older adults). Within the studies focusing on PwMS, half that measure pace collected free-living data, while only one study explored gait variability in free-living conditions. No studies explore gait asymmetry or complexity in free-living conditions.

Summary Wearable technology has the ability to provide objective, comprehensive, and sensitive measures of gait in PwMS. Future research should investigate this technology's ability to accurately assess free-living measures of gait quality, specifically gait asymmetry and complexity.

Keywords Multiple sclerosis · Wearable technology · Community ambulation · Gait · Gait quality

Introduction

Multiple sclerosis (MS) is an inflammatory autoimmune disease that affects roughly 2.3 million individuals worldwide [1]. Although the underlying cause of MS is unknown, many believe it to be influenced by factors such as age, environment, gender, infection, and genetics [2, 3]. Pathologically, the disease targets the body's central nervous system (CNS) through the demyelination of nerve fibers, resulting in altered or lost communication from the CNS to effector organs. This altered neural conduction affects sensory and motor functions which ultimately lead to impairments in gait, balance, and locomotion [4, 5].

Walking is a highly involved motor skill which integrates the locomotor stepping pattern with the cyclic biomechanical phases of gait [6]. To achieve an efficient and reproducible walking pattern, neural control must integrate step timing with appropriate trunk and limb postures for specific phases of the gait cycle (See Fig. 1) [7]. This neural control provides a framework for gait quality, or an individual's efficiency within the gait cycle, which can be broken into five measurable parameters: pace, rhythm, variability, asymmetry, and complexity [8]. Pace refers to the rate of movement (i.e., gait speed), rhythm describes the temporal characteristics within an individual's gait cycle (i.e., cadence, time in stance, time in swing, time in double support), variability is the amount of variance or change experienced across gait cycles (e.g., stride time variability), asymmetry captures the lack of similarity in movement patterns between each lower limb during the gait cycle, and complexity refers to nonlinear measures that capture the temporal evolution of movement variability (e.g., sample entropy). For instance, healthy individuals are seen

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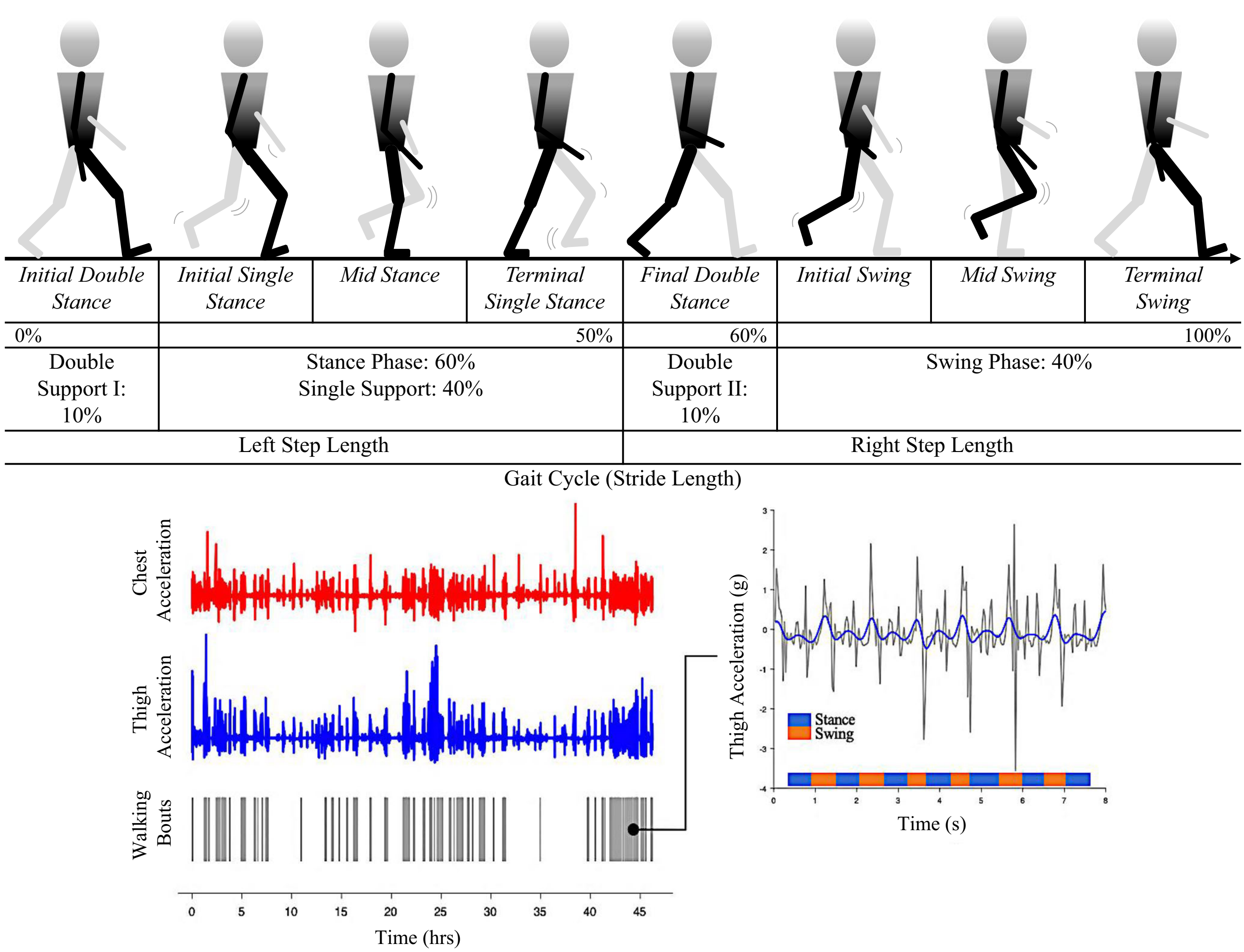

