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Validation of the French version of the Multiple Sclerosis Intimacy And Sexuality Questionnaire-19: A preliminary study

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ABSTRACT

Introduction: Patients with multiple sclerosis (MS) suffer from various symptoms, including sexual dysfunction. The Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19) is a scale that explores the impact of MS on sexual activity and satisfaction.
Aim: This observational cohort study aimed to provide a validated, cross-cultural, French version of the MSISQ-19 in patients with MS.
Methods: The original version of MSISQ-19 was translated into French according to standardized guidelines. Patients were asked to complete all questionnaires during the inclusion visit and the MSISQ-19 a second time two weeks later. Content validity was assessed by face validity. Internal consistency was evaluated using Cronbach's alpha. Construct validity was checked by the exploratory factor analysis. Concurrent validity was assessed by performing Spearman's correlation coefficient with the Female Sexual Function Index (FSFI), the Male Sexual Health Questionnaire (MSHQ), and the Multiple Sclerosis International Quality of Life questionnaire (MusiQoL). Spearman's correlation coefficient was also used to evaluate the relationship with the Expanded Disability Status Scale (EDSS), age, and disease duration. Test-retest reliability was assessed by intraclass correlation coefficient (ICC). Responsiveness was assessed by the standard error of measurement (SEM) and the minimum detectable change (MDC).
Main outcome measures: MSISQ-19 is the main outcome measure.
Results: We enrolled 71 patients with MS (49 female, 22 male). The mean age was 42.6 ± 9.7 years with a median disease duration of 8 [3–16] years. Sixty-four (90%) patients had relapsing-remitting MS, 4 (6%) primary progressive MS, and 3 (4%) secondary progressive MS. French MSISQ-19 showed a Cronbach's alpha coefficient of 0.89. MSISQ-19 scores correlated significantly and moderately between each other and correlated significantly and moderately with scores on the FSFI, MSHQ, MusiQoL and EDSS. Reproducibility was excellent with intraclass correlation coefficients > 0.80. Exploratory factor analysis was performed using principal component analysis. A three-factor solution was adopted giving eigenvalues higher than 1, supporting the primary, secondary, and tertiary dimensions. SEM was 4.55 and MDC was 12.6 (13.3%).
Conclusion: This study provides a preliminary validation of the French version of the MSISQ-19 which could be a reliable, and reproducible instrument to assess sexual dysfunction in patients with MS. These results need to be confirmed in a larger cohort which will be more representative of the general MS population.

1. Introduction

Multiple sclerosis (MS) is a chronic, dysimmune, inflammatory, demyelinating, neurodegenerative disease of the central nervous system and the most common cause of neurological disability in young adults. Among the wide range of clinical manifestations, sexual dysfunction

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(SD) represents one of the symptoms which may have a harmful impact on patients' quality of life (Tepavcevic et al., 2008; Schairer et al., 2014; Nazari et al., 2020). Sexual dysfunction's prevalence is greater in patients with MS (PwMS) than in the general population and in other chronic neurological diseases (Rees et al., 2007; Zorzon et al., 1999). A recent meta-analysis including 20 articles showed a prevalence of SD in adult men with MS ranging from 31% to 92% with a pooled prevalence of 62.9% (Dastoorpoor et al., 2021). In another recent systematic meta-analytic review including 9 articles, the prevalence of SD in adult women with MS was extremely discrepant, ranging from 27% to 95%, and the pooled estimate was calculated as 55% (Azimi et al., 2019). SD does not only affect PwMS in advanced disease stages but can occur in the early stages of the disease, even in patients with mild or moderate disability. Tzortzis and colleagues evaluated 63 women with MS with no major neurological impairment (mean Expanded Disability Status Scale (EDSS) score 2.3, range 0–3.5). Female SD was diagnosed in 22 (34.9%) out of the 63 patients (Tzortzis et al., 2008).

