

Validity and Reliability of the Persian Version of Fatigue Scale for Motor and Cognitive Functions (FSMC) in Patients with Multiple Sclerosis (MS)

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ABSTRACT

Background: Fatigue is one of the most common symptoms in patients with multiple sclerosis (MS), and the cognitive aspect of fatigue is not fully evaluated in these patients. After reviewing existing questionnaires and noting that the fatigue scale for motor and cognitive functions (FSMC) questionnaire has not been validated in Persian, we designed this study to assess the validity and reliability of the Persian version of the FSMC questionnaire in patients with MS.

Methods: One hundred and forty patients and 63 healthy participants who met the inclusion criteria for healthy controls (age-matched with cases, no history of neurological or psychiatric disorders and not taking anti-depressant medications in the past three months) were enrolled in the present study. Both groups completed the FSMC questionnaire, while the patient group was asked to fill out the valid and reliable Persian version of the modified fatigue impact scale (MFIS), fatigue severity scale (FSS) and Beck depression inventory (BDI). Internal consistencies, content, convergent and discriminant validities were evaluated. We considered the MFIS score as the comparator with a cut-off value of 33 to dichotomize fatigued and non-fatigued individuals, then we plotted the ROC curves of total FSMC, cognitive and motor sub-scales to estimate the best cut-off value of FSMC.

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Results: The Cronbach's alpha for the total FSMC was calculated as 0.95, for the FSMC cognitive subscale as 0.92, and the motor subscale as 0.94. The ICC for the motor subscale was 0.962, and for the cognitive subscale was 0.963. Content validity index (CVI) and content validity ratio (CVR) for all questions of FSMC questionnaire were 100% (content validity). There were significant positive correlations between FSMC and its subscales with MFIS, FSS, BDI and expanded disability status scale (EDSS) (convergent validity). The FSMC score and its subscales were significantly different between patients and healthy individuals (discriminant validity).

Conclusion: The Persian version of FSMC provides a valid and reliable tool for evaluating motor and cognitive aspects of MS fatigue, which could be applied in clinical practice and research purposes.

Keywords: fatigue, validity, reliability.

PRACTICE POINT

As fatigue is a common symptom in patients with multiple sclerosis (MS), the Persian version of the fatigue scale for motor and cognitive functions (FSMC) could be applied for MS-related fatigue evaluation by clinicians in Iran.

INTRODUCTION

Fatigue is one of the most common and disabling symptoms of patients with multiple sclerosis (MS) (1, 2). Between 65% and 90% of affected patients experience fatigue and report fatigue as a symptom interfering with their daily activities and quality of life (3). The exact cause of fatigue in MS is not determined (4), while the brain and immune system changes, as well as comorbidities, such as depression, insomnia and pain may contribute to the fatigue experience in people with MS (5).

Fatigue is not a unidimensional symptom and it has both physical and mental aspects (6). In clinical practice, assessment of fatigue is based on patient reports or evaluations via the application of questionnaires (7). Up to now, there are different questionnaires developed to assess fatigue in MS and other conditions and each one has its own advantages and disadvantages.

Penner *et al* developed the fatigue scale for motor and cognitive functions (FSMC) for evaluating fatigue including 20 questions (10 for the motor dimension of fatigue and 10 for the cognitive aspect of fatigue). Each question is scored based on a Likert scale (4). It is a self-report instrument that could be easily applied in different settings and can evaluate mental and physical fatigue. It is not too long or too short and evaluates all aspects of physical and mental fatigue. Other question-

naires may have less questions for each domain. For instance, MFIS includes two questions evaluating psychological-related fatigue. According to wider range of values, FSMC could provide better discrimination within motor or cognitive domains.

In a recent systematic review, Cohen *et al* evaluated measurement characteristics of subjective fatigue and found that the modified fatigue impact scale (MFIS) was a comprehensive measurement of fatigue and fatigue severity scale (FSS) was an excellent tool to screen subjective fatigue (8).

Fatigue, as a key symptom in patients with MS, is typically assessed through self-reporting by the patients using validated interviews and questionnaires. This is because the experience of fatigue is largely based on the individual's perspective and cannot be easily measured by conventional metrics. Therefore, having a validated questionnaire that has been culturally and linguistically adapted for the patients is of great importance for assessing the level of fatigue in MS patients. In this context, after reviewing existing questionnaires and noting that the FSMC questionnaire has not been validated in Persian, we designed this study to assess the validity and reliability of the Persian version of the FSMC questionnaire. □

METHODS

This cross-sectional study was done in the MS Research Center of Sina Hospital (affiliated hospital of Tehran University of Medical Sciences (TUMS)) between June–December 2022. All participants signed a written informed consent form. The study was approved by the ethics committee of the TUMS. This study was conducted according to the Declaration Helsinki and all patient in-

formation was kept confidential during the study and after its completion.