Fig. 1 Phases and components of the gait cycle. Walking bouts (gray) identified from the chest (red) and thigh (blue) accelerometer data using a statistical classification model during the 48 h a volunteer with MS was instrumented with wearable sensors during their daily life. Accelerometer data (gray) during the walking bouts (see callout) can be filtered (blue) and processed to identify spatiotemporal gait parameters during every walking bout completed by the subject during the 48-h monitoring period

to have highly complex movement patterns, and thus a high amount of complexity within their gait, while complexity decreases with aging and disability [9–11]. Due to the decline in sensory and motor function within multiple sclerosis, persons with MS (PwMS) have altered gait quality [12••, 13] characterized by declines in pace, rhythm, and complexity as well as increases in variability and asymmetry [14–16].

Approximately 40–60% of (PwMS) report having a gait impairment [17, 18]. Of those who self-reported walking difficulties, 74% claimed it interferes with their daily life [17]. Alterations in gait have been observed early in the disease course, even in the absence of other indicators of the disease, making it a prime marker for disease presence and progression [19–21]. Walking impairment is strongly correlated with the disease severity of MS [19, 22, 23] and risk for adverse outcomes such as falls [4], reduced quality of life [17], and increased caregiver burden [17].

Fortunately, early identification of altered gait quality allows for early intervention. In order to do this effectively, sensitive, objective, easy-to-use, and ecologically valid measures of gait impairment are critical for assessing the impact of MS on the functional ability of patients, and for identifying appropriate interventions to improve these abilities early in the disease course. To date, no such method exists, yet an emerging body of literature suggests that wearable technology may embody all of these characteristics. Therefore, the purpose of this review is to investigate the feasibility of wearable technology in providing a sensitive, objective, and easy-to-use assessment of community ambulation in individuals with MS.

Traditional Assessments of Mobility

Within clinical practice and research, there are a number of different approaches used to quantify gait quality in PwMS.

These measures run the gamut from clinician-rated scales (e.g., dynamic gait index scale), self-report measures (e.g., 12-item multiple sclerosis walking scale (MSWS12)), performance-based measurements (e.g., timed 25-ft walk test (T25FW), 6-min walk test (6MWT), and timed up and go test (TUG)), and lab-based advanced movement analysis measures which leverage technology such as optical motion capture and force plates. Although widely utilized, each of these tests is limited in some way (see Table 1).

To date, fully characterizing the five aspects of gait quality (pace, rhythm, variability, asymmetry, and complexity) has required advanced movement analysis. These methods of collecting data are highly sensitive to subtle changes in impairment, responsive, reliable, comprehensive, and standardized, yet they require expensive laboratory equipment and trained personnel, and have a high level of administrative burden [34] (see Table 1). The combination of these factors prevents the use of these technologies in clinical practice. On the other hand, performance-based measures, or clinical assessments, are easy to administer and cost-effective. While these simple performance measures have been related to mobility impairment [35], they do not provide information about the underlying biomechanics of the task itself. These tests also have limitations including floor and ceiling effects [24], poor sensitivity in mildly impaired PwMS [24], non-comprehensive, and limited ecological validity [36•, 37•]. Similarly, measures of self-report and rating scales are easy to administer, cost-effective, and standardized, yet they are subjective and have the ability to be impacted by mood disturbances, such as depression [25].

