Correlations between Inertial Body Sensor Measures and Clinical Measures in Multiple Sclerosis

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ABSTRACT
Gait assessment using inertial body sensors is becoming popular as an outcome measure in multiple sclerosis (MS) research, supplementing clinical observations and patient-reported outcomes with precise, objective measures. Although numerous research reports have demonstrated the performance of inertial measures in distinguishing healthy controls and MS subjects, the relationship between these measures and the impact of MS on gait impairment remains poorly understood. In contrast, although clinical evaluation has limited variability in scores, it is meaningful and interpretable for clinicians.

Therefore, this paper investigates correlations between two inertial measures and three clinical measures of walking ability. The clinical measures are the MS Walking Scale (MSWS-12), the Expanded Disability Status Scale (EDSS), and the six minute walk (6MW) distance. The inertial measures are the double stance time to single stance time ratio (DST/SST) and the causality index, both of which have been proven effective in MS gait assessment in previous work.

28 MS subjects and 13 healthy controls were recruited from an MS outpatient clinic. Most correlations among measures were strong and significant. Experimental results suggested that combining all five measures may improve separability performance for tracking MS disease progression.

Categories and Subject Descriptors
G.3 [**Mathematics of Computing**]: Probability and Statistics–*correlation and regression analysis.*

General Terms
Algorithms, Measure, Performance, Experimentation, Human Factors, Theory, Verification

Keywords
12-item Multiple Sclerosis Walking Scale, 6-minute Walk, Inertial Body Sensors, Separability Enhancement

1. INTRODUCTION
Gait impairment is a common marker of disease progression in persons with multiple sclerosis (MS). MS is a chronic autoimmune disorder of the central nervous system (CNS) that results in neurologic impairment and functional disability over time, leading to decreased mobility, independence and quality of life. Gait performance is, therefore, an important outcome to assess severity of disease, disease progression, and therapeutic efficacy.

There are many measures of gait impairment that have been used in research and clinical practice. They can be divided into two groups: clinical measures and inertial measures from body sensors.

Clinical measures include assessments completed by patients and assessments completed by physicians or other care providers. Several clinical measures are routinely used to assess the impact of MS on mobility. These measures have been developed using standard methods of test construction and validated in community and hospital-residing samples of individuals with MS. For instance, the Expanded Disability Status Scale (EDSS) [1] is a physician-assessed composite score based on neurological examination of walking ability along with seven functional systems: pyramidal, cerebellar, brainstem, sensory, vision, bowel and bladder, and cognitive. The 12-item Multiple Sclerosis Walking Scale (MSWS-12) [2] is a patient-reported outcome questionnaire developed by a panel of experts that is used to assess the impact of MS on walking. Otherwise, measures from timed walk tests (25-ft or 6-min walk tests) such as gait speed, and distance walked are also widely used in MS clinics and research.

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Gait measures using inertial body sensors are gaining popularity in MS research. The measures drawn from the walk tests and movement analysis include gait cycles and interactions among body parts. Although several studies have demonstrated the performance of inertial measures in distinguishing between healthy controls and MS subjects, the relationship between inertial measures and the impact of MS on gait impairment is not well understood. In contrast, although measures from clinical evaluation have limited variability in scores, their meaning is well-known to care providers, making them easy to interpret; relationships between them have been extensively studied; and they are known to be effective outcome measures when evaluating treatment or monitoring disease progression.

To understand the relationship between gait measures from inertial body sensors and the impact of MS on gait impairment, this paper further investigated the most recent and best validated measures of walking performance. Experimental results from 28 MS subjects recruited from a MS outpatient clinic and 13 healthy controls show separability enhancement in MS and illustrate the efficacy of the proposed analysis.

