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Validation of the Modified Fatigue Impact Scale in Parkinson's disease

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ABSTRACT

Introduction: Fatigue is a common symptom in Parkinson's disease (PD); however, a multidimensional scale that measures the impact of fatigue on functioning has yet to be validated in this population. The aim of this study was to examine the validity of the Modified Fatigue Impact Scale (MFIS), a self-report measure that assesses the effects of fatigue on physical, cognitive, and psychosocial functioning, in a sample of nondemented PD patients.
Methods: PD patients ($N = 100$) completed the MFIS, the Positive and Negative Affect Schedule (PANAS-X), and several additional measures of psychosocial, cognitive, and motor functioning. A Principal Component Analysis (PCA) and item analysis using Cronbach's alpha were conducted to determine structural validity and internal consistency of the MFIS. Correlational analyses were performed between the MFIS and the PANAS-X fatigue subscale to evaluate convergent validity and between the MFIS and measures of depression, anxiety, apathy, and disease-related symptoms to determine divergent validity.
Results: The PCA identified two viable MFIS subscales: a cognitive subscale and a combination of the original scale's physical and psychosocial subscales as one factor. Item analysis revealed high internal consistency of all 21 items and the items within the two subscales. The MFIS had strong convergent validity with the PANAS-X fatigue subscale and adequate divergent validity with measures of disease stage, motor function, and cognition.
Conclusion: Overall, this study demonstrates that the MFIS is a valid multidimensional measure that can be used to evaluate the impact of fatigue on cognitive and physical/social functioning in PD patients without dementia.

1. Introduction

Fatigue is a common symptom in Parkinson's disease (PD) with prevalence rates of 33–70% [1]. While there is no universally accepted definition of fatigue, it has been defined as a "feeling of abnormal and overwhelming tiredness and lack of energy, distinct both qualitatively and quantitatively from normal tiredness" [2]. It is generally accepted that fatigue is multidimensional and may be comprised of distinct constructs including physical and cognitive fatigue.

The most prevalent method of assessing fatigue is by self-report rating instruments. Recently, the International Movement Disorders Society (IMDS) task force on fatigue rating scales reviewed all nine fatigue-specific rating instruments that had been used in previous PD studies [3]. Only two scales, the Fatigue Severity Scale (FSS) [4] and the Multidimensional Fatigue Inventory (MFI) [5] were "recommended" for rating fatigue severity in PD. The FSS is a brief, nine-item unidimensional scale that does not specifically measure cognitive fatigue. While the MFI addresses a larger array of items, including cognitive (mental) fatigue, it does not evaluate the *impact* of fatigue on functioning. Rather, the MFI measures fatigue by sampling items that could be caused by alternative etiologies, rather than fatigue. For example, the MFI requires individuals to rate whether they can concentrate well or if their thoughts wander, difficulties that may be due to cognitive dysfunction, rather than fatigue per se. The IMDS acknowledged that their

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recommendations were limited by the lack of published studies on certain scales [3], suggesting that research on alternative measures of fatigue in PD may be warranted.

One scale that has not been used or evaluated in PD is the Modified Fatigue Impact Scale (MFIS), a 21-item self-report measure of fatigue derived from the 40-item Fatigue Impact Scale [6]. The Multiple Sclerosis Council for Clinical Practice Guidelines recommends the MFIS for use in clinical practice and research [7] and empirical studies have supported the utility of the MFIS in multiple sclerosis patients [8]. In contrast to the FSS and MFI, the MFIS is a multidimensional measure that assesses the *impact* of fatigue on physical, cognitive, and psychosocial function. In addition, the MFIS contains six additional items on each of the cognitive (mental) and physical subscales compared to the MFI, suggesting the possibility of a stronger and more thorough assessment of these factors.

The aim of this study was to evaluate the utility of the MFIS in PD by examining the factor structure of the scale, internal consistency of the scale items, as well as convergent and divergent validity of the MFIS in a nondemented PD sample.