Two very important and shared limitations between current assessment approaches (lab-based motion analysis and clinical assessments) are that they (i) provide information at a single time-point and (ii) do not take into consideration environmentally induced tradeoffs when walking in real-world conditions. It is very common for the presence of disease-related symptoms to vary within [38] and between days [39] for PwMS. A measurement recorded at a single time-point fails to provide insight on this inherent variability and could thereby misrepresent the individual's functional ability. Furthermore, these gait assessments are typically performed in a stable environment such as a research laboratory or clinical setting. When walking within the community, an individual is faced with environmentally induced tradeoffs, which inadvertently result in behavior modifications to the peripheral neuromechanical/environmental system that adjust gait for the present task's demands [40, 41]. Simply put, an individual will adjust their gait to prioritize safety, in exchange for a less efficient walking pattern [6]. Indeed, a recent study indicated that traditional lab-based walking assessments are

Table 1 Advantages and disadvantages to varying types of mobility assessments

Mobility assessment types	Advantages	Disadvantages	References
Performance measures (e.g., 6MWT, T25FW)	- Easy to administer - Inexpensive - Standardized - Objective	- Single time-point - Limited responsiveness to subtle changes in impairment - Limited ecological validity - Floor and ceiling effects - Not comprehensive	- Goldman et al., 2010 [24] - Motl et al. 2017 [25] - Gjibels et al., 2012 [26]
Self-report (i.e., MSWS12)	- Easy to administer - Inexpensive - Standardized	- Single time-point - Subjective - Impacted by depression - Not comprehensive	- Hobart et al., 2013 [27]
Rating scales (i.e., Dynamic Gait Index)	- Easy to administer - Standardized	- Single time-point - Subjective - Limited reliability - Not comprehensive	- Kalron & Aloni 2018 [28] - Bennet et al., 2017 [29]
Biomechanical assessments (i.e., motion capture)	- Highly sensitive to subtle changes in impairment - Highly responsive - Reliable - Comprehensive - Standardized	- Single time-point - Costly - Requires expertise - High administration burden	- Cofré Lizama et al., 2016 [30] - Peebles et al., 2016 [31]
Wearable technology (i.e., IMU)	- Easy to administer - Continuous data collection - Community ambulation - Sensitive - Comprehensive? - Reliable? - Highly sensitive?	- Usability? - Adoption? - Compliance?	- Moon et al., 2017 [32••] - McGinnis et al., 2017 [33••]

6MWT 6-min walk test, *T25FW* timed 25-ft walk test, *MSWS12* 12-item multiple sclerosis walking scale not in line with older adults' walking in a free-living environment [42]. Due to the discussed limitations of traditional approaches, it is paramount to develop an inexpensive, objective, and easy-to-use tool for frequent gait assessment during community ambulation in PwMS.

The Implications of Wearable Technology

Wearable technology may provide a solution to the limitations of current clinical and lab-based measures by enabling easy-to-administer continuous remote gait quality monitoring outside of a typical laboratory or clinical context (see Table 1). These technologies have been popularized in recent years, thanks to advances in MEMS (microelectromechanical systems) realizations of inertial sensors, including accelerometers and angular rate gyroscopes, which have resulted in decreased size, cost, and power consumption. When incorporated in appropriate packaging and secured to the human body, these miniaturized, low-cost sensors provide a direct measurement of body segment kinematics. When paired with novel signal processing and machine learning algorithms, these measures can be used to capture the five aspects of gait quality previously assessed using expensive, laboratory-based measurement modalities (e.g., force platforms, optical motion capture).

Since the advent of MEMS accelerometers, considerable research has focused on using these measurements to capture the amount of daily physical activity in terms of activity and/or step counts. In fact, step counts are the most common means for capturing free-living ambulation and physical activity in healthy and diseased populations, including MS [43, 44]. However, the *amount* of physical activity is influenced by numerous factors—above and beyond MS-related symptoms (e.g., only 20% of the variance in daily physical activity explained by MS-induced mobility impairment, fatigue, and depression [45]). As such, this review focuses on the use of wearable technology for capturing gait *quality* rather than gait *quantity*.

