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Short communication

Minimal clinically important difference of the Modified Fatigue Impact Scale in Parkinson's disease

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ABSTRACT

Objective: Fatigue is a common and debilitating symptom of Parkinson's disease (PD) with no evidence-based treatments. While several fatigue scales are partially validated in PD the minimal clinically important difference (MCID) is unknown for any scale but is an important psychometric value to design and interpret therapeutic trials. We thus sought to determine the MCID for the Modified Fatigue Impact Scale (MFIS).
Methods: This is a secondary data analysis from 94 PD participants in an acupuncture trial for PD fatigue. Standard psychometric approaches were used to establish validity and an anchor-based approach was used to determine the MCID.
Results: The MFIS demonstrated good concurrent validity with other outcome measures and high internal consistency. MCIDs values were found to be 13.8, 6.8 and 6.2 for the MFIS total, MFIS cognitive, and MFIS physical subscores respectively.
Conclusions: The MFIS is a valid multidimensional measure of fatigue in PD with demonstrable MCID.

1. Introduction

Fatigue affects approximately half of all Parkinson's disease (PD) patients and a third report fatigue as their single most disabling symptom [1]. A recent meta-analysis found insufficient evidence to support the use of any available pharmacologic or non-pharmacologic therapies [2]. Future work to develop and test therapeutic interventions for this symptom are needed. A Movement Disorders Society (MDS) Task Force reviewed and gave recommendations on seven fatigue outcome measures for PD and Schiehser et al. subsequently provided validation of the Modified Fatigue Impact Scale (MFIS), a scale which was not included in the MDS manuscript [3,4]. The minimal clinical important difference (MCID) describes the minimal clinically important difference or change on a scale and is useful for study design and interpretation. While MCID data exists for the MFIS in multiple sclerosis (MS) and other clinical populations there is currently no MCID data for any fatigue scale in PD. Our objective was thus to determine the MCID of the MFIS in PD and provide further validation of this scale through secondary analysis of a published randomized controlled trial (RCT) of acupuncture for fatigue in PD [5].

2. Methods

This is a secondary analysis of a previously published RCT of acupuncture for PD fatigue [5].

2.1. Participants

Participants were recruited from the University of Colorado Hospital and Denver Health Medical Center Movement Disorders Clinics and community referrals. Inclusion criteria included: United Kingdom Brain Bank criteria for probable PD; age 40–99 years; fluent in English; stable medication use for 30 days; and self-reported moderate or severe fatigue using the Movement Disorder Society Unified Parkinson Disease Rating Scale fatigue item [6]. Patients with deep brain stimulation (DBS) or on medications for fatigue (e.g. stimulants) were included provided they had ongoing fatigue. Exclusion criteria included dementia or a score below 24 on

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the Montreal Cognitive Assessment; presence of another medical condition expected to produce fatigue; active depression or Hospital Anxiety and Depression Scale (HADS) depression subscale score greater than 10; presence of an untreated sleep disorder; or exposure to acupuncture within the past six months. This study was approved by the Colorado Multiple Institutional Review Board and written informed consent was obtained from all participants. This trial was registered with ClinicalTrials.gov (NCT01360229).

2.2. Randomization and intervention

Eligible participants were randomized in a 1:1 fashion without stratification to real or sham acupuncture using permuted blocks. Acupuncturists were provided a code linking group assignment to study identification number. All other study team members were blinded.

Treatment consisted of twice-weekly sessions at least one day apart for six weeks using a fixed-point prescription based on TCM theory and prior papers in PD and fatigued populations [5]. Participants lay supine on the acupuncture table and were blindfolded. For real treatment, acupuncture needles were inserted to a depth of 0.5–1 cm twisted three times to the right and removed after 30 min in the same order as they were inserted.

We utilized a previously validated sham procedure in which a sharp round toothpick in a guide tube was placed on the sham point and tapped on the skin. Toothpicks were “inserted” in the same order as the real protocol using non-acupuncture points, located 0.5 inches lateral to the real acupuncture point, or to the right for midline points. Acupuncturists “removed” toothpicks by slowly pressing a toothpick into the sham point and quickly removing it in the same order they were inserted. Data from the RCT demonstrate that participants were adequately blinded [5].

