Monitoring exertion-induced changes in gait parameters in patients with relapsing-remitting MS

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Background

Gait disturbance is a common element of the physical disability caused by multiple sclerosis (MS),[1] and deviations in gait parameters in MS have been noted in patients with early MS and no observable gait abnormality.[2] Motor fatigue has been demonstrated in individuals with MS and generally does not correlate well with self-report measures of fatigue.[3] Motor fatigue can also be measured via exertion-related alteration of gait parameters, and summarized in a Fatigue Index (FI).[4]

Study Goals

The main goal of this study was to further validate the Fatigue Index (FI) in patients with relapsing-remitting MS (RRMS), a low level of neurologic disability, no evidence of disease activity on disease modifying therapy over the past year, but who reported changes in their gait with exertion.

Methods

- MS patients with RRMS were screened for enrollment based on the inclusion/exclusion criteria listed in **Table 1**.
- Exertion-induced gait parameters were measured at baseline and after a 6-month period, and validated clinical and self-report measures were administered as shown in **Table 2**.
- Diffusion tensor imaging (DTI) was performed on a subset of 10 patients at baseline and 6 months.

Table 1. Inclusion / Exclusion Criteria

Inclusion criteria	Exclusion criteria
• age 18 to 65 inclusive • diagnosis of RRMS based on revised MacDonald Criteria • stable DMT for a minimum of 12 months • no relapses or new MRI lesions in the last 12 months • EDSS score 1.0-4.0 • patient-reported changes in gait with exertion while walking	• comorbidity representing a contra-indication to the exercise test • documented worsening of 20% or more on the Timed 25 Foot Walk over the 12 months prior to enrollment, • severe cognitive impairment compromising the subject's ability to safely perform study procedures • MRI subgroup only: factor compromising the feasibility of MRI (e.g. weight inappropriate for height, ferrous objects in the body, severe tremor, history of claustrophobia).

Table 2. Data collected

Domain	
Demographics	age, sex, ethnicity, education years, BMI, date of onset of MS symptoms, current disease course, concomitant medications, active comorbidities.
MS-related disability	Expanded Disability Status Scale (EDSS)
Activity level	Godin Leisure Time Questionnaire (GLTQ)
Gait parameters	Spatiotemporal, kinetic, and kinematic gait parameters were collected while the subjects walked in the Computer Assisted Rehabilitation ENvironment (CAREN) system.
Walking performance tests	Walking Speed Test (WST) of the MS Performance Test (MSPT) 2-minute walk test (2MW)
Self-report measures	Fatigue Scale for Motor and Cognition (FSMC) MS Walking Scale-12 (MSWS-12) Quality of Life in Neurological Disorders (Neuro-QOL) Center for Epidemiological Studies Depression Scale (CESD-10)
DTI	Transverse (TD), longitudinal (LD), and mean (MD) diffusivity Fractional anisotropy (FA)

Methods

Exertion Test

- Subjects walked on a treadmill at a speed set 10% above their observed comfortable walking speed, until they reached a Rate of Perceived Exertion (RPE) score of 7 (Very Hard), or for a maximum of 60 minutes. They wore a harness for safety and we obtained clearance from the patient's treating physician beforehand. Gait parameters were collected every 5 minutes for a period of 2 minutes while the subjects are walking.
- The following parameters were used to calculate the FI, adapted from the formula proposed by Sehle et al.[4]: step length, step width, step height, maximum circumduction, and maximum knee flexion angle. Possible values for the FI range from 0 to 1, with greater values indicating greater motor fatigue from exertion.

$$\text{Fatigue Index} = \frac{1}{2}\left(\frac{\text{N sig mean changes}}{\text{N gait parameters}} + \frac{\text{N sig SD changes}}{\text{N gait parameters}}\right)$$

- We used the Computer Assisted Rehabilitation ENvironment (CAREN) system, which allowed to collect gait parameters during the exertion test. (**Figure 1**)

Figure 1. Computer Assisted Rehabilitation ENvironment (CAREN)

Results

- 29 patients were enrolled and completed baseline assessments. (**Table 3**)
- There were significant associations between individual gait parameters (step height, step length, knee flexion), but not FI, and clinical / self-report measures of walking. (**Table 4**)
- In before-after exertion comparisons, a significant increase was observed for circumduction on both median values and area under the curve (**Figure 2**), while significantly increased variation was detected on step length, step width, step height and circumduction. (**Table 5**)
- In the analysis of the DTI subgroup, some gait parameters, but not FI, were associated with DTI metrics as shown in **Table 6**.