The pathogenesis of SD in PwMS is multidimensional and can be categorized in three different dimensions: primary, secondary and tertiary SD (Schmidt et al., 2005). Primary SD results from demyelination and axonal damage within areas of the brain and spinal cord that are directly engaged in sexual response. The most common primary dysfunctions in MS are reduction or loss of libido, impaired genital sensation, decreased vaginal lubrication, erectile dysfunction, difficulties in reaching orgasms/anorgasmia. Secondary SD includes the impact of common MS symptoms that indirectly influence sexual functioning, such as fatigue, muscle overactivity, muscle weakness, bladder and bowel dysfunction, impaired mobility, tremor, pain. Finally, tertiary SD refers to the influence of psychological, emotional, and sociocultural aspects of MS on sexual function. Despite this classification, SD often results from a complex interplay of factors across the three dimensions.

SD in MS is highly underdiagnosed, probably given the sensitive nature of the topic, and undertreated (Lew-Starowicz and Rola, 2014). Despite the fact that patients may desire their physician to initiate discussion about sexual concerns, embarrassment is an important barrier to addressing this topic for both healthcare professionals and patients (Tudor et al., 2018). Given the intimate nature of the subject and the taboos around it, one way to improve screening of SD in PwMS should be the use of self-reported validated questionnaires. In a recent systematic review evaluating available patient reported outcome measures (PROM) for SD in neurological patients, Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19) and its shorter version Multiple Sclerosis Intimacy and Sexuality Questionnaire-15 (MSISQ-15) appeared as the best tools to assess SD in MS (Hoen et al., 2017).

The MSISQ-19 is a validated self-reported questionnaire that explores the impact of MS on sexual activity and satisfaction over the previous 6 months. It assesses the three dimensions of sexual dysfunction: primary SD (items 12,16,17,18,19), secondary SD (items 1,2,3,4,5,6,8,10,11) and tertiary SD (items 7,9,13,14,15). Each item is rated on a five-point Likert scale (1=never, 2=rarely, 3=occasionally, 4=almost always, 5=always). The total score is the sum of the 19 items. The maximum total score is 95. The higher the score, the greater the impact of SD on patient's life. The original version of the MSISQ-19 was developed in English in 2000 (Sanders et al., 2000). The internal consistency was rated moderately to strongly positive, as was the content validity because of the active involvement of experts and patients in the development. Moderate evidence was found for positive construct validity (Sanders et al., 2000). The original English version has been translated and validated in Persian (Mohammadi et al., 2014), Brazilian Portuguese (da Silva et al., 2015), Ukrainian (Nehrych et al., 2019) and Italian (Carotenuto et al., 2021). A re-evaluation on a large sample of US patients resulted in a validated 15 item version (Foley et al., 2013). This shorter version of the MSISQ has been translated and validated in Dutch for patients with MS and spinal cord injury (Noordhoff et al., 2018) as well as in Italian for patients with spinal cord injury (Monti et al., 2020).

To the best of our knowledge, no specific instrument assessing sexual dysfunction in MS is available for French-speaking patients. With this study, we aimed at (i) translating the English version of the MSISQ-19 into French taking into account a cross-cultural adaptation; (ii) evaluating the content validity, construct validity, concurrent validity, reliability (internal consistency and test-retest reproducibility), and responsiveness of the French version of the MSISQ-19.

2. Materials and methods

2.1. Subjects

In this multicenter cross-sectional study, patients diagnosed with MS (all subtypes) according to the 2017 McDonald's criteria (Thompson et al., 2018) were prospectively enrolled at the Department of Neurology of the "Cliniques Universitaires Saint-Luc" (Brussels, Belgium), and the Department of Neurology of the "centre Hospitalier Universitaire CHU UCL Namur » (Yvoir, Belgium) between January 2021 and December 2021. Inclusion criteria were as follows (i) age $\geq$ 18 years old, (ii) French native speaking, (iii) Expanded Disability Status Scale (EDSS) $\leq$ 8.0 (Kurtzke, 1983). We excluded patients with (i) any other pathological condition that might lead to SD such as hormonal dysfunctions, major depression, major cardiovascular risk factor, (ii) concomitant treatment that may lead to SD such as antidepressant, beta-blockers,… (iii) clinical relapse in the 3 months preceding screening, (iiii) a change in the disease-modifying treatment, (iiiii) no sexual experience.

This study was approved by the relevant ethics committee and all patients signed a written informed consent after comprehensive explanation of the procedures, according to the Declaration of Helsinki.

