Short inertial sensor-based gait tests reflect perceived state fatigue in multiple sclerosis

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Abstract

Background: Multiple sclerosis (MS) is a chronic autoimmune inflammatory disease of the central nervous system, affecting more than 2.3 million people worldwide. Fatigue is among the most common symptoms in MS, resulting in reduced mobility and quality of life. The six-minute walking test (6MWT) is commonly used as a measure of fatigability for the assessment of state fatigue throughout treatment or rehabilitation programs. This 'gold standard' test is time-consuming and can be difficult and exhausting for some patients with high levels of disability or high rates of fatigue.

Research question: Can **short** inertial sensor-based gait tests assess perceived state fatigue in MS patients?

Methods: Sixty-five MS patients equipped with one sensor on each foot performed the 6-minute walk test (6MWT) and the 25-foot walk (25FW, at both preferred and fastest speed). Perceived state fatigue was measured after each minute of the 6MWT, using the Borg rating. The highest of these ratings served as a measure of overall perceived state fatigue. Stride-wise spatio-temporal gait parameters were extracted from the 25FW and from the first minute, first 2 minutes, and first 4 minutes of the 6MWT. Principal component analysis was performed. Perceived state fatigue was predicted in a regression analysis, using the principal components of gait parameters as predictors. Statistical tests evaluated differences in performance between the full 6MWT, the shortened 6MWT, and the 25FW.

Results: A mean absolute error of less than 2 points on the Borg rating was obtained using the shortened 6MWT and the 25FW. There were no significant differences between the prediction accuracy of the full 6MWT and that of the shortened gait tests.

Significance: It is possible to use shortened gait tests when evaluating perceived state fatigue in MS patients using inertial sensors. Substituting them for long gait tests may reduce the burden of the testing on both patients and clinicians. Further, the approach taken here may prompt future work to explore the use of short bouts of real-world walking with unobtrusive inertial sensors for state fatigue assessment.

Background

Multiple sclerosis (MS) is a chronic autoimmune inflammatory disease in which the immune system mistakenly attacks the central nervous system (CNS), leading to inflammatory demyelinating CNS lesions and thus to location-specific neurological symptoms. More than 2.3 million people worldwide have a diagnosis of MS [1]. Gait impairment and fatigue are among the most common symptoms, resulting in reduced mobility and quality of life [2]. Fatigue affects 50% to 90% of MS patients [3], even at an early stage of the disease [4]. The assessment of fatigue is therefore of importance to clinicians as guidance for treatment or rehabilitation programs [5].

Due to the strong correlation between motor function, gait and fatigue [6], gait analysis is used to monitor disability and fatigue in MS patients. Novel approaches to the technique employ systems such as electronic gait mats [7], optical tracking [8], instrumented treadmills [9], and wearable inertial sensors [10]. Wearable systems are among the least obtrusive of the various gait analysis systems and are clinically reliable for monitoring gait in MS [11].

Gait analysis is typically used to assess two types of fatigue: trait fatigue measured via self-report questionnaires (e.g. the Modified Fatigue Impact Scale (MFIS)), and state fatigue, or perception of exertion after an exhaustive task, quantified by the Borg rating of perceived exertion (RPE) [12]. Several standardized walking tests, such as the six-minute walk test, the 25-foot walk, and the 2-minute walk test (6MWT, 25FW, 2MWT), are commonly used for assessing gait in MS. Fatigue is mostly evaluated using long gait tests [13], which assess endurance and have been reported as providing a good measure of walking fatigability [14]. In addition to the assessment of the total distance covered, gait analysis systems can record more specific features of gait. Engelhard et al. used an accelerometer at the hip to measure gait deterioration due to fatigue induced in the 6MWT [15]. They used the acceleration signal of gait cycles from the first and second minutes as a baseline for comparison with cycles from each of the later minutes via dynamic time warping (DTW). In the comparison with each subsequent minute from third to sixth minute, a warp score was calculated that represented the length of the warping path needed for alignment; a higher score therefore indicated higher dissimilarity between baseline minutes and subsequent minutes. They observed that the warp score increased with time due to deterioration of gait. Assessing minutes 3 to 6, they reported the strongest correlation as occurring between the warp score of minute 6 and patient-reported fatigue as measured by MFIS, a self-report questionnaire for rating the effects of fatigue on MS patients' physical, psychosocial, and cognitive performance. They concluded that fatigue is measurable from long bouts of walking. Additionally, Shiratzky et al. [16] studied the relationship between fatigue (MFIS) and decline in gait performance. They used lower back and ankle sensors to measure gait features during the 6MWT. Segmenting the signal into 1-minute windows, they compared gait features occurring across those windows to the end of evaluating the decline in gait patterns that took place due to long and exhausting periods of walking. They found that in moderately disabled patients as measured by the expanded disability status scale (EDSS), sample entropy and cadence declined from the second minute of the test. The authors also found a significant correlation between stride regularity and patient-reported fatigue, and concluded that long durations of walking (e.g. in the 6MWT) could serve as biomarkers for measuring fatigability in MS. Ibrahim et al. [10] used sensors worn on the foot during the 6MWT to predict perceived state fatigue in MS. They calculated the change in gait parameters between the start and the end of the test and used regression analysis for predicting patient-reported state fatigue as measured by the RPE Borg rating. They reported that some gait parameters (stride length, heel strike angle, maximum toe clearance, and stride time) had the largest effects on state fatigue; they were able to predict state fatigue with a mean error of 1.4 on the RPE Borg rating.