Gait quality measures, including pace, rhythm, variability, asymmetry, and complexity, have been captured in a variety of populations with gait impairments. Table 2 provides a summary of studies that have used wearable devices for capturing each of the five aspects of gait quality and in populations of patients with MS, Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), dementia, mild cognitive impairment (MCI), stroke, and older age. These studies have collected data in both laboratory and free-living environments, and with devices placed on the head, chest, lumbar, torso, pelvis, thigh, shank, knee, ankle, foot, and combinations thereof.

The vast majority of studies (47 out of 60) examining gait quality have been conducted in a laboratory environment. Laboratory-based studies have been important in demonstrating the validity and reliability of gait quality measures extracted from wearable technologies (e.g., [32••, 33••]) and improving the sensitivity of standard functional assessments [34]. However, they fall short of realizing the potential of wearable sensors—which is the remote analysis of gait in naturalistic, free-living environments. While the measurement of physical activity has made the transition outside of the lab, the analysis of gait quality in free-living environments is just beginning. This is especially important in neurological disorders like MS, where symptoms are known to fluctuate daily, and even from one hour to the next within a given day [91]. There may be additional technical challenges in advancing gait quality measures outside of the laboratory, not the least of which is robustly and automatically identifying when patients are walking so that appropriate algorithms can be deployed for capturing gait quality. Activity classification using statistical models trained with machine learning techniques provides a potential solution that has been leveraged for this goal in other populations [92, 93]. Figure 1 provides example data from our group illustrating the use of machine learning for automatically identifying periods of walking and processing those walking bouts to yield free-living measures of gait quality for PwMS.

The physical form of wearables remains a technical challenge that has slowed the transition of devices outside of the lab. These devices need to balance power, storage, and computational requirements in a package that is able to interface closely with the human body for long periods of time. Notably, the power drawn by MEMS angular rate gyroscopes is orders of magnitude above that drawn by accelerometers (e.g., see [94]). While this is suitable for short-duration monitoring in the clinic or laboratory, in practice, it means that wearables are only able to leverage accelerometer data for capturing measures of free-living gait quality, limiting the scope of possible analyses and potentially their clinical relevance (e.g., an angular rate gyroscope would be required for estimating joint angles or foot trajectory). Moreover, wearable devices that are strapped to body segments may be sufficient for short-duration assessments conducted in the clinic or laboratory but are uncomfortable and impractical for long-term wear. The notable exception to this is for devices strapped to the wrist, where commercial activity trackers have demonstrated that devices can be worn for long periods, but the resulting data does not necessarily provide sufficient information to quantify all aspects of gait quality (see Table 2 and description below). This points toward the need for flexible wearable sensors that can be secured directly to the skin (i.e., adherable sensors) and provide a non-invasive measurement of body segment kinematics (e.g., see [32••, 92, 93, 95–97]) at locations critical for assessing gait quality. It also points toward the need for improvements in MEMS gyroscope power draw and/or data collection strategies that are designed to minimize

Table 2 References examining each aspect of gait quality, with the indication of the population studied, location where data was collected, and the placement of wearable devices