2.3. Primary outcome and anchor

Our primary outcome was change from baseline on the Modified Fatigue Impact Scale (MFIS) at six weeks [7]. The MFIS is a 21-item self-report scale that rates the impact of fatigue on various functions and includes a total score (primary outcome) as well as cognitive, physical, and psychosocial subscales. The MFIS has been validated for use in PD and may be more responsive to change than other commonly used fatigue scales. Each item is rated based on frequency of symptoms from 0 (“Never”) to 4 (“Almost Always”) with a range of 0–84 for the total score, 0–36 for the physical subscore, and 0–40 for the cognitive subscore. In a study ($n = 415$) to investigate the construct validity of the MFIS using a Rasch analysis, Mills et al. concluded that the physical and cognitive subscales should be modified by eliminating questions 4, 14, and 17 from the physical scale and questions 1, 2, 3, 5, and 11 from the cognitive scale. Mills et al. recommended against using the MFIS total due to poor psychometric properties.[19] Therefore, we chose to include five MFIS scores for the purposes of this secondary analysis: 1) MFIS total, 2) MFIS cognitive subscale, 3) MFIS physical subscale, 4) Mills modified MFIS cognitive subscale, and 5) Mills modified MFIS physical subscale. The anchor used in the analysis was obtained from the Clinical Global Impression of Improvement scale which participants completed at the six-week visit; overall improvement was rated on a 7-point scale ranging from “very much improved” to “very much worse [8].”

2.4. Secondary outcomes to assess concurrent validity

Mood was assessed using the Hospital Anxiety and Depression Scale (HADS) [e-1]. Sleep quality and excessive daytime somnolence were assessed using the Parkinson's Disease Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS) [e-2, e-3]. Apathy was assessed using the Apathy Scale (AS) [e-4]. QOL was assessed using the Parkinson Disease Questionnaire 39 (PDQ-39) [e-5]. We also examined fatigue items from the PDQ-39, the single fatigue item from the MDS UPDRS, and a standalone question of “How much of a problem is fatigue in your life right now?” answered on a scale from 1-Not at all to 6-A Great Deal.

2.5. Statistical procedures

Summary statistics (e.g., means, frequencies) were computed to describe the study sample. The MFIS total, cognitive subscale, and physical subscales were calculated for each study participant [7,9]. We did not calculate the psychosocial subscale as prior analyses suggest this is not an independent factor [4]. Concurrent validity was examined by correlating the MFIS measures with the secondary outcome measures described above using Spearman correlation. Internal consistency was established by calculating Cronbach's alpha. While there are different approaches to establishing a minimal clinically important difference (MCID) [10], Revicki et al. recommend that the MCID “be based on appropriate patient-based and clinical anchors that are correlated with a correlation coefficient that is greater or equal to 0.30 with the patient reported outcomes [11].” Anchor-based approaches use an external indicator, either clinical or patient-based, to assign subjects into groups reflecting no change, small positive changes, large positive changes, small negative changes, or large negative changes in clinical or health status. The patient-based anchors available for the Fatigue Acupuncture Study were: “very much worse,” “much worse,” “minimally worse,” “no change,” “minimally improved,” “much improved,” and “very much improved.” The change scores were calculated by subtracting each patient's six-week score from the baseline score and were then used to determine the MCID using the anchor-based mean change score technique. Mean change scores with corresponding 95% confidence intervals were then calculated in each of the anchor groups. The MCID was defined as the mean of the absolute value of change score in the group of participants ($n = 44$) who reported that they were “minimally worse” or “minimally improved.” Spearman correlation was used to assess relationship between each of the MFIS difference measures and the patient anchor score. Linear regression was applied to relate the difference in MFIS total to patient anchor score. All seven values of anchor score were used for both the regression and correlational analyses. All analyses were performed using SAS, version 9.4 (Cary, N.C.) specifying a level of significance of 0.05.

3. Results

Of the 94 individuals participating in the Acupuncture study, 63% ($n = 59$) were men, with mean age of 65.4 years, mean disease duration of 4.4 years, and high fatigue with a mean total MFIS of 49.4 (see Appendix for Clinical and Demographic Information).

Table 1 reports the results of correlational analyses to establish the concurrent validity for the MFIS total scale, MFIS cognitive subscale, and MFIS physical subscale. The MFIS total was significantly correlated with all measures selected for concurrent validity. The MFIS cognitive subscale showed similar patterns and was significantly correlated with all measures except the MDS fatigue scale item. Similarly, the MFIS physical subscale was significantly correlated with all measures except the HADS anxiety and ESS.

All of the MFIS measures showed good internal consistency. The Cronbach's alphas were: 0.91 for the MFIS total scale, 0.90 for the MFIS cognitive subscale, and 0.84 for the MFIS physical subscale.

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