The 25FW, a short gait test, has been validated for clinical use in MS patients due to its reliability in measuring gait dysfunction and in distinguishing between patients and healthy controls and among patient groups with different levels of disability [17]. Further, the 25FW is more suitable for clinical usage than long gait tests [14], is applicable to a wider range of disability levels than those applied in long gait tests, and reflects clinically relevant changes that may occur during treatment or rehabilitation programs [18]. Moreno-Navarro et al. [19] used various gait tests, including the 25FW, to measure gait deterioration and perceived fatigue (MFIS) in MS patients classified in three groups on the basis of their EDSS level. Measuring gait speed during the 25FW, the authors found a significant difference among the patient groups, which indicated that gait speed could serve as a distinguishing factor between patients with different levels of disability. No significant relationship was observable between perceived fatigue and gait speed; this said, the authors measured only overall gait speed, and did not address stride-wise parameters or additional gait features which may relate to fatigue and are assessable using wearable sensors.

The 2MWT has further been validated for the measurement of gait capability in patients with various neuromuscular conditions (sporadic inclusion body myositis, myotonic dystrophy, limb-girdle muscular dystrophy and other muscular diseases) [20]. Gijbels et al. [21] compared the walking distance between the 2MWT and 6MWT in MS patients. They measured the distance covered in each minute and found that MS patients exhibited the same walking pace after the second minute and that the distances covered in each of the last 4 minutes appeared repeatedly in the measurement series, with values that were almost constant. Further, they found no significant difference between the distance completed in the 2MWT and the distance completed in the first 2 minutes of the 6MWT. They additionally observed a strong correlation between distances and EDSS scores, which was similar in relation to both walking tests. However, weak correlations were found between fatigue measured by MFIS and walking distances. An additional study by Scalzitti et al. [22] compared the distance completed between the 2MWT and the 6MWT performed on a gait mat. The authors divided MS patients into subgroups based on their disability and found significant correlations between the two tests in each subgroup. They further showed that the distance completed in the 2MWT could predict the distance completed in the 6MWT and consequently distinguish between patient subgroups with differing levels of disability. Similarly, Langeskov-Christensen et al. [23] studied the relationship between disability level (EDSS) and walking speed in the 6MWT, the 2MWT, the first 2 minutes of the 6MWT, and the 25FW. They found significant correlations between EDSS and walking speed in all gait tests, with a slightly better correlation in relation to the 2MWT than the 25FW.

To the best of our knowledge, no published work has compared gait tests of different lengths for perceived state fatigue assessment in MS using inertial sensors worn on the foot. This study therefore aims to predict perceived state fatigue in MS patients using short gait tests. These shorter tests may be able to replace exhausting, time-consuming longer tests (e.g. the 6MWT) commonly used for fatigue assessment at present and may therefore, reduce the burden of performance testing on patients and clinicians.

Methods

Participants

102 patients were recruited from the MS center of the University Hospital Erlangen (Germany) and the Neurological Rehabilitation Center Quellenhof (Bad Wildbad, Germany) for a cross-sectional study [11]. The inclusion criteria were age over 18 years and an EDSS score below 7 (this ensured the study included only such patients as were able to walk) [11]. All subjects gave their informed consent to participation in the study. Patients were excluded if they were

unable to give informed consent due to problems with cognition [11]. The study included sixty-five patients who were able to complete the 6MWT; the remaining patients were excluded because high levels of disability or high rates of fatigue precluded them from completing the 6MWT (Table 1). The local ethics committee (IRB-No. 166_18 B, Medical Faculty, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany) granted ethical approval to the study.