Participants

Inclusion criteria for participants with MS comprised MS diagnosis based on the latest McDonald criteria (9), age more than 18 years, no definite relapses during the past three months, no corticosteroids treatment within the past four weeks, no substance abuse and no other neurological/psychiatric disorders.

Inclusion criteria for healthy controls were age-matched with cases, no history of neurological or psychiatric disorders and not taking antidepressant medications in the past three months.

Instruments

Patients were asked to fill out the valid and reliable Persian version of MFIS, FSS (10), Beck depression inventory (BDI) (11) and FSMC.

Fatigue scale for motor and cognitive functions has 20 questions, including 10 questions evaluating motor-related fatigue and 10 questions evaluating cognitive-related fatigue. Each question can be rated between 1 (Does not apply at all) and 5 (Applies completely). The total score ranges between 20 and 100, with higher scores indicating more severe fatigue.

Based on Penner *et al*'s study, a cognitive subscale score ≥ 22 is considered mild fatigue, ≥ 28 moderate fatigue and ≥ 34 is determined as severe cognitive fatigue. For the motor subscale, scores equal to or greater than ≥ 22 are considered as mild motor-related fatigue, ≥ 27 moderate motor-related fatigue and ≥ 32 severe motor-related fatigue (4).

Modified fatigue impact scale has 21 questions, including three subscales: physical (nine questions), cognitive (10 questions) and psychological (two questions). Each question could be scored between 0 and 4, and a total score is the sum of all scores. Higher scores indicate more severe fatigue (2).

Fatigue severity scale is a nine-item questionnaire that is designed to assess the severity of fatigue. Each question is graded between 1 and 7 (1: strong disagreement; 7: strong agreement). The sum of all scores provides the final score and higher scores indicate more severe fatigue (12). Fatigue severity scale scores are commonly reported both as a total score (/63) or a mean score (/7).

Beck depression inventory consists of 21 questions, each rating between 0 and 3. The sum of all questions is the total score of the questionnaire. Scores between 10 and 18 indicate mild to moderate depression, those between 19 and 29 show moderate to severe depression and scores higher than 30 correspond to severe depression (11). As depression is highly correlated with fatigue in MS, we applied BDI for validity evaluation.

Using forward-backward translation method, the English version of FSMC was translated into Persian by a bilingual researcher. Afterwards, another bilingual researcher translated the Persian version into English.

A neurologist who is an expert in the MS-fatigue research compared the two versions.

Validity

Content validity – Five neurologists who had a subspecialty of MS assessed the content validity of the questionnaire to determine if all questions were relevant and necessary. The content validity ratio (CVR) and content validity index (CVI) were recorded for each question; CVR reflects how many specialists within a section rate an item as essential and CVI shows experts' ratings of item relevance.

Convergent validity – To evaluate convergent validity, we calculated the correlation coefficient between the Persian versions of FSMC, FSS, MFIS, BDI and EDSS scores.

Discriminant validity – Discriminant validity was done by comparing the scores of healthy participants and patients with MS.

Reliability

Twenty patients were asked to complete the FSMC questionnaire two weeks after the first assessment to assess the reliability of the questionnaire.

The intra-class correlation coefficient (ICC) was used for test-retest reliability and the ICC coefficient > 0.70 was considered excellent. Cronbach's alpha was applied to assess the internal consistency. Cronbach's alpha coefficient ≥ 0.70 reflected an excellent internal consistency.

Statistical analysis

We performed all the statistical analyses using SPSS version 23 (SPSS, Inc., Chicago, IL, USA). Data is presented as mean $\pm$ standard deviation

(SD) for continuous variables and frequencies for categorical variables; for EDSS, we reported median and interquartile range (IQR). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test.

We categorized patients based on EDSS into three groups: 0-3 (mild disability); 3.5-6 (moderate disability); and ≥ 6.5 (severe disability) to compare participants based on disability level.

Internal consistency was evaluated using Cronbach's alpha coefficient, with values ≥ 0.70 being considered acceptable. Test-retest reliability was assessed by calculating the intraclass correlation coefficient (ICC), with values > 0.70 indicating acceptable reliability. Convergent validity was examined using Pearson correlation coefficients between FSMC scores and established measures of fatigue (MFIS, FSS), depression (BDI) and disability (EDSS).

Discriminant validity was assessed by comparing FSMC scores between MS patients and healthy controls using independent samples t-test. Comparisons across EDSS categories were performed using one-way ANOVA, with post-hoc

pairwise comparisons conducted using Tukey's HSD test to identify significant group differences. Also, to compare fatigue scores between MS types and sex groups, we applied independent sample t-test.