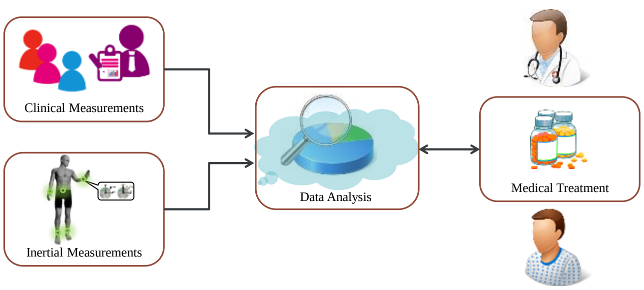

Figure 1. This paper further investigated the correlations between clinical measures including the 12-item Multiple Sclerosis Walking Scale (MSWS-12), Expanded Disability Status Scale (EDSS), and distance walked during 6MW, and two gait measures drawn from inertial body sensor data including the ratio between double stance time and single stance time (DST/SST) and the causality index, providing enhanced separability for tracking MS disease progression.

2. RELATED WORK

2.1 Clinical Measures

Validation of measures in clinics has been investigated in numerous studies. The EDSS has long been a popular outcome for validation, but research demonstrated that it was not sensitive to clinical change over a 9-month follow-up period, it was unresponsive to disease progression in moderate to severe disability, and it had limited variability in scores. Therefore, recently, another measure, MSWS-12, has gained popularity as an outcome measure partly based on its correlation to other objective measures.

McGuigan et.al [3] was the first attempt to validate the MSWS-12. Results from 149 patients illustrated that the psychometric properties of the MSWS-12 were excellent, and in particular the scale is responsive to change. Motl et al. [4] investigated the MSWS-12 scores of 133 participants based on confirmatory factor analysis and the experimental results demonstrated strong evidence of internal consistency. Motl et al. [5] further validated the MSWS-12 based on correlation with a physiological marker, the oxygen cost of walking. Pilutti et.al [6] also conducted further validation of the MSWS-12 using correlation analysis with spatiotemporal gait parameters such as gait speed, cadence, step length, and step time from 6MW. Sidovar et.al [7] mapped the MSWS-12 to the EuroQol 5-dimension (EQ-5D) in North American MS patients and proved the MSWS-12 scores also have strong correlation with EQ-5D scores.

Apparently, as described in [4], the MSWS-12 is the most recent and best validated patient-reported outcome for the effect of MS on walking ability, and plenty of experimental results from different research groups had proved it. However, the MSWS-12 appears to have variable sensitivity across the MS walking disability spectrum The traditional objective measures in clinics were based on manual measures, for instance, the patients followed instructions to walk in the clinic hallway, and then the doctors recorded the distance walked during each specified period and the total distance. We evaluated the characteristics of the 6MW in MS subjects and healthy controls and proved the strong correlation between objective measures from 6MW and subjective measures of physical impairment, including the MSWS-12 [10].

2.2 Inertial Measures from Body Sensors

In recent years, gait assessment using inertial body sensors is gaining more and more attention from MS researchers, because the sensors provide more precise and accurate measures than human observation and manual measures. Many methods for gait assessment based on inertial body sensors using gait cycle detection [8], gait pattern recognition [9], etc., had been reported in the literature. Often temporal gait features based on gait phase decomposition are used. These include gait speed [10, 11], stride length [12], joint angles [13], swing time [14], double stance time, single stance time [15] or other derived parameters [16].

Most recently, we proposed another novel view of the gait assessment based on using a causal model to describe and estimate the interactions among body parts [17]. Compared to other objective measures, this estimated representation of interactions among body parts, named as Causality Index, provides the best separability performance between the healthy controls and MS patients. This paper is the first attempt to validate the Causality Index based on the correlations with other measures, including EDSS, MSWS-12, gait speed, and other quantitative parameters from gait analysis.

Therefore, the main contributions of this paper are:

- A complementary validation of clinical measures including EDSS, MSWS-12 and distance walked during 6MW based on correlations with gait measures using inertial body sensors including the ratio between double stance time and single stance time (DST/SST) and the causality index.
- First attempt to validate the causality index drawn from inertial body sensors with other measures.
- Separability enhancement between MS subjects and healthy controls based on combined clinical and inertial measures.

