Research paper

Symptom variability, affect and physical activity in ambulatory persons with multiple sclerosis: Understanding patterns and time-bound relationships

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ABSTRACT

Background: Individuals with multiple sclerosis (MS) experience a clinical course that is highly variable with daily fluctuations in symptoms significantly affecting functional ability and quality of life. Yet, understanding how MS symptoms co-vary and associate with physical and psychological health is unclear.
Objective: The purpose of the study was to explore variability patterns and time-bound relationships across symptoms, affect, and physical activity in individuals with MS.
Methods: The study employed a multivariate, replicated, single-subject repeated-measures (MRSRM) design and involved four individuals with MS. Mood, fatigue, pain, balance confidence, and losses of balance were measured daily over 28 days by self-report. Physical activity was also measured daily over this same time period via accelerometry. Dynamic factor analysis (DFA) was used to determine the dimensionality and lagged relationships across the variables.
Results: Person-specific models revealed considerable time-dependent co-variation patterns as well as pattern variation across subjects. Results also offered insight into distinct variability structures at varying levels of disability.
Conclusion: Modeling person-level variability may be beneficial for addressing the heterogeneity of experiences in individuals with MS and for understanding temporal and dynamic interrelationships among perceived symptoms, affect, and health outcomes in this group.

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Multiple sclerosis (MS) is a chronic and disabling disorder of the central nervous system with a highly individualized presentation and progression. The disease manifests in a broad spectrum of associated sensory, motor, and psychological dysfunction. While MS symptoms are heterogeneous among individuals, the most commonly reported symptoms include impaired balance and mobility, fatigue, pain, and mood disturbances.[1,2] This constellation of symptoms not only interferes with daily performance[3,4] and quality of life,[5–7] it also associates with reduced participation in physical activity and other health behaviors among those with MS.[8,9]

While impairments by themselves are challenging, the variability and uncertainty of MS symptoms are equally impactful. Individuals with MS experience a clinical course that is often unpredictable with day-to-day fluctuations in symptoms profoundly affecting both physical and psychological functioning.[10,11] Short-term variability of within-subject performance has been shown in relation to cognitive processing,[12] walking distance and speed,[13] as well as postural control and gait.[14] Still, limited empirical attention has been directed toward the co-morbidity of MS symptoms and the functional consequences of symptom fluctuations across days. While one previous study found that variability in underlying impairments was generally larger than variability in performance of daily tasks,[15] how MS symptoms co-vary and associate with physical and psychological health remains unclear. Moreover, it is unclear how regular physical activity is directly and acutely impacted by fluctuating MS symptoms irrespective of its

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reported benefit on both symptom management,[16,17] and life satisfaction.[18,19] Directed assessment of variability in symptoms and their consequences may therefore prove useful when developing prescriptive guidelines effective for managing symptoms and improving health outcomes in those with the disease.

Uncovering the temporal dynamics of symptom fluctuations and their effects thus requires person-specific models that more clearly elucidate biological, psychological, and behavioral processes at the individual level. As such, the overall aim of the study was to examine how specific MS symptoms co-vary with affect and physical activity in individuals with MS by employing a single subject design[20,21] and analysis that afforded insight into the complexity and structure of systematic change for the individual.[22] Specifically, the purposes of the study were to 1) determine the magnitude of day-to-day fluctuations in pain, fatigue, balance, and mood 2) identify person-specific co-variation patterns in these symptoms and physical activity, and 3) examine co-variation patterns across subjects with various functional levels.

Methods

Design

A multivariate, replicated, single-subject repeated-measures (MRSRM) design[20,21] was employed for the study. MSRSM designs allow for sufficient repeated measurement to reveal uniqueness of intra-individual variability patterns and, when including others, insights into commonalities of factors across individuals. Dynamic factor analysis (DFA)[22,23] often accompanies such an approach as it can not only determine factors used to explain patterns of co-variation between variables but can also reveal the effect of these latent variables across time. Given that impairments and functional constraints may persistently influence physical activity and affect, a factor analysis that accounts for possible lagged relationships and serial dependence is necessary.