2.2. Translation and cross-cultural adaptation

Translation and cross-cultural adaptation were performed according to relevant guidelines (Beaton et al., 2000). Two professional French-speaking translators separately forward-translated the English MSISQ-19 in French. Differences were discussed with the translators, a sexologist, a neurologist and the primary investigator until consensus was reached. The consensus translation was then backward-translated into English by an independent native English professional translator. The back-translated English version and the original version were compared and both versions were similar with neither misinterpretation nor ambiguity.

A pilot study was carried out for pre-test analysis of cultural equivalence and ensure face validity. The MSISQ-19 was applied to a group of 15 PwMS selected randomly at the Cliniques Universitaires Saint-Luc (Brussels, Belgium).The purpose of this pre-test was to identify issues that were not understood by the population and were therefore deemed culturally inappropriate. The content and wording of the questions were discussed with the neurologist. All patients confirmed their understanding of the items, so that no cross-cultural adaptation was made. Furthermore, all patients judged the content validity to be appropriate and confirmed the importance of all questions to assess the broad range of SD in PwMS, thus the final version of the French MSISQ-19 was generated (Fig. 1).

2.3. Questionnaires

This study made use of five questionnaires: 1) a study-specific questionnaire on demographic, clinical, and medical characteristics. For each patient, data was collected regarding gender, age, disease duration, MS subtype, MS treatment, EDSS, and previous attempts to solve their sexual dysfunction (sexologist, psychologist, medication,…); 2) the French MSISQ-19; 3) the Multiple Sclerosis International Quality of Life questionnaire (MusiQoL); 4)the Female Sexual Function Index (FSFI); 5) the Male Sexual Health Questionnaire (MSHQ). Patients were asked to complete anonymously all questionnaires during the inclusion visit and the MSISQ-19 a second time two weeks later at home.

Au cours des 6 derniers mois, les symptômes suivants ont perturbé mon activité ou ma satisfaction sexuelle	Jamais 1	Rarement 2	Occasion nellement 3	Presque toujours 4	Toujours 5
1. Rigidité musculaire ou spasmes aux bras, aux jambes ou au corps					
2. Symptômes urinaires ou au niveau de la vessie					
3. Symptômes intestinaux					
4. Sentiments de dépendance à cause de la SEP					
5. Tremblements ou secousses dans les mains ou le corps					
6. Douleurs, sensations de brûlure ou inconfort dans le corps					
7. Sentiment que mon corps est moins attirant					
8. Difficultés à me mouvoir comme je le veux lors d'une activité sexuelle					
9. Sentiment d'être moins féminine ou viril à cause de la SEP					
10. Problèmes de concentration, de mémoire ou de réflexion					
11. Exacerbation ou aggravation significative de ma SEP					
12. Diminution de la sensibilité ou engourdissement au niveau des parties génitales					
13. Crainte d'être rejeté(e) sexuellement à cause de la SEP					
14. Inquiétudes de ne pas pouvoir satisfaire sexuellement mon/ma partenaire					
15. Avoir moins confiance en ma sexualité en raison de la SEP					
16. Manque d'intérêt ou de désir sexuel					
17. Orgasmes moins intenses ou moins agréables					
18. Trop de temps nécessaire pour atteindre l'orgasme					
19. Lubrification/ « humidité » vaginale insuffisante (femmes) / difficultés à obtenir ou à maintenir une érection satisfaisante (hommes)					

Résultats

Items de la sous-échelle de dysfonction sexuelle primaire = 12,16,17,18,19

Items de la sous-échelle de dysfonction sexuelle secondaire = 1,2,3,4,5,6,8,10,11

Items de la sous-échelle de dysfonction sexuelle tertiaire = 7,9,13,14,15

Tout item obtenant un score de « 4 » ou « 5 » doit faire l'objet d'une discussion avec votre professionnel de la santé SEP.

Fig. 1. French Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19)
INSTRUCTIONS : Afin de mieux comprendre l'impact de la sclérose en plaques (SEP) sur l'intimité et la sexualité, ce questionnaire de 19 items vous demande d'évaluer dans quelle mesure divers symptômes de la SEP ont perturbé votre activité ou votre satisfaction sexuelle au cours des 6 derniers mois. Vous pouvez répondre aux questions en cochant la case située à côté de la question et sous le chiffre correspondant. Il n'y a pas de bonnes ou mauvaises réponses. Si vous avez un doute sur la manière de répondre à une question, veuillez choisir la réponse qui vous semble la plus adéquate.
Résultats
Items de la sous-échelle de dysfonction sexuelle primaire = 12,16,17,18,19
Items de la sous-échelle de dysfonction sexuelle secondaire = 1,2,3,4,5,6,8,10,11
Items de la sous-échelle de dysfonction sexuelle tertiaire = 7,9,13,14,15
Tout item obtenant un score de « 4 » ou « 5 » doit faire l'objet d'une discussion avec votre professionnel de la santé SEP.