Current measures for MS disease state assessment are generally based on clinical measures (e.g. MSWS-12, gait speed) separately. Based on the complementary results of this paper, we can say that combining the measures from clinical measures and inertial measures from body sensors has the potential to enhance the assessment of MS disease severity and progression.

3. METHODS

3.1 Participants

Participants (N = 41) were recruited from a MS outpatient clinic via telephone and e-mail messages from a member of the research team. This was followed by a screening for inclusion criteria that included a neurologist-confirmed diagnosis of MS; relapse free during the previous 30 days, ambulatory with minimal assistance, age between 18 and 65 years, and absence of risk-factors for undertaking strenuous physical activity (e.g., cardiovascular diseases, diabetes, hyperlipidemia, and hypertension). There were 60 individuals who underwent screening and 41 of those individuals satisfied inclusion criteria and volunteered for participation. All the measures including EDSS, MSWS-12 and 6MW data including gait speed, distance walked, and data from inertial body sensors were collected during a single clinic visit.

3.2 6MW Data Collection

The 6MW procedure followed Goldman's previous research [10]. We have left the details of this protocol to Appendix 1 of reference [10]. All the participants were assisted by the examiners to wear 5 inertial sensors, named "Technology-Enabled Medical Precision Observation (TEMPO) [21]", which contains 3 axes of accelerometers and gyroscopes on each sensor node for 6 degrees-of-freedom sensing, on the left/right wrists, left/right ankles and sacrum while completing the 6MW.

The distance walked was recorded in 1-minute epochs by a research assistant using a measure wheel. Subjects were asked to walk as far and as fast as possible (without running) up and down a 175-foot hallway. The inertial sensor data was wirelessly transmitted to a laptop for post-processing.

The inertial sensor sampling rate is 128Hz, sufficient to capture the frequency band of body motion while walking. The operator of the data collection system was required to make timestamp annotations in order to indicate the beginning and end of the walk.

132 data sessions were collected over 3 years and each subject performed at least one 6MW. All the data sessions were calibrated with recorded calibration parameters determined prior to data collection [18]. There is no general normalization in the data preprocessing. However, due to the technical issues of our custom data collection system and human factors in real-world deployment, 11 data session failed in the calibration process; 6 of them had too many dropped packets during wireless transmission to the laptop for data collection, 3 of them have timestamp errors due to system operator error, and 2 of them had lost calibration parameters in the calibration records. Finally, 36 data sessions were successfully collected from 13 healthy controls while 85 data sessions were successfully collected from 28 MS subjects.

3.3 Clinical Measures

The EDSS is used to categorize the severity of disability as mild (EDSS 0-2.5), moderate (EDSS 3.0-4.0), and severe (EDSS 4.5-6.5). In this pilot study, we did not recruit any participants with severe walking disability (EDSS $\geq$ 4.5).

MSWS-12 scores were collected every time the participant visited the MS outpatient clinic. We did not collect MSWS-12 scores from healthy controls; because they do not have any walking impairment due to MS, their score is 12, the minimum score.

Gait speed and distance walked during the 6MW were calculated based on the manual measures. However, based on the evaluation results of [10], we selected distance walked as the only one measure in next-step correlation analysis, because there is strong correlation (r=0.91) between gait speed and distance walked.

3.4 Inertial Measures from Body Sensors

Measures from inertial body sensors came from two types of gait assessment techniques; one is the temporal decomposition of the inertial sensor signals, such as stride length, single stance time (SST), swing time, and double stance time (DST); another is the causality estimation among the sensor signals which is used to represent the interactions among the body parts. This paper adopted two typical measures from inertial body sensors: Ratio between DST and SST (DST/SST) [16] and Causality Index [17].