2. Methods

2.1. Participants

Participants were one hundred individuals diagnosed with PD by a board-certified neurologist specializing in Movement Disorders based on the UK Brain Bank criteria [9]. PD patients were recruited from the Movement Disorders Clinics at the University of California, San Diego (UCSD) and the VA San Diego. Each patient was determined to be nondemented based on a clinical assessment using the Diagnostic and Statistical Manual of Mental Disorders-IV criteria [10] and the criteria set forth by Emre et al. [11] as well as a cutoff score of ≥124 [12] on the Mattis Dementia Rating Scale (MDRS) [13]. Medication information was gathered from all but one patient. Of those 99 participants with known medication, all but eight (8%) were on at least one medication for their PD symptoms, while the majority of participants were on a combination of two or more medications. Participants were tested on their normal dosages of medication. Table 1 provides the levodopa equivalent dosage along with other disease characteristics. Informed consent was obtained from all participants and this study was approved by the local ethics committee.

2.2. Materials and procedure

All patients were administered the MFIS as part of a comprehensive neuropsychological evaluation. The MFIS measures the impact of fatigue on functioning by having participants rate 21 items on a scale from 0 (never) to 4 (almost always). Scores range from 0 to 84, with higher scores indicating greater impact of fatigue. The items can be aggregated into a total score (21 items) as well as three subscales: physical (9 items), cognitive (10 items) and psychosocial (2 items) [7].

To evaluate convergent validity, the MFIS total score was compared to the fatigue subscale of the Positive and Negative Affect Schedule (PANAS-X) [14]. The PANAS-X fatigue subscale consists of 4 fatigue-related words ("tired", "sluggish", "sleepy", and "drowsy") that participants rate as experiencing on a scale from 1 (very slightly or not at all) to 5 (extremely) at the present moment.

To evaluate divergent validity, the MFIS total score was compared to several measures of psychological functioning: the Hamilton Depression Rating Scale (HAM-D) [15], the Geriatric Depression Scale (GDS) [16], the State-Trait Anxiety Inventory (STAI) [17], and the Apathy Scale (AS) [18]. Divergent validity was also measured by examining the relationship between the MFIS total score and disease-related symptoms, including disease stage and motor function as well as overall cognition. Motor symptoms were evaluated with the Movement Disorder Society-sponsored revision of Part III of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [19] and the modified Hoehn and Yahr scale was used to stage the disease [20]. Overall cognitive functioning was measured by the MDRS [13]. Levodopa equivalents were calculated using the criteria of Hobson et al. [21]. Please see Table 1 for these variables.

Table 1
Demographic and clinical characteristics for sample ($N = 100$).

Variable	Mean (SD)
Age (years)	68.14 (7.3)
Gender (total number of Males:Females)	66:34
Education (years)	16.5 (2.6)
Duration of disease (months)	67.5 (62.5)
MDRS total score	138.2 (4.3)
UPDRS-part III score	24.5 (12.1)
Modified Hoehn & Yahr stage[a]	2.0; 0.0–5.0
Stage 0	1.0%
Stage 1	15.0%
Stage 1.5	2.0%
Stage 2	56.0%
Stage 2.5	6.0%
Stage 3	15.0%
Stage 4	3.0%
Stage 5	2.0%
Levodopa equivalent (mg/day)[b]	562.2 (601.5)
MFIS total score	31.7 (16.6)

Note: MDRS = Mattis Dementia Rating Scale; UPDRS = Unified Parkinson's Disease Rating Scale; MFIS = Modified Fatigue Impact Scale.

[a] Median and Range presented for modified Hoehn and Yahr stage followed by percentage of patients at each stage.

[b] Levodopa equivalent (mg/day) is based on the criteria of Hobson et al. (2002), $N = 99$.

2.3. Statistical analyses

Based on the information from the published scale [7] and the previous work of Kos et al. [8], we predicted a similar three factor structure of the MFIS representing the impact of fatigue on physical, cognitive, and psychosocial functioning. We further predicted high internal consistency of the items, and adequate convergent and divergent validity with a measure of fatigue (PANAS-X fatigue subscale) and other measures of psychological functioning and disease-related symptoms, respectively.