- The FSFI (Rosen et al., 2000) is a self-reported instrument for the assessment of female sexual function not specific for MS. It consists of 19 items measuring the following dimensions: desire, arousal, lubrification, orgasm, satisfaction, and pain. The validity and reliability of the French version of the FSFI have been published (Wylomanski et al., 2014).
- The MSHQ (Rosen et al., 2004)is a 25-item self-administered questionnaire for assessing erection, ejaculation, desire, and satisfaction in older men with low urinary tract symptoms and sexual dysfunction. The validity and reliability of the French version of the MSHQ have been confirmed.
- The MusiQoL (Simeoni et al., 2008) is a multi-dimensional, self--administered, disease-specific scale assessing quality of life. It comprises 31 items describing nine dimensions: activity of daily living, psychological well-being, symptoms, friendly relationships, family relationships, satisfaction with healthcare, sentimental and sexual life, coping, and rejection. The French version of the MusiQoL has been shown a reliable and valid instrument to assess SD in French-speaking patients with MS (Baumstarck-Barrau et al., 2011).

2.4. Statistical analysis

Statistical analyses were performed using SPSS (version 27, 2020). Continuous data are presented as mean and standard deviation or median and first-third quartile. Categorical data are presented as counts and percentages. Normal distribution of variables was evaluated with

statistical and graphical approaches (Shapiro-Wilk). In order to validate the French version of the MSISQ-19, we followed the standards proposed by Instrument Review Criteria (SAC) (Aaronson et al., 2002; Lohr et al., 1996) and the Consensus-Based Standards for the Selection of Health Measurement Instruments (COSMIN) checklist (Mokkink et al., 2010a). We assessed the content validity, construct validity, concurrent validity, internal consistency, reproducibility, and responsiveness.

The content validity reflects the degree to which the content of a health-related PROM is an adequate reflection of the construct to be measured. Content validity was assessed by face validity (Mokkink et al., 2010b).

Construct validity was explored with the exploratory factor analysis (EFA) which was used to determine the underlying factor structure of the set of items. EFA was performed using a principal component analysis with promax rotation. Only components with eigenvalues higher than 1 were included in the final model. Kaiser-Meyer-Olkin (KMO) value was calculated and Bartlett's sphericity test was performed.

Concurrent internal validity was evaluated by exploring the Spearman's correlation (ρ) between MSISQ-19 and its subscales, while external validity was estimated computing the Spearman's correlation between (i) MSISQ-19 and its subscales with physical disability as captured by EDSS and (ii) MSISQ19 and the other administered questionnaires (MuSIQoL, FSFI and MSHQ).

The degree to which patients can be differentiated from each other, despite the measurement error, reflects the reliability. The reliability was assessed based on internal consistency obtained by Cronbach's alpha, and test-retest stability (reproducibility), obtained by Pearson's correlation, paired *t*-test, and intraclass correlation coefficient (ICC). A Cronbach's alpha between 0.70 and 0.99 was considered to reflect adequate internal consistency and ICC scores over 0.70 are acceptable (Terwee et al., 2007). The systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured, i.e. the measurement error, was also calculated. Measurement error was evaluated by use of the standard error of measurement (SEM), which was calculated as: SEM x SD_x x $\sqrt{(1 - R_x)}$, where SD_x is the standard deviation for all observations from test sessions 1 and 2 and R_x is the test-retest reliability coefficient (ICC) (Wagner et al., 2008).

The measurement property responsiveness shows the ability of a PROM to detect change over time in the underlying construct (Mokkink et al., 2010). It was measured by the minimum detectable change (MDC). The MDC, which represents the magnitude of change necessary to exceed the measurement error of 2 repeated measures at a specified CI was calculated for the 95% CI (MDC_{95}) as: MDC_{95} = SEM x 1.96 x $\sqrt{2}$, where 1.96 is the 2-sided tabled z value for the 95% CI and $\sqrt{2}$ is used to account for the variance of 2 measurements (Wagner et al., 2008).