3.5 Statistical Analysis

All analyses were performed using SPSS, version 19 (SPSS, Chicago, IL). Descriptive data are presented as mean and standard deviation. The differences in EDSS, MSWS-12, distance walked, causality index, and DST/SST across the 6MW tests were examined using one-way, within-subjects ANOVAs; disability measure (EDSS) was the within-subjects factor with three levels (healthy, mild, and moderate). The relationships between scores from the EDSS, MSWS-12, distance walked, causality index, and DST/SST across the 6MW tests were estimated using Pearson product-moment correlations (r) as the scores for all variables approximated a normal distribution with minimal skewness and kurtosis and had continuous measure properties. Cohen's guidelines of .1, .3, and .5 were used for judging the magnitude of the correlation coefficients as small, moderate, and large, respectively [19].

4. RESULTS

4.1 Bivariate Correlation Analysis

Table 1 presents a matrix of correlations among MSWS-12 scores, EDSS scores, distance walked, and other quantitative measures drawn from inertial sensor data including DST/SST index and causality index. Scatter plots of the stronger associations among the measures are provided in Fig. 1.

It is noteworthy that most of the correlations among these measures are significant and strong (r>0.500), except the associations between EDSS scores and quantitative measures drawn from inertial sensor data. This is because of the limited variability in the EDSS scores.

Distance walked during 6MW correlated significantly and strongly with causality index (r = 0.822, p = 0.001) and DST/SST index (r = 0.748, p = 0.001), while these two objective measures from inertial sensor data also correlated to each other significantly and strongly (r = 0.772, p = 0.001). MSWS-12 scores correlated significantly and strongly with distance walked during 6MW (r=-0.678, p=0.001). As we can see in Figure 2 (d-f), there is similar