To evaluate the underlying structure of the MFIS, individual scores were subjected to a Principal Component Analysis (PCA) with varimax rotation. Cronbach's alpha was used to examine the internal consistency of the 21 total items and items within the subscales identified in the PCA. To examine convergent and divergent validity, Spearman rank correlations were used to correlate the MFIS with the PANSAS-X fatigue subscale, HAM-D, GDS, STAI, and the AS, as well as with demographic information and clinical characteristics. Significant correlation coefficients that were greater than 0.5 were interpreted as strong, coefficients of 0.3–0.5 were interpreted as moderate, and coefficients less than 0.3 were interpreted as weak [22]. Gender differences on the MFIS were examined using an independent samples *t*-test. All analyses were based on a sample size of 100, unless otherwise indicated.

3. Results

There were no significant correlations between the MFIS total score and age ($r_s = -0.153$, $p = 0.13$), education ($r_s = -126$, $p = .21$), or disease duration ($r_s = 0.040$, $p = .69$). Males and females did not significantly differ on their total MFIS scores (t (98) $= -0.585$, $p = .56$).

The PCA revealed two factors that had eigenvalues > 1.0. These factors were rotated using the varimax rotation procedure that yielded two interpretable factors, which we term "cognitive" and "physical/social" based on the existing or combination of the original subscale names. As shown in Table 2, all items clearly loaded onto one factor versus the other, with the exception of the first item ("alertness"), which had a loading of 0.592 on the cognitive factor and 0.561 on the physical/social factor; such a small difference between these loadings does not allow this item to be associated uniquely to one of the subscales.

Item analysis using Cronbach's alpha suggested high internal consistency of all 21 items and the items within the two PCA-identified subscales, with an overall Cronbach's alpha of 0.96 for all 21 items, 0.95 for the 10 items (including "alertness") of the cognitive subscale, and 0.95 for the 11 items of the physical/social subscale. None of the items had a score that was higher than the overall alpha (all alphas = 0.96). As the first item "alertness" was not uniquely assigned to either one of the subscales, we conducted an item analysis without this item; the deletion of this item did not affect the overall alpha (0.96) or the cognitive subscale alpha (0.95). Means, standard deviations, and ranges for each of the MFIS items are presented in Table 3.

Convergent validity, as measured by the correlation between the MFIS total score and the Positive and Negative Affect Schedule

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Table 2
Principal-component factor analysis with varimax rotation.

Item	Description	Factor	
		Cognitive	Physical/social
1	Alertness	0.592	0.561
2	Attention	**0.778**	0.365
3	Clear thinking	**0.814**	0.304
4	Coordination	0.380	**0.617**
5	Forgetfulness	**0.656**	0.304
6	Pace physical activities	0.289	**0.755**
7	Motivation-physical	0.297	**0.781**
8	Motivation-social	0.383	**0.624**
9	Outside activities	0.275	**0.698**
10	Maintain physical effort	0.385	**0.721**
11	Decision-making	**0.740**	0.359
12	Motivation-mental	**0.732**	0.315
13	Muscle weakness	0.278	**0.696**
14	Physically uncomfortable	0.316	**0.604**
15	Mental task completion	**0.761**	0.359
16	Thought organization	**0.771**	0.275
17	Physical task completion	0.437	**0.764**
18	Slow thinking	**0.692**	0.444
19	Concentration	**0.771**	0.331
20	Physical activities	0.304	**0.784**
21	Need for rest	0.311	**0.764**

Note. Item description does not reflect the MFIS item text in its entirety; bold-faced type indicates highest factor loading for each variable.

(PANAS-X) fatigue subscale, was strong, with $r_s = 0.585$, $p < .001$; $N = 93$. Correlations between the MFIS and additional measures of psychological functioning were moderate to strong: State-Trait Anxiety Inventory (STAI)-State ($r_s = 0.518$, $p < .001$), Hamilton Depression Rating Scale (HAM-D; $r_s = 0.497$, $p < .001$), Geriatric Depression Scale (GDS; $r_s = 0.599$, $p < .001$), and Apathy Scale (AS; $r_s = 0.564$, $p < .001$). Correlations between the MFIS and UPDRS-Part III score ($r_s = 0.155$, $p = .12$), Hoehn & Yahr stage ($r_s = 0.176$, $p = .08$), and Mattis Dementia Rating Scale (MDRS) score ($r_s = -0.124$, $p = .22$) were non-significant. Higher levels of fatigue (MFIS total score) were significantly associated with higher levels of daily levodopa equivalent usage ($r_s = 0.228$, $p = .024$; $N = 99$).