Finally, if more than 15% of the respondents would achieve the lowest or highest possible score, floor or ceiling effects are considered. The floor and ceiling effects were assessed for the MSISQ-19 total score, primary, secondary and tertiary SD subscale score at baseline (Terwee et al., 2007).

Results were considered statistically significant for p-value < 0.05.

3. Results

We enrolled 83 patients with MS in the study. Twelve patients were excluded because they did not return the second questionnaire. In all, 71 MS patients completed the study with no missing data. Of those patients, 49 (69%) were female and 22 (31%) male. The mean age was 42.6 ± 9.7 years and median disease duration was 8 [3–16] years. Sixty-four (90%) patients had relapsing-remitting MS, 4 (6%) primary progressive MS, and 3 (4%) secondary progressive MS. The prevalence of SD, defined as a total MSISQ-19 score greater than 30 or any response 4 (often) or 5 (always) was 75.5% in female PwMS and 72.7% in male PwMS. The detailed sample characteristics are shown in Table 1. All variables were abnormally distributed except for age and total MusiQOL score.

Table 1
Demographic and clinical characteristics of the sample.

Characteristics	
Gender	
Female, N (%)	49 (69)
Male, N (%)	22 (31)
Age, mean ± SD, (years)	42.6 ± 9.7
Disease duration, median [Q1-Q3]	8 [3–16]
Disease phenotype	
Relapsing-remitting, N (%)	64 (90)
Secondary-progressing, N (%)	3 (4)
Primary-progressing, N (%)	4 (6)
EDSS, median [Q1-Q3] (range)	2 [1–3] (0–6.5)
MSISQ-19 score, median [Q1-Q3]	39 [31–54]
Primary sexual dysfunction subscale	11 [8–15]
Secondary sexual dysfunction subscale	18 [12–22]
Tertiary sexual dysfunction subscale	11 [7–15]
FSFI score, median [Q1-Q3]	25.75 [19.2–30.275]
MSHQ score, median [Q1-Q3]	98 [83–106.5]
MusiQoL score, mean ± SD	69.17 ± 16.79

EDSS = Expanded Disability Status Scale; MSISQ-19 = Multiple Sclerosis Intimacy and Sexuality Questionnaire-19; FSFI = Female Sexual Function Index; MSHQ = Male Sexual Health Questionnaire; MusiQoL = Multiple Sclerosis International Quality of Life Questionnaire.

3.1. Construct validity

EFA was used to evaluate the latent factor structure of the MSISQ-19. The Kaiser-Meyer-Olkin statistic was 0.84, and Bartlett's test of sphericity was significant ($p < 0.001$), indicating sampling adequacy for principal component analysis. EFA was thus performed using principal component analysis with oblique promax rotation. As for the original version of the MSISQ-19, a three-factor solution was adopted giving eigenvalues higher than 1, supporting the primary, secondary, and tertiary dimensions. Item were assigned to corresponding subscales based on the highest component loading. All items loaded onto the same subscales as in the original version at the exception of items 2, 3, 14, and

Table 2
Exploratory factor analysis of the MSISQ-19.

	F1	F2	F3
1. Muscle tightness or spasms in my arms, legs, or body	/	0.774	0.174
2. Bladder or urinary symptoms	0.592	0.377	−0.259
3. Bowel symptoms	0.504	0.197	−0.264
4. Feelings of dependency because of MS	0.376	0.506	0.125
5. Tremors or shaking in my hands or body	/	0.748	−0.123
6. Pain, burning, or discomfort in my body	−0.163	0.766	0.231
7. Feeling that my body is less attractive	−0.241	0.245	0.901
8. Problems moving my body the way I want during sexual activity	0.280	0.385	0.389
9. Feeling less masculine or feminine due to MS	0.304	/	0.539
10. Problems with concentration, memory, or thinking	−0.123	0.519	0.104
11. Exacerbation or significant worsening of my MS	0.391	0.526	/
12. Less feeling or numbness in my genitals	0.823	0.195	−0.312
13. Fear of being rejected sexually because of MS	−0.163	/	0.518
14. Worries about sexually satisfying my partner	0.584	−0.139	0.398
15. Feeling less confident about my sexuality due to MS	0.532	/	0.511
16. Lack of sexual interest or desire	0.646	−0.366	0.308
17. Less intense or pleasurable orgasms or climaxes	0.857	/	/
18. Takes too long to orgasm or climax	0.846	/	/
19. Inadequate vaginal wetness or lubrication	0.924	−0.148	/
Eigenvalue	7.52	2.13	1.55
Variance explained (%)	39.56	11.21	8.16
Cumulative variance explained (%)	39.56	50.77	58.92