Gait tests

The patients performed the following tests:

- The 6MWT, in which patients walked back and forth for 6 minutes along a 20-meter corridor at a self-selected speed. The gait parameters were extracted from the first minute, first 2 minutes, first 4 minutes, and the full test, for the purpose of investigating whether perceived state fatigue can be predicted using shorter bouts of walking.
- The 25FW, involving patients walking along a corridor to a mark placed at 25ft/7.6m. The test was performed twice: once at the patient's preferred speed, and a second time at the patient's fastest possible speed. The 25FW has been validated for use in MS patients and correlates strongly with disease status and mobility measures [18].

Gait features

Each patient was equipped with one inertial measurement unit consisting of a tri-axial accelerometer and gyroscope (SHIMMER 3 sensor, Shimmer Research Ltd., Dublin, Ireland) at the lateral side of each foot [24]. Data was captured at a sampling rate of 102.4 Hz, saved on a tablet and transferred to a computer for further analysis. Strides were segmented using multi-sequence dynamic time warping as proposed by Barth et al. [24]; spatio-temporal gait parameters were calculated for each stride using the algorithm proposed by Rampp et al. [25].

Rating of perceived fatigue

The RPE Borg rating was used as a subjective measure of patients' self-reported difficulty in performing a task [26]. The RPE Borg rating measures the level of effort and state fatigue that patients feel during an exercise. It has been validated as a measure of fatigue and exertion level in MS patients [27]. Drebinger et al. [12] reported that state fatigue as measured by the RPE Borg rating after the 6MWT was correlated with performance fatigability and gait impairment. After each minute of the test, the patients were asked to rate their state fatigue on a scale of 6 to 20. The highest rating of these served as a representation of overall perceived state fatigue for that patient.

Principal components and regression analysis

For each of the gait tests, the mean gait parameters were calculated (mean stride time, swing time, stance time, stride length, gait velocity, maximum toe clearance, maximum lateral excursion, toe-off angle, and heel strike angle). As some gait features were correlated, principal component analysis (PCA) was performed to remove multicollinearity. PCA components that explained high variance within the data (> 90%) were used for training different regression models (random forest regressor, decision tree regressor, and support vector regressor). In order to evaluate the generalization error, the different models were validated using 10-fold cross-validation. Hyper-parameter tuning was performed in a nested cross validation using Bayesian search, with the minimum absolute error as an optimization criterion. The outer loop split the data into 10 subsets. In each of the 10 folds, one subset was held out for testing and the rest for training to estimate the generalization error. An inner 10-fold cross-validation was used for the data of the remaining 9 subsets for hyperparameter tuning. The best hyperparameters obtained from the inner loop were used to calculate the prediction error on the held-out set from the outer loop.

Statistical analysis

The prediction error from the 6MWT was used as a baseline for comparing the other gait tests to the end of identifying statistically significant differences between the performance of different gait tests. 5x2 cross-validation with a modified t-test [28] [29] was used to statistically compare the performance of the baseline 6MWT model with the models using the 25FW (preferred and fastest speed), the first minute, first 2 minutes, and first 4 minutes of the 6MWT. In this analysis, for each gait test, five iterations were performed. In each iteration, the data was split into two stratified folds, with one fold used as a training set and the other as a test set. In each fold, PCA and hyperparameter tuning were performed on the training set and the performance of the prediction model was evaluated using the test set. After this, the training and test folds were swapped, and the same process was repeated in order to calculate the performance of the model on the new test set; then the average of the two scores was calculated in each iteration. This means that five performance measures were calculated for each gait test using the same cross-validation folds. The Shapiro–Wilk test was used to assess normality due to its reliability for small datasets [30]. The performance measures of the different tests were then compared to the 6MWT using the modified t-test [29]. Additionally, we calculated Pearson's correlation between state fatigue and gait features. The significance level was set at α =.05. Fig. 1 shows the complete data flow of the methodology.

Results

Mean gait parameters were calculated for each of the gait tests (Table 2, Fig. 2, 3). Principal components of these parameters were used as independent variables and the RPE Borg rating as the dependent variable for training different regression models. The models were evaluated using nested 10-fold cross-validation. The mean absolute errors resulting from different gait tests differ only slightly (Table 3). A mean error of 2 represents one level on the RPE Borg rating. Statistical tests were used to compare the performance of the model that used the 6MWT against the performances of the models using the other gait tests. The model with the lowest mean absolute error in the 5x2 cross-validation was selected for comparison. The support vector regressor was selected for the 6MWT and the random forest regressor was selected for the other gait tests. There was no significant difference in prediction accuracy between the 6MWT and the other gait tests (Table 4). The first minute of the 6MWT had the smallest effect size, indicating that it had the smallest difference compared to the full 6MWT and may be suitable as a substitute for the 6MWT.