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off values for FSMC total and subscales scores in differentiating fatigued and non-fatigued individuals as it was done in the original work (4). The MFIS cut-off score of 33 was used as a reference based on prior literature, where this threshold effectively distinguishes clinically significant fatigue in MS patients (13). The optimal FSMC cut-off values were determined by maximizing the Youden index and a p-value less than 0.05 was considered significant. $\square$

RESULTS

We administered the questionnaires to 160 patients with MS and 80 healthy controls. One hundred and forty patients and 63 healthy participants completed the question-

Variables	Case group	Control group	P value
Age (mean $\pm$ SD)	38.3 $\pm$ 7.5	36.4 $\pm$ 9.4	0.03
Sex			0.1
Female	118 (84.3%)	48 (76.1%)	
Male	22 (15.7%)	15 (23.9%)	
Education			0.01
≤ 12 years	63 (45%)	29 (46%)	
>12 years	77 (55%)	34 (54%)	
Duration of the disease in years (mean $\pm$ SD)	9 $\pm$ 5.7		
EDSS [median (IQR)]	2.5 (2.1)		
Marital status			
Single	39 (27.9%)		
Married	90 (64.3%)		
Divorced	11 (7.9%)		
Type of MS			
Relapsing remitting	107 (76.4%)		
Progressive	33 (23.6%)		
FSMC			
Motor	29.3 $\pm$ 10.7	15.4 $\pm$ 5.9*	
Cognitive	32 $\pm$ 10.7	14.5 $\pm$ 6.7*	
Total	61.3 $\pm$ 20.6	29.9 $\pm$ 11.1*	
MFIS			
Physical	13.7 $\pm$ 9.2		
Psychological	2.8 $\pm$ 2.6		
Cognition	13 $\pm$ 9.9		
Total	28.6 $\pm$ 17		
BDI	17.4 $\pm$ 11.9		
FSS	37.1 $\pm$ 16.7		

*Comparing patients and healthy individuals (p-value is less than 0.05).

SD=standard deviation; EDSS=expanded disability status scale; IQR=interquartile range;

MS=multiple sclerosis; FSMC=fatigue scale for motor and cognitive functions;

BDI=Beck depression inventory; FSS= fatigue severity scale.

TABLE 1. Demographics, disease characteristics and questionnaire scores

	MFIS _{Ph}	MFIS _C	MFIS _P	Total MFIS	BDI	FSS	EDSS
Motor	0.5*	0.68*	0.36*	0.83*	0.35*	0.75*	0.3*
Cognitive	0.83*	0.53*	0.47*	0.84*	0.23*	0.72*	0.23*
Total FSMC	0.59*	0.63*	0.43*	0.86*	0.3*	0.7*	0.22*

*P-value<0.05. MFIS=modified fatigue impact scale;
MFIS_{Ph}=physical subscale of MFIS;
FSMC=fatigue scale for motor and cognitive functions;
MFIS_C=cognitive subscale of MFIS; MFIS_P=psychosocial subscale of MFIS;
FSMC=fatigue scale for motor and cognitive functions; FSS=fatigue severity scale;
EDSS=expanded disability status scale.

TABLE 2. Correlation coefficients between FSMC and its two subscales with other variables

Variables	Motor aspect of FSMC	Cognitive aspect of FSMC	Total FSMC
Sex			
Female	29±10.9	31.4±10.7	60±20.7
Male	31.4±9.7	34.7±11	66.1±19.6
P-value	0.3	0.1	0.2
EDSS			
0-3 (N=103)	29.2±10.5	30.5±10.9	59.7±20.8
3.5-6 (N=33)	29.6±11.4	35.6±9.5	65.3±19.7
≥6.5 (N=4)	32±13.2	38±10.4	70±21.2
P-value	0.8	0.03	0.2
MS subtype			
RR (N=107)	29±10.6	30.6±10.6	59.6±20.7
Progressive MS (N=33)	30.7±11.2	37.3±9.5	68±19.2
P-value	0.4	0.003	0.05

FSMC=fatigue scale for motor and cognitive functions; MS=multiple sclerosis;
EDSS=expanded disability status scale; RR=relapsing-remitting.

TABLE 3. Association of FSMC and its subscales with patients' sex, disability level and MS subtype

TABLE 4. Area under the curve, cut-off values, sensitivity and specificity of fatigue scale for motor and cognitive functions and its subscales

	Total FSMC	Motor subscale	Cognitive subscale
AUC	0.83	0.82	0.8
Cut off value	54	22	22
Sensitivity	93%	95%	96%
Specificity	60%	47%	48%

AUC=area under the curve;
FSMC=fatigue scale for motor and cognitive functions.