Results *cont.*

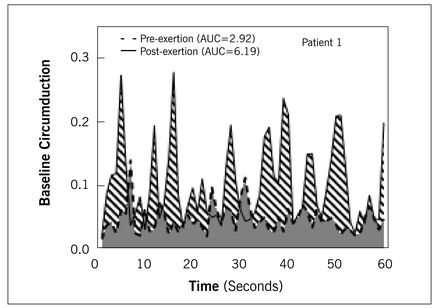
Table 3. Participant characteristics

	Whole sample	No MRI	With MRI
Patients, N	29	19	10
Age (years)	46.0 (41.0,55.0)	50.0 (45.0,56.0)	39.5 (38.0,48.0)
BMI (kg/cm2)	29.1 (24.5,35.0)	28.5 (23.7,35.0)	33.6 (24.5,38.9)
Sex, Female N (%)	20 (69.0)	12 (63.2)	8 (80.0)
Race, White N (%)	22 (75.9)	16 (84.2)	6 (60.0)
College or higher N (%)	12 (41.4)	8 (42.1)	4 (40.0)
MS duration (years)	10.0 (6.0,15.0)	13.0 (5.0,19.0)	8.5 (6.5,10.5)
No active comorbidities N (%)	18 (62.1)	10 (52.6)	8 (80.0)
GLTEQ (how often do you engage in any regular activity…)			
Often	5 (17.2)	4 (21.0)	1 (10.0)
Sometimes	12 (41.4)	9 (47.4)	3 (30.0)
Rarely or Never	12 (41.4)	6 (31.6)	6 (60.0)

Table 4. Correlations with Clinical and Self-Report Measures

	Pre-Exertion Gait Parameters					Fatigue Index		
	Step Length	Step Width	Step Height	Circumduction	Knee Flexion	FI-mean	FI-variability	FI
Age	-0.16 (0.4)	**-0.44 (0.016)**	-0.19 (0.33)	0.28 (0.14)	0.2 (0.29)	0.29 (0.13)	0.04 (0.84)	0.17 (0.37)
MS duration	-0.3 (0.12)	0.17 (0.38)	-0.31 (0.097)	-0.01 (0.96)	-0.31 (0.11)	0.34 (0.074)	0.26 (0.17)	0.36 (0.055)
MSWS-12	**-0.43 (0.021)**	0.1 (0.59)	**-0.45 (0.015)**	0.13 (0.49)	**-0.39 (0.039)**	-0.29 (0.12)	-0.24 (0.21)	-0.27 (0.15)
FSMC, physical	0.04 (0.85)	-0.15 (0.44)	0.08 (0.69)	0.02 (0.93)	0.11 (0.58)	-0.28 (0.14)	-0.14 (0.47)	-0.22 (0.25)
FSMC, cognitive	0.16 (0.41)	-0.07 (0.7)	0.14 (0.47)	-0.19 (0.33)	0.11 (0.58)	-0.19 (0.32)	0 (0.99)	-0.09 (0.65)
FSMC, Total	0.04 (0.83)	-0.11 (0.56)	0.04 (0.82)	-0.08 (0.7)	0.1 (0.62)	-0.24 (0.22)	-0.11 (0.58)	-0.17 (0.38)
CESD	0.2 (0.29)	0.05 (0.81)	0.17 (0.36)	0.06 (0.75)	0.1 (0.62)	-0.2 (0.3)	**-0.55 (0.002)**	-0.37 (0.051)
NeuroQoL LE	-0.1 (0.59)	-0.11 (0.58)	-0.12 (0.54)	0.05 (0.78)	-0.15 (0.45)	-0.15 (0.43)	-0.28 (0.15)	-0.21 (0.27)
EDSS	-0.15 (0.45)	0.2 (0.31)	-0.18 (0.36)	-0.05 (0.8)	0.07 (0.72)	-0.01 (0.96)	-0.09 (0.64)	-0.03 (0.87)
2MW	**0.53 (0.003)**	-0.3 (0)	**0.46 (0.011)**	-0.06 (0.75)	**0.35 (0.064)**	0.1 (0.62)	0.34 (0.075)	0.2 (0.29)