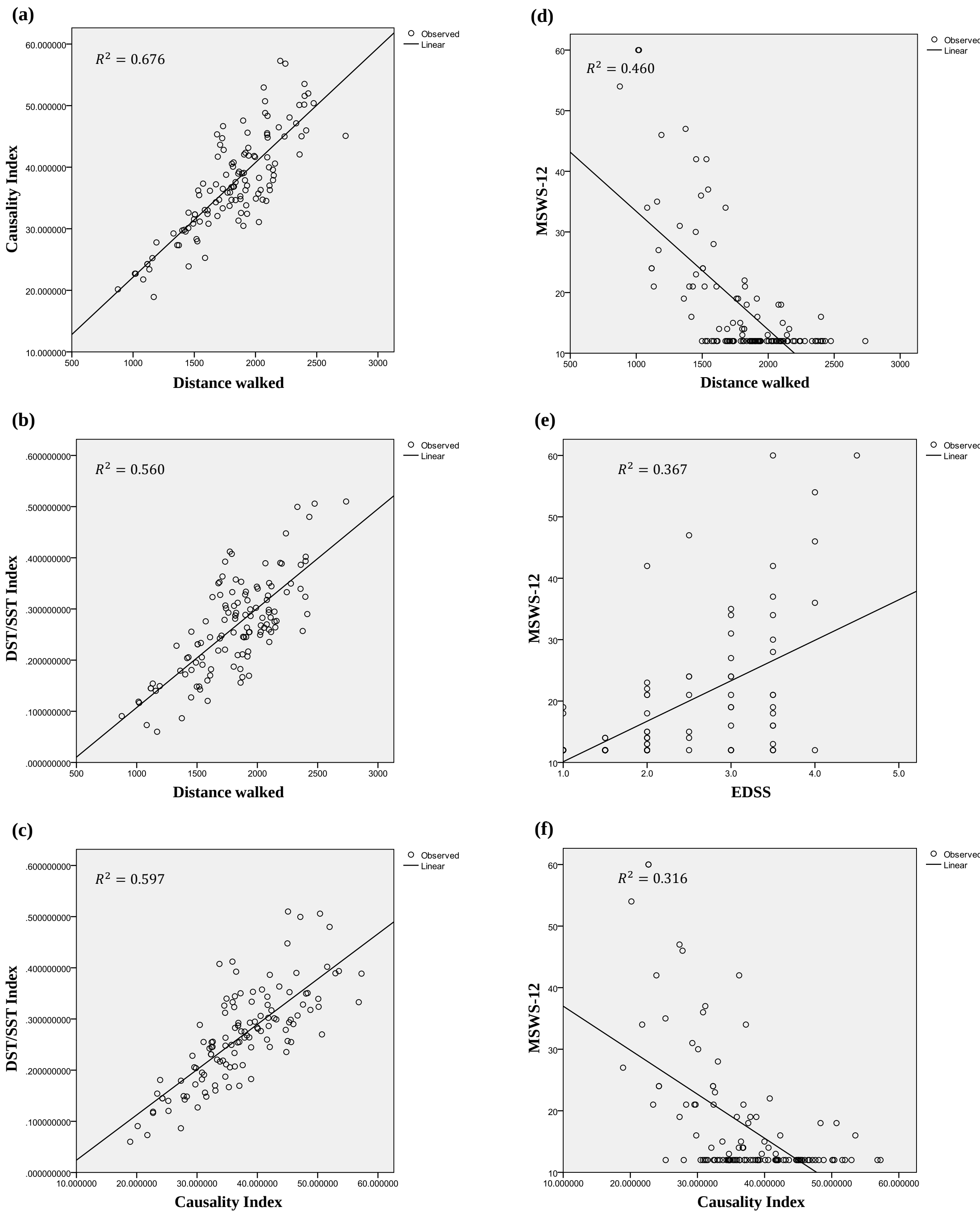

Figure 2. Scatter plot, linear trend-line, and squared multiple correlation (R2) for the stronger associations among the measures: associations between distance walked and (a) causality index, and (b) DST/SST index; (c) association between causality index and DST/SST index; and associations between MSWS-12 and (d) distance walked, and (e) EDSS, and (f) causality index. Apparently, the strongest association is the one between distance walked and causality index.