Gait feature	Population	References	Location	Placement
Pace	MS	McGinnis et al. (2017) [33••]	Lab	Pelvis, thigh, shank
	MS	Supratak et al. (2018) [46•]	Free-living	Lumbar
	MS	Pau et al. (2018) [41]	Lab	Lumbar
	MS	Shammas et al. (2014) [47]	Free-living	Pelvis
	MS	Sosnoff et al. (2012) [48]	Free-living	Pelvis, foot, thigh
	MS	Motl et al. (2012) [49]	Lab	Pelvis
	PD	Combs-Miller et al. (2019) [50]	Lab	Foot, shank, thigh
	PD	Del Din et al. (2016a) [51]	Lab, free-living	Lumbar
	PD	Mitchell et al. (2019) [52]	Lab	Chest, pelvis, wrist, shank
	PD	Nero et al. (2015) [53]	Lab	Wrist
	PD	Raccagni et al. (2018) [54]	Lab	Foot
	Stroke	Moore et al. (2017) [55]	Lab	Lumbar
	Stroke	Yang et al. (2013) [56]	Lab	Shank
	Stroke	Meijer et al. (2011) [57]	Lab	Pelvis
	Stroke	Taylor-Piliae et al. (2016) [58]	Free-living	Chest
	Stroke	Sánchez et al. (2015) [59]	Free-living	Chest, thigh
	Older adults	Takayanagi et al. (2019) [36•]	Free-living	Pelvis
	Older adults	Van Ancum et al. (2019) [37•]	Free-living	Lumbar
Rhythm	MS	Spain et al. (2012) [34]	Lab	Wrist, ankle, sternum, lumbar
	MS	Pau et al. (2016) [60•]	Lab	Lumbar
	MS	Moon et al. (2017) [32••]	Lab	Lumbar, shank
	MS	Pau et al. (2017) [61]	Lab	Lumbar
Variability	MS	Storm et al. (2018) [62]	Lab, free-living	Lumbar, shank
	PD	Del Din et al. (2016a) [51]	Lab, free-living	Lumbar
	PD	Del Din et al. (2016b) [63]	Lab	Lumbar
	PD	Ellis et al. (2015) [64]	Lab	Navel
	Stroke	Moore et al. (2017) [55]	Lab, free-living	Lumbar
	MCI	Schwenk et al. (2016) [65]	Lab	Thigh, shank
	Dementia	Ijmker and Lamoth (2012) [66]	Lab	Lumbar
	Older adults	Brodie et al. (2016) [67]	Lab	Chest
	Older adults	Hickey et al. (2016) [68]	Lab	Lumbar
	Older adults	Urbanek et al. (2017) [69]	Lab	Pelvis, wrist
	Older adults	Wang et al. (2017) [70]	Lab	Lumbar, ankle
	Older adults	Grimpampi et al. (2015) [71]	Lab	Lumbar
	Older adults	Howcroft et al. (2016) [72]	Lab	Head, pelvis, shank
Asymmetry	MS	Psarakis et al. (2018) [73•]	Lab	Head, pelvis
	MS	Brodie et al. (2016) [67]	Lab	Pelvis
	PD	Mitchell et al. (2019) [52]	Lab	Chest, pelvis, wrist, shank
	PD	Del Din et al. (2016a) [51]	Lab, free-living	Lumbar
	PD	Del Din et al. (2016b) [63]	Lab	Lumbar
	PD	Sant' Anna et al. (2011) [74]	Lab	Ankle, wrist
	Stroke	Prajapati et al. (2011) [75]	Lab, hospital	Ankle
	Stroke	Lien et al. (2017) [76]	Lab	Lumbar, knee, ankle, foot
	Stroke	Meijer et al. (2011) [57]	Lab	Pelvis
	Stroke	Moore et al. (2017) [55]	Lab, free-living	Lumbar
	Stroke	Oyake et al. (2017) [77]	Lab	Lumbar
	Stroke	Wang et al. (2018) [78]	Lab	Shank, thigh
	Stroke	Yang et al. (2013) [56]	Lab	Shank

Table 2 (continued)

Gait feature	Population	References	Location	Placement
	Stroke	Zhang et al. (2018) [79]	Lab	Lumbar, foot
	Neuro	Qiu et al. (2019) [80]	Lab	Ankle
Complexity	MS	Craig et al. (2019) [81]	Lab	Ankle, lumbar
	MS	Craig et al. (2017) [82]	Lab	Chest, ankle
	MS	Huisinga et al. (2013) [83]	Lab	Lumbar, wrist, shank
	MS	Peebles et al. (2017) [84••]	Lab	Chest
	PD	Afsar et al. (2016) [85]	Lab	Feet
	PD	Warlop et al. (2018) [86]	Lab	Ankle
	PD	Combs-Miller et al. (2019) [87]	Lab	Foot, thigh, shank
	PD	Jehu and Nantel (2018) [88]	Lab	Wrist, ankle, lumbar, chest
	PD/HD/ALS	Liao et al. (2008) [89]	Lab	Feet
	Stroke	Tamburuni et al. (2018) [90]	Lab	Lumbar
	Stroke	Dugan and Combs-Miller (2019) [50]	Lab	Pelvis, thigh, shank, foot

MS multiple sclerosis, *PD* Parkinson's disease, *MCI* mild cognitive impairment, *Neuro* neurological diseases, *HD* Huntington's disease, *ALS* amyotrophic lateral sclerosis

power requirements. Collectively, these approaches will allow for the creation of smaller wearables that integrate seamlessly with the human body and can record data for long periods of time in free-living environments.