Subjects

Individuals with MS were recruited through advertisement by local neurologists and the Greater New England Chapter of the National Multiple Sclerosis Society. To qualify for the study, individuals had to have doctor-diagnosed MS. Given the focus on physical activity, each individual had to be able to ambulate on a daily basis with no or only intermittent use of a unilateral assistive device (Expanded Disability Status Scale (EDSS)[24] score between 1 and 5.5). They also had to report a history of balance loss within the past 3 months as falls and near falls were assessed as a self-reported measure of balance impairment. Subjects were excluded from participation if they had an unrelated medical condition that prohibited participation in physical activity or presented with a cognitive impairment that could hinder understanding of the questionnaires to be completed. All criteria were assessed via self-report. The Institutional Review Board at the principal author's institution approved the study and all subjects gave written informed consent prior to their involvement.

Four adults with a medical diagnosis of MS who met the above-mentioned criteria and were willing to commit to the extended study period volunteered and completed the study (Table 1). Given the ideographic nature of the study, no additional subjects were recruited. Subjects were not selected for achieving any specific physical activity level and all were encouraged to follow their typical daily routines and to carry out their individual MS management regiments as usual.

Table 1
Subject characteristics.

Subject	Gender	Age	Type of MS	Yrs post Dx	EDSS	Falls	LOB
1	M	36	RR	11	2.5	0	3
2	M	66	RR	10	3.0	1	42
3	F	58	RR	6	3.5	4	29
4	M	80	RR	13	5.5	1	61

RRMS = Relapse Remitting MS; Dx = Diagnosis; EDSS = Expanded Disability Status Sore; LOB = Losses of Balance.

Measures

Loss of balance

Each subject was asked to record the number of falls or near falls that occurred each day on a balance log and provide a description of each incident. A fall was defined as any event leading to an unexpected contact with a support surface (i.e., ground)[25]; a near fall was defined as any time that the person felt that he or she may fall but did not[26] or as any unexpected contact with an environmental object (e.g., wall, piece of furniture, person) that prevented a fall.

Mood

Mood state was assessed using the 30-item Profile of Mood States-Brief (POMS).[27] Subjects were asked to respond to each of the POMS items for "how they generally felt throughout that day" on a scale from 0 (Not at all) to 4 (Extremely). A Total Mood Disturbance (TMD) score was calculated by adding the total points for the five subscales of Tension, Depression, Anger, Fatigue and Confusion and then subtracting the points for the subscale of Vigor. The POMS has sound psychometric properties[28] and has been used in research involving individuals with MS.[29,30]

Fatigue

Fatigue was measured using the 21-item self-report Modified Fatigue Impact Scale (MFIS) that focuses on the ways in which MS-related fatigue affects everyday life.[31] Each item is anchored from 0 (Not at all) to 4 (Almost always) with a total score ranging from 0 to 84. The MFIS has been found valid and reliable for patients with MS.[32]

Balance confidence

The Activities-specific Balance Confidence Scale (ABC)[33] was used to assess the subject's degree of confidence (from 0% indicating no confidence to 100% indicating complete confidence) for completing 16 activities of daily living without losing balance. The ABC scale was designed specifically to detect loss of balance confidence in individuals with different functional levels and has been employed in other MS research.[34,35]

Pain

The Pain Effects Scale (PES)[31] provides an assessment of the ways in which pain and unpleasant sensations interfere with mood, ability to walk or move, sleep, work, recreation, and enjoyment of life. Each item is scored from 1 (Not at all) to 5 (To an extreme degree) with a total score ranging from 6 to 30. The PES has shown acceptable reliability and validity in the MS population.[31,36]

Physical activity

The ActiGraph bi-axis accelerometer (model GT1M, Manufacturing Technology Incorporated, Fort Walton Beach, FL) is a small electronic device that can objectively measure physical activity. The devise detects dynamic accelerations within specified ranges and frequencies with resulting physical activity data reported in "counts." Counts are the summation of the accelerations