F1 = primary sexual dysfunction, item 12, 16–19; F2 = secondary sexual dysfunction, item 1–6, 10,11; F3 = tertiary sexual dysfunction, item 7–9, 13–15.

15. This three-factor solution explained 59% of the total variance. Detailed results are presented in Table 2.

3.2. Concurrent validity analysis

Primary, secondary and tertiary subscales were correlated moderately between each other (primary vs secondary $\rho = 0.60$, $p < 0.001$; secondary vs tertiary $\rho = 0.59$, $p < 0.001$; primary vs tertiary $\rho = 0.62$, $p < 0.001$). Similarly, MSISQ-19 total score also highly correlated with primary ($\rho = 0.83$, $p < 0.001$), secondary ($\rho = 0.89$, $p < 0.001$) and tertiary ($\rho = 0.83$, $p < 0.001$) subscales.

MSIQ-19 total score and subscale scores showed significant correlation with other measures and questionnaires. A summary for correlation coefficient between MSISQ-19 and all other questionnaires is presented in Table 3. A significant, moderate, negative relationship was found between the total score of FSFI and the total score of MSISQ-19 ($\rho = -0.67$, $p < 0.001$), the primary SD subscale score ($\rho = -0.66$, $p < 0.001$), the secondary SD subscale score ($\rho = -0.53$, $p < 0.001$), and the tertiary SD subscale score ($\rho = -0.51$, $p < 0.001$). As shown in Table 3, a significant negative, moderate to high relationship was found between the total score of MSHQ and the total score of MSISQ-19 ($\rho = -0.71$, $p < 0.001$), the primary SD subscale score ($\rho = -0.83$, $p < 0.001$), the secondary SD subscale score ($\rho = -0.50$, $p = 0.02$), and the tertiary SD subscale score ($\rho = -0.65$, $p = 0.001$). A significant negative, moderate relationship was found between the total score of MusiQoL and the total score of MSISQ-19 ($\rho = -0.66$, $p < 0.001$), the primary SD subscale score ($\rho = -0.46$, $p < 0.001$), the secondary SD subscale score ($\rho = -0.67$, $p < 0.001$), and the tertiary SD subscale score ($\rho = -0.56$, $p < 0.001$). The score of MusiQoL' item "Satisfaction with sexual function" significantly and moderately correlated with MSISQ-19 total score ($\rho = -0.56$, $p < 0.001$), and with primary ($\rho = -0.56$, $p < 0.001$), secondary ($\rho = -0.44$, $p < 0.001$), and tertiary SD subscale score ($\rho = -0.47$, $p < 0.001$).

Disability level, measured by the EDSS, correlated moderately but significantly with total MSISQ-19 score ($\rho = 0.51$, $p < 0.001$), primary SD subscale score ($\rho = 0.48$, $p < 0.001$), secondary SD subscale score ($\rho = 0.50$, $p < 0.001$), and tertiary SD subscale score ($\rho = 0.30$, $p = 0.01$).

Age significantly but weakly correlated with the MSISQ-19 total score ($\rho = 0.26$, $p = 0.03$), and with primary SD subscale score ($\rho = 0.35$, $p = 0.002$) but not with secondary ($\rho = 0.18$, $p = 0.14$), and tertiary SD subscale score ($\rho = 0.18$, $p = 0.13$).

Disease duration did not significantly correlate with the MSISQ-19 total scale or subscales.

Table 3
Spearman's correlations of scores on MSISQ-19 and subscales with MusiQoL, FSFI, MSHQ, EDSS scores, and demographics.