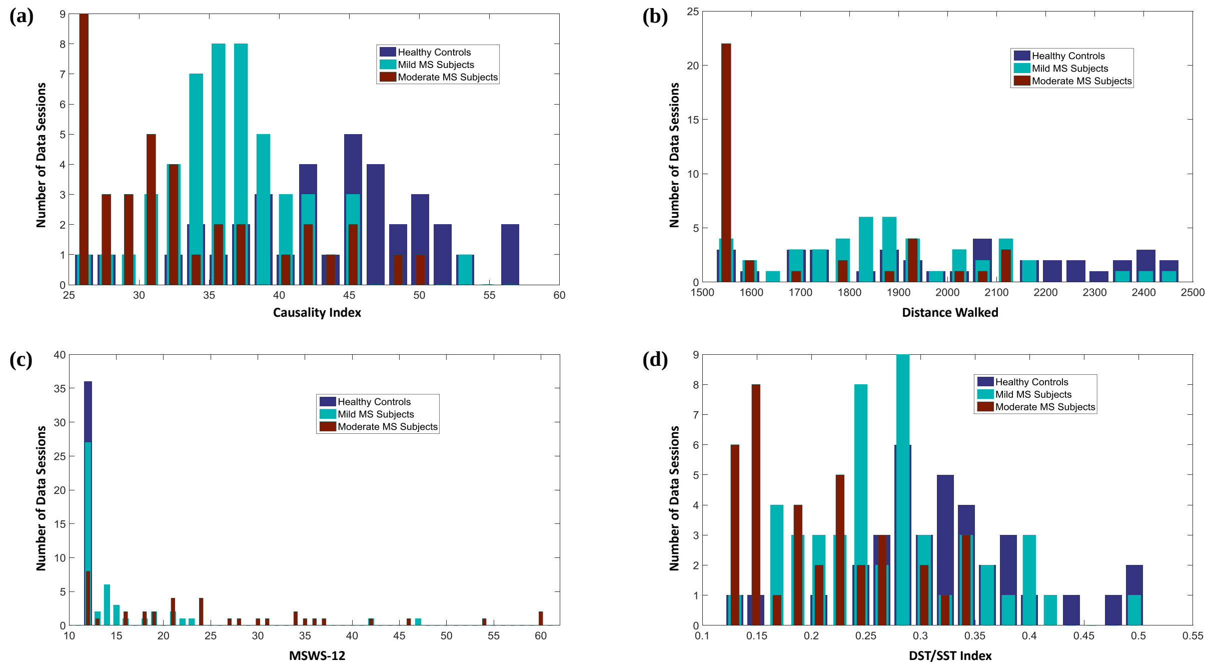

Figure 3. Distribution of (a) Causality Index, (b) Distance walked, (c) MSWS-12 scores, and (d) DST/SST index in three groups: healthy controls, mild and moderate MS subjects. The causality index distinguishes the three groups most clearly.

limited variability in MSWS-12 scores, impeding correlations between the MSWS-12 and other measures.

Table 1. Bivariate correlations among MSWS-12 scores, EDSS scores, distance walked, other quantitative measures drawn from inertial sensor data (causality index and DST/SST index)

Measure	1	2	3	4	5
1. MSWS-12	-				
2. EDSS	0.606	-			
3. Distance walked	-0.678	-0.510	-		
4. DST/SST index	-0.500	-0.358	0.748	-	
5. Causality Index	-0.562	-0.436	0.822	0.772	-

4.2 Separability Performance

A measure of walking ability can be used to provide assistance to doctors when evaluating and monitoring MS disease progression. This assistance comes from the ability of the measure to distinguish the within-subjects factors and then estimate the impact of MS in subjects. As we mentioned before, we use one-way, within-subjects ANOVAs using disability measure as the within-subjects factor with three levels (healthy (EDSS 0), mild (EDSS 0-2.5), and moderate (EDSS 3-4)). Our participants included 13 healthy controls, 17 mild MS subjects and 11 moderate MS subjects.

4.2.1 Separability for Three Groups

Figure 4 illustrates the analysis results of effect size from one-way, within-subjects ANOVAs. We adopted the MES toolbox V1.4 [20] as our analysis method, which provide appropriate effect size value rather than p value. The distributions of the measures are plotted in figure 3. As we can see, the distribution of the causality index better distinguishes between the three groups. Figure 4 shows the same results: causality index has the best effect size in separability of the three groups.

4.2.2 Combined Measures

Based on above analysis in correlations and separability, we selected MSWS-12 as the best validated subjective measure in clinics and the causality index as the measure with best separability performance. Combining the causality index and MSWS-12, Figure 4 shows that the combined index has the best separability performance and Figure 5 presents a better illustration of the separability among the three groups. As you can see, most of the moderate MS subjects are in the red area, most of mild MS subjects are in the blue area, while most of the healthy controls are in the black area. It is worth noting that there is a boundary in the plane which can be used to validate the data. This means it is less likely that any measures from a subject will fall outside the boundary.

5. DISCUSSION

The gait measures from inertial body sensors and clinical measures correlated to each other mostly strongly and significantly ($r>0.500$). This is consistent with the previous validation study of MSWS-12 scores and EDSS scores. This study shows not only the EDSS scores, but also MSWS-12 scores with limited variability. This limited variability greatly impacts the correlations with other measures and the ability to distinguish gait impairment due to MS. Therefore, although the MSWS-12 shows strong and significant correlations to other measures, it provides worse separability performance in experimental data. Figure 3 (c) presents its limited variability in scores.

Distance walked during 6MW is an outcome measure with growing application and utility in MS clinical research. Correlation analysis shows that gait measures using inertial body sensors have strong and significant correlation ($r = 0.822$, $p = 0.001$) with distance walked during the 6MW. This gives promising evidence that inertial body sensors can be a useful and convenient gait assessment tool for MS gait impairment. Otherwise, measures from inertial body sensors provide better separability (effect size = 1.26) in three groups in our experiments.