4. Discussion

The MFIS appears to be a promising measure for evaluating multidimensional fatigue in nondemented individuals with Parkinson's disease. Our results confirmed that all 21 items that comprise the MFIS were homogenous. Our findings also revealed that the 9 items that comprised the original physical subscale loaded onto one factor and the items that comprised the original cognitive subscale loaded onto another factor, with the exception of "alertness", in which the difference was too small to confidently assign it to the cognitive over the physical/social subscale. The ambiguity of the "alertness" item was also found in Kos et al.'s [8] validation study of multiple sclerosis patients.

In contrast to the original scale and the findings of the Kos et al. study [8], our analysis did not reveal a third factor; and therefore, did not confirm a unique "psychosocial" subscale in this sample. Rather, our results demonstrated that the two items that comprised the original psychosocial scale loaded solidly with the physical items onto one factor. While Kos and colleagues [8] found a third "psychosocial" factor, it was statistically weak and the authors concluded that there was limited value of this subscale. Thus, two valid subscales of the MFIS, the "cognitive" subscale, with the 9 of the 10 original items, and the newly named "physical/social" subscale, with 11 total items, were confirmed in this PD sample. Including or excluding the first item, "alertness", does not appear to significantly alter the integrity of the overall scale or the cognitive subscale.

Convergent validity of the MFIS was established with the fatigue subscale of the PANAS-X, suggesting a strong level of association. Divergent validity varied when the MFIS was correlated with other measures of psychological functioning (depression, anxiety, and apathy), while adequate divergent validity was established between the MFIS and disease-related variables (i.e., motor symptoms, disease stage) and overall cognition. The MFIS did not correlate with age, education, disease duration, motor symptoms, disease severity or overall cognition, nor differ between males and females. However, there was a significant, albeit weak, association between levodopa levels and fatigue, indicating that future research exploring the relationship between medication and fatigue may be warranted.

It is important to note that this PD cohort was fairly early in their disease course, with an average time since diagnosis of less than 6 years, suggesting that generalizability of these results to more advanced patients may be limited. Evaluating the MFIS within an advanced, less educated population as well as within a treatment study is recommended to expand the validity of this scale. Additionally, we were unable to calculate sensitivity and specificity or establish a cut-off score for the MFIS because of the absence of a gold standard or control group; future studies may be informative in this regard.

To our knowledge, this is the first study to evaluate the validity of the MFIS in PD patients. In sum, our analyses determined that the MFIS has strong convergent validity with another measure of fatigue and adequate divergent validity with measures of disease-related symptoms and cognition. Our analyses also revealed two viable subscales: cognitive and physical/social fatigue. We did not confirm an independent psychosocial scale; rather these two items loaded onto the physical/social scale. Overall, these analyses demonstrate the utility of the MFIS in evaluating cognitive and physical/social aspects of fatigue in PD patients without dementia.

Table 3
Means, standard deviations (SD) and ranges for MFIS items.

Item	Description	Mean (SD)	Range
1	Alertness	1.58 (0.92)	0–4
2	Attention	1.55 (1.0)	0–4
3	Clear thinking	1.28 (0.93)	0–4
4	Coordination	1.54 (1.0)	0–4
5	Forgetfulness	1.54 (0.95)	0–4
6	Pace physical activities	1.84 (1.1)	0–4
7	Motivation-physical	1.66 (1.1)	0–4
8	Motivation-social	1.43 (1.1)	0–4
9	Outside activities	1.39 (1.1)	0–4
10	Maintain physical effort	1.71 (1.1)	0–4
11	Decision-making	1.15 (0.97)	0–4
12	Motivation-mental	1.07 (1.0)	0–4
13	Muscle weakness	1.87 (1.1)	0–4
14	Physically uncomfortable	1.57 (1.0)	0–4
15	Mental task completion	1.12 (0.98)	0–4
16	Thought organization	1.25 (0.98)	0–4
17	Physical task completion	1.57 (1.0)	0–4
18	Slow thinking	1.59 (1.1)	0–4
19	Concentration	1.49 (1.0)	0–4
20	Physical activities	1.69 (1.1)	0–4
21	Need for rest	1.88 (1.1)	0–4

Note: Item description does not reflect the MFIS item text in its entirety.

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