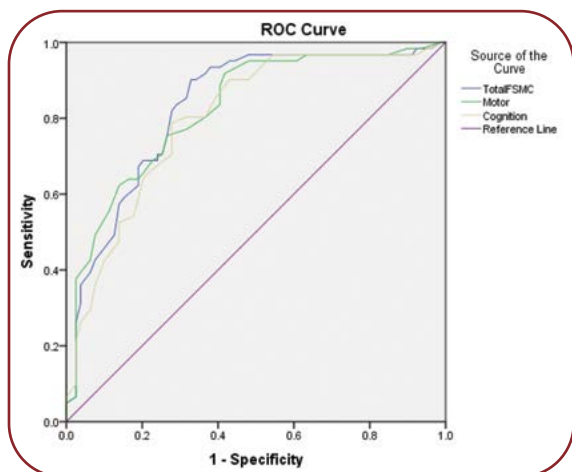


FIGURE 1. Receiver operating characteristic analysis for FSMC over MFIS

Reliability

The Cronbach's alpha for total FSMC was calculated as 0.95, for FSMC cognition subscale as 0.92, and for motor subscale as 0.94.

The ICC for the motor subscale was 0.962, and for the cognition subscale was 0.963.

The area under the curve (AUC) was higher for total FSMC (Table 4). □

DISCUSSION

The current study aimed to determine the validity and reliability of the Persian version of the FSMC questionnaire.

We showed that the ICC of each subscale and the total score of the questionnaire was high, indicating that the test-retest reliability of the Persian version of FSMC questionnaire was excellent. The high Cronbach's alpha of two subscales, and the entire questionnaire indicated that the internal consistency of FSMC, and its two subscales are excellent (14).

We found that total FSMC and its subscales had significant positive correlations with MFIS, and its three sub-scales, as well as FSS, EDSS, and BDI. These findings confirm the results reported by Penner *et al* and Oervik *et al* (4, 7), which showed the high convergent validity of the FSMC questionnaire. In the studies conducted by Penner *et al* and Oervik *et al*, the correlation coefficient between total FSMC and MFIS was 0.82, and 0.85, respectively (4, 7).

Interestingly, we found that patients with a higher physical disability had higher cognitive fatigue scores. The results also demonstrate that patients with progressive types of the disease had significantly higher cognitive subscale score, as well as total fatigue scores, but the motor subscale score was not different. This may indicate that patients with progressive forms of MS and higher physical disability may suffer more from cognitive fatigue.

There are inconsistencies in the results of studies regarding the relationship between physical disability and fatigue experience. Some researchers found a positive correlation, while others did not show an association (2, 15-17).

The mean score of the FSMC questionnaire and cognitive and motor subscales were significantly different between patients with MS and healthy participants confirming the discriminant validity of the questionnaire.

Depression is the most common mood disorder in people living with MS, which affects more than half of MS patients (3). We showed a significant positive correlation between FSMC score, and its subscales with BDI score, which confirms previous findings (4, 7). It has been shown that fatigue and depression are strongly correlated and depression is an independent predictor of fatigue in patients suffering from MS (2).

In this study, the AUC for total FSMC was higher than its two subscales and the sensitivity for provided cut-off values was higher. In con-

trast, specificity values were lower than Penner *et al*'s study (4).

Fatigue is a disabling symptom in patients with MS. A valid and reliable tool for measuring MS fatigue and differentiating cognitive from physical aspects of fatigue is essential for developing therapeutic interventions. It is shown that mental and physical parts of fatigue are not necessarily correlated, and treatment goals for each component could be different.

Based on possible cultural and linguistic differences, every single questionnaire should be translated and validated for the targeted population.

Our study has several strengths. Firstly, we administered the questionnaire to both MS patients and healthy controls. Secondly, we utilized several validated questionnaires for assessing the convergent validity assessment, including FSS, BDI and MFIS.

The Persian version of FSMC provides a valid and reliable tool for evaluating cognitive and motor aspects of fatigue in patients living with MS.

This study had some limitations. Firstly, the translation process involved only one translator who compared the backward-translated version of the questionnaire with the original. This limited approach may have introduced biases or overlooked nuances in the language, which could affect the validity of the translated instrument. A collaborative effort among a team of translators would likely enhance the accuracy and reliability of the translation. Secondly, the sample included primarily young individuals with lower levels of disability. This demographic characteristic raises concerns about the external validity of the findings. The results may not be generalizable to older patients or those with more severe forms of MS, as these groups might experience fatigue differently. Future studies should aim to include a more diverse sample to better understand the applicability of the findings across different populations. Also, case and control groups differences regarding age and education level may affect the fatigue score which should be considered in future studies. □

CONCLUSION

In conclusion, this study supported the validity and reliability of Persian version of the FSMC

for assessing motor and cognitive fatigue in Iranian MS patients. Cognitive fatigue was notably higher in patients with progressive MS and greater physical disability. Also, significant correlations with depression, disability level and esta-

blished fatigue measures support the FSMC scale's convergent validity. ◻

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