Figure 2. Example of Pre-Post Exertion Change in **Circumduction**



Results *cont.*

Table 5. Changes in gait parameters before and after exertion

	Baseline		
Factor	**Pre (A)**	**Post (B)**	**p (A vs B)***
Mean			
Step Length	0.59±0.13	0.60±0.14	0.4159
Step Width	0.16±0.03	0.15±0.05	0.8344
Step Height	0.10±0.03	0.10±0.03	0.6803
Circumduction	0.05±0.01	0.07±0.02	<.0001
Knee Flexion	64.9±6.1	65.6±6.6	0.3474
Variability (SD)			
Step Length	0.021±0.012	0.024±0.013	0.041
Step Width	0.022±0.008	0.027±0.009	0.001
Step Height	0.007±0.003	0.009±0.005	0.0019
Circumduction	0.015±0.007	0.021±0.012	<.0001
Knee Flexion	1.41±0.639	1.603±1.08	0.1852
AUC%			
Step Length	35.5±6.5	36.3±6.9	0.403
Step Width	9.3±2.0	8.4±2.1	0.0107
Step Height	5.9±1.3	6.0±1.6	0.5131
Circumduction	3.1±0.87	4.0±1.3	<.0001
Knee Flexion	3905.2±364.8	3942.8±412.3	0.426

Table 6. Correlations with Imaging Parameters

	Association among Baseline Values			
	FA	**MD**	**TD**	**LD**
Clinical measures				
MSWS-12	-0.62 (0.056)	0.58 (0.077)	**0.81 (0.005)**	0.4 (0.26)
FSMC, physical	-0.5 (0.14)	0.24 (0.51)	0.22 (0.53)	0.22 (0.53)
FSMC, cognitive	**-0.66 (0.039)**	-0.01 (0.97)	0.2 (0.58)	-0.38 (0.27)
FSMC, total	**-0.74 (0.015)**	0.1 (0.78)	0.28 (0.43)	-0.11 (0.76)
CESD	**-0.66 (0.038)**	0.19 (0.6)	0.51 (0.13)	-0.26 (0.47)
NeuroQoL, LE	-0.32 (0.37)	-0.33 (0.35)	0.03 (0.93)	-0.58 (0.077)
NeuroQoL, Sleep	0.16 (0.66)	**-0.87 (0.001)**	-0.58 (0.079)	**-0.84 (0.003)**
NeuroQoL, UE	-0.23 (0.52)	0.06 (0.88)	0.21 (0.57)	-0.06 (0.86)
NeuroQoL, Cognitive	-0.45 (0.19)	-0.06 (0.88)	0.1 (0.77)	-0.39 (0.27)
EDSS	**-0.92 (<0.001)**	0.48 (0.16)	**0.76 (0.011)**	0.06 (0.88)
2MW	0.35 (0.33)	-0.43 (0.21)	**-0.66 (0.038)**	-0.23 (0.52)
Pre-Exertion mean				
Step Length	0.39 (0.26)	**-0.68 (0.029)**	**-0.81 (0.005)**	-0.52 (0.13)
Step Width	-0.12 (0.75)	0.32 (0.37)	0.56 (0.09)	0.31 (0.38)
Step Height	0.61 (0.06)	-0.5 (0.14)	**-0.79 (0.006)**	-0.21 (0.56)
Circumduction	-0.02 (0.96)	0.5 (0.14)	0.21 (0.56)	0.42 (0.23)
Knee Flexion	0.08 (0.83)	-0.09 (0.8)	-0.26 (0.47)	-0.18 (0.63)
Fatigue Index*				
Fatigue Index	-0.13 (0.72)	0.11 (0.76)	-0.05 (0.89)	-0.12 (0.74)
Index-mean	-0.04 (0.92)	-0.22 (0.55)	-0.29 (0.42)	-0.41 (0.23)
Index-variability	0.04 (0.92)	0.15 (0.68)	-0.08 (0.84)	0.08 (0.84)

Conclusions

- We were able to calculate the FI in 29 patients with RR-MS and low disability. However, individual gait parameters exhibited better convergent validity and sensitivity to exertion than the FI in our sample.
- The validity of the FI needs to be further explored in MS patients with a wide range of walking disability, including sensitivity to change over time.

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Disclosures

The authors have no conflict of interest to report.