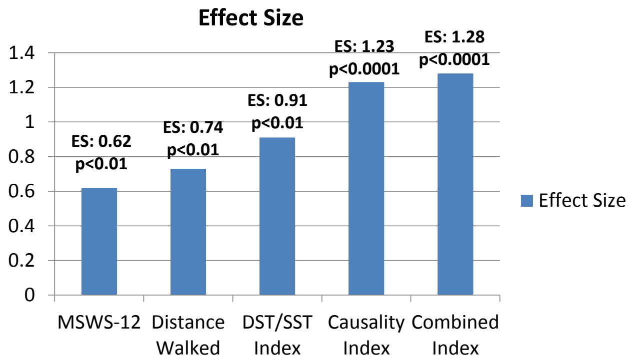

Figure 4. Analysis of effect size from one-way, within-subjects ANOVAs. The EDSS scores were used as the within-subjects factor with three levels (healthy, mild, and moderate). Combined index is a combination of the causality index and MSWS-12.

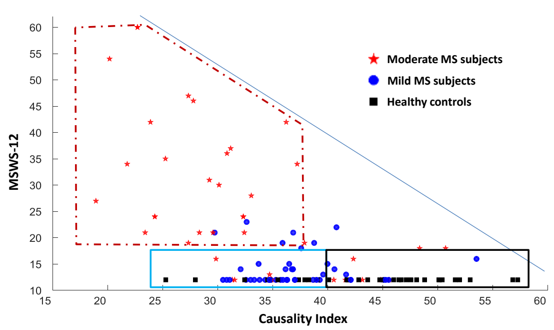

Figure 5. Causality index and MSWS-12 together provide better illustration of separability in three groups.

Strong evidence had been provided to prove the successful validation of causality index of inertial body sensors based on the obvious strong and significant correlations with MSWS-12, distance walked, and DST/SST index. Since the causality index is used to represent the interactions among body parts, we can say that the interactions among body parts can be a common measure to provide strong ability to distinguish three groups: healthy controls, mild MS subjects, and moderate MS subjects.

Combing the measures together is another promising method to enhance separability of MS among patients. Comparing to other measures, a simple data visualization combing causality index and MSWS-12 provided better illustration of separability for the three groups. Therefore, this preliminary result suggested that the information processing and integration between clinical and inertial measures will be next-step work in the near future since the importance of some information in the clinical measures is not well understood yet.

There are some limitations to this study. The first is the size of the sample. This study included three groups of 13 healthy controls, 17 mild MS subjects and 11 moderate subjects. However, the results are consistent with previous studies. Another limitation is the limited understanding of other effects on the 6MW. This study was conducted over a period of 3 years, and many potential issues that may affect the 6MW test were less well understood. A future study with a larger sample size will be needed to evaluate the impact of sample size on separability performance among MS subjects. Finally, there was no baseline assessment of fitness, exercise routine, or other impairment factors such as other pains or injuries. Therefore, it is possible that some of the differences between the groups could be due to level of fitness. This study shows that some MS subjects perform better in MSWS-12 and causality index. Future work should monitor and track energy expenditure in daily life to account for other impact factors, then explore the relationship between 6MW and gait impairment caused by MS.

6. Conclusion

This paper is motivated by the validation requirements of the most current measures from inertial body sensors for understanding the relationship between the gait measures from inertial body sensors and the impact of MS on gait impairment. Therefore, this paper further investigated the correlations between inertial measures from body sensors and measures in clinical evaluation then compared the separability performance of these measures. The experimental results suggested that combining the inertial and clinical measures provides better separability performance for tracking MS disease state and progression.

Future work will focus on larger validation studies for gait measures from inertial body sensors, optimal combination of inertial and clinical measures, and extraction of intuitional meaning for clinicians.

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