Discussion

The main aim of this study was to investigate the use of inertial sensors worn on the foot for perceived state fatigue assessment of MS patients using short gait tests. The motivation behind the study was the difficulty some MS patients experience in performing long walking tasks due to fatigability or other constraints associated with their level of disability. We sought to investigate whether short walking tests have the same predictive accuracy as long ones. For most of the walking tests, the mean prediction error was less than 2 points with respect to the best regression model, which represents one level on the RPE Borg rating. Statistical tests were used to ascertain whether the differences in performance between the 6MWT and other short gait tests were significant or occurred due to random sources of variation, such as random selection of training and test sets or randomness of learning algorithms. 10-fold cross validation was used for reporting the generalization errors of the various models (Table 3), whereas 5x2 cross-validation was used only for statistical comparison and was not usable for estimating generalized performance due to the small size of the dataset. We found no significant difference in prediction errors between the full 6MWT and the different short gait tests investigated (25FW; first minute, first 2 minutes, and first 4 minutes of 6MWT). The findings of this study therefore indicate that spatio-temporal gait parameters obtained from short walking tests may predict perceived state fatigue as accurately as those derived from long gait tests. Accordingly, the results indicate that short gait tests may be good substitutes for the full 6MWT in terms of assessing perceived state fatigue in MS. Additionally, the initial minutes of the 6MWT may be representative of the entire 6MWT; it may thus be possible to use them for state fatigue assessment in patients whose high levels of fatigability or issues associated with their level of disability preclude their completing the full 6 minutes.

Previous studies had revealed the validity of short gait tests for predicting MS disease disability level, but had been unable to identify a relationship between fatigue and characteristics of short walking bouts [19] [21]. However, they had investigated only overall walking speed or total walking distance, without looking at other gait parameters. Our study, by contrast, recorded other parameters, such as stance time and heel strike angles, which previous work had omitted. We have been able to show that spatio-temporal features obtained from foot sensors, in combination with principal component analysis, reflected perceived state fatigue even in short walking tests. Consequently, the initial minutes of the 6MWT or 25FW may have the same validity regarding state fatigue prediction as does the full 6MWT, which is commonly used in the literature [10][15][16]. The inclusion of these additional gait parameters has enabled our findings to suggest that clinicians may use shorter gait tests for assessing perceived state fatigue in MS where longer tests are not feasible. This may make the process of monitoring fatigue during treatment or rehabilitation measures easier and less exhausting for highly disabled or fatigued patients, additionally saving time and supervisory work during the tests. Further, our findings indicate that wearable sensors alongside short gait tests may be usable in fatigue monitoring at home or in real-world walking scenarios, which would help to provide better management and better quality of life for MS patients.

The limitations of the study include the restricted number of participants. A similar study using a larger sample may help improve the generalization of the models and generate further insights about patients who experience difficulties completing long walking tests. Additionally, our study included only a small number of patients with high fatigue scores. Future work should therefore seek to study a wider spectrum of patients, including those with higher fatigue levels. Another limitation of the study appears in its analysis of mean gait parameters only; investigation of the dynamics of, or changes in, gait parameters may be able to provide more insights into fatigue [10]. However, some of the short gait tests the study used (e.g. the 25FW) consisted of only a few strides, making it unfeasible to reliably calculate changes in gait parameters. Further, the RPE Borg rating is a subjective measure susceptible to individual differences and the occurrence of human errors that can result from cognitive impairment; objective measurements of fatigue, such as heart rate and oxygen consumption, may have the potential to generate more accurate results and remove this study's dependence on patients' self-reporting. Future work should investigate the association between trait fatigue as measured by standard questionnaires and shortened gait tests, as well as checking the validity and reliability of short bouts of walking in assessing fatigue in home or real-world settings.

Conclusion

The 6MWT test is a common measure of fatigability in MS, yet may be problematic for patients with high levels of disability or high fatigue scores. Upon comparing the prediction performance of various inertial sensor-based gait tests, we found no significant differences between long and short gait tests used to assess perceived state fatigue. This implies that short gait tests may be an appropriate substitute for more burdensome longer tests in assessing state fatigue in MS. Wearable sensors may also pave the way to the use of short tests to monitor fatigue in real-world environments across periods of treatment or rehabilitation programs, reducing the time taken to complete these assessments and the associated burden on MS patients and clinicians.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Conflict of interest statement

The authors confirm that there are no known conflicts of interest regarding the work described in the current manuscript.

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