Recent evidence suggests that free-living pace and rhythm can be estimated from wearable devices secured to the wrist [98, 99] in healthy individuals. However, as illustrated in Table 2, wrist-worn devices have not yet been deployed in patients with mobility impairment nor have they been extended to address the other aspects of gait quality. One study explores the use of wrist sensors for capturing lab-based gait variability, but the authors note that the method would be unlikely to generalize to free-living environments as patients often walk without arm swinging [69]. This is especially true in cases when participants utilize walking aids. Similarly, one study also explores the use of wrist sensors for capturing gait asymmetry, but their data is specifically used to capture upper extremity asymmetry and is paired with sensors on the lower extremities [74]. Collectively analysis of device locations used previously suggests that a single accelerometer placed at the lumbar region of the back could be used to capture most gait quality measures. The primary limitation of other locations is the inability to calculate asymmetry, which requires recording bilaterally. It is likely that locations above the lumbar attenuate the accelerometer signal too significantly to yield accurate measures of gait quality from accelerometer data alone. Indeed, the majority of gait quality measures require devices deployed to the lumbar or lower extremities.

Many of the studies included in Table 2 focus on capturing various aspects of gait quality in clinical populations other than MS. Collectively, this highlights the potential to capture each aspect of gait quality in PwMS. Within the studies focusing on PwMS, the majority explore free-living measures of pace and rhythm, while only one study explores gait variability. To date, no publications examine gait asymmetry or complexity in free-living conditions. This highlights the need for additional research exploring free-living measure of gait quality in PwMS. It is also important to note that there are very limited data on which aspects of gait quality are sensitive markers to disease progression and/or intervention. Moreover, many of the studies that do examine free-living, or laboratory, measures of gait quality leverage proprietary technologies with black-box algorithms for extracting these measures from the wearable sensor data. The rate of development in these areas would likely increase if more open-source tools were available for processing data from wearable sensors that are increasingly commercially available. For example, the authors have recently released an open-source toolbox for the analysis of free-living gait (see Fig. 1) [100].

As we continue to develop free-living measures of gait quality, care needs to be taken in interpretation. Studies suggest that these measures may be capturing different constructs than laboratory-based functional assessments of gait and mobility (see [36•, 37•] for pace examples in older adults). As we begin to deploy these technologies for assessing gait quality in MS, it is important that we do not treat these measures as replacements for functional assessments, but instead as another rich source of information that we can use for quantifying MS symptoms (potentially progression) and their impact on daily function. Moreover, the reality that these measurements are made continuously during daily life suggests that this approach could be leveraged in the future for improving patient-provider interactions or informing the development of novel digital therapeutics for improving MS symptom management.

Conclusion

Biomechanical measurements of gait quality are highly sensitive yet are not easily accessible or cost-effective. Traditional clinical measures of performance are widely accepted yet results are limited in their ability to be transferred to a real-world environment. Wearable technology may have the ability to provide comprehensive, reliable, and highly sensitive measures of gait in a real-world setting for PwMS. However, additional studies are needed to establish the measurement of each aspect of gait quality in free-living conditions in this population.

Future Directions

Future wearable technologies need to evolve to be less invasive and more comfortable to wear for long durations in free-living environments and to employ smart strategies that enable the inclusion of additional data modalities. Prior to implementing wearable technology for capturing free-living measures of gait quality, researchers need to establish its validity and reliability. For PwMS in particular, research on each aspect of gait quality are needed, but with particular emphasis on gait asymmetry and complexity. In these studies, researchers could also explore the tradeoffs between the development of individualized and general algorithms in terms of performance and ease-of-use. As with any new technology, human factor considerations need to be thoroughly investigated such as patient and clinician usability, adoption, and compliance.

Compliance with Ethical Standards

Conflict of Interest Mikaela L. Frechette, Brett Meyer, Lindsey Tulipani, and Reed D. Gurchiek each declare no potential conflicts of interest.

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Ryan S. McGinnis reports other from Impellia, Inc. (Scientific advisor, consultant) and other from MC10, Inc. (Own stock, consultant), outside the submitted work; in addition, Dr. McGinnis has a patent METHODS AND APPARATUS FOR PROVIDING PERSONALIZED BIOFEEDBACK FOR THE TREATMENT OF PANIC ATTACKS pending (Claims and description include language about providing personalized biofeedback for preventing falls), a patent Method and System for Neuromodulation and Stimulation pending, a patent Method and System for Crowd-Sourced Algorithm Development pending, a patent Automated detection and configuration of wearable devices based on on-body status, location, and/or orientation pending, a patent Athlete Speed Prediction Method Using Data from Attached Inertial Measurement Unit issued, and a patent Apparatus and Methods for Employing Miniature IMU's for Deducing Forces and Moments on Bodies pending.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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