	MSISQ-19 Total	Primary	Secondary	Tertiary
MSISQ-19				
Primary	0.83**	1	0.60**	0.62**
Secondary	0.89**	0.60**	1	0.59**
Tertiary	0.83**	0.62**	0.59**	1
MusiQoL				
Total	−0.66**	−0.46**	−0.67***	−0.56**
Satisfaction with sexual life	−0.56**	−0.56**	−0.44**	−0.47**
FSFI	−0.67**	−0.66**	−0.53**	−0.51**
MSHQ	−0.71**	−0.83**	−0.50*	−0.65***
EDSS	0.51**	0.48**	0.50**	0.30**
Age	0.26**	0.36**	0.18	0.18
Disease duration	0.03	0.16	−0.02	0.001

MSISQ-19 = Multiple Sclerosis Intimacy and Sexuality Questionnaire-19; MusiQoL = Multiple Sclerosis International Quality of Life Questionnaire; FSFI = Female Sexual Function Index; MSHQ = Male Sexual Health Questionnaire; EDSS = Expanded Disability Status Scale.

* Correlation is significant at the $p < 0.05$ level.

** correlation is significant at the $p < 0,01$ level.

3.3. Internal consistency

The MSISQ-19 showed a good internal consistency with Cronbach's alpha α=0.89 for the MSISQ-19 as a whole, and values of 0.88 and 0.83 for primary and secondary sexual dysfunction, respectively. The internal consistency for tertiary sexual dysfunction was adequate with Cronbach's alpha α=0.71.

3.4. Reproducibility

Seventy-one MS patients completed the test after a period of 14.1 ± 1.1 days in order to assess test-retest reproducibility. The average MSISQ-19 total scores for the test and retest did not differ (41.7 ± 14.6 vs 41.3 ± 14.3). MSISQ-19 test and retest total scores highly correlated between each other ($r = 0.93$, $p < 0.001$). Paired *t*-test showed no statistically significantly difference between MSISQ-19 test and retest total score ($p = 0.553$). The ICCs for agreement for the total MSISQ-19 and the three domains were all high with ICC= 0.90, ICC=0.92, ICC=0.87, ICC=0.89 for total scale, primary, secondary and tertiary sexual dysfunction subscale score, respectively, indicating a good to excellent reliability.

3.5. Responsiveness

SEM was 4.55 and MDC was 12.6 (13.3%).

3.6. Floor and ceiling effects

No floor effects were seen for the MSISQ-19 total score, primary, and secondary subscale scores. Two (2.8%), six (8.5%), and seven (9.9%) subjects had the lowest possible score on the total score, primary subscale score, and secondary subscale score respectively. Floor effects were seen in the tertiary domain (16% of the patients). No ceiling effects were seen for the MSISQ-19 total score and subscales scores. No subject obtained the maximum score on the total score, primary subscale score, secondary subscale score, and tertiary subscale score.

4. Discussion

The present study assessed content validity, construct validity, concurrent validity, internal consistency, reproducibility, and responsiveness of the French MSISQ-19. All measurement properties obtained significant, moderate to high scores. This French version of the MSISQ-19 appears to be a reliable, reproducible, and responsive instrument for evaluation of SD in French speaking PwMS.

The prevalence of sexual dysfunction in PwMS ranges from 30 to 95% (Dastoorpoor et al., 2021; Azimi et al., 2019), which is greater than in the general population and in other neurological diseases (Rees et al., 2007; Zorzon et al., 1999). Despite the high prevalence, SD in MS remains underdiagnosed and 63% of PwMS report that they have never talked to physicians about their sexual problems (Cordeau and Courtois, 2014). Similarly, Mahajan et al. reported that only 20% of patients with MS were being asked about sexual dysfunction by their healthcare provider (Mahajan et al., 2014).Barriers to discussing SD are various (embarrassment, lack of time,…) and are related to healthcare professionals as much as to patients themselves (Tudor et al., 2018). Sexual function is now recognized as an essential component of quality of life. According to the World Health Organization and the current working definition, sexual health is: "…a state of physical, emotional, mental and social well-being in relation to sexuality" (World Health Organization, 2022). Failure to consider sexual problems prevents these patients from receiving proper sexual counselling and thus improving their quality of life. Using standardized questionnaires to assess sexual dysfunctions in patients with MS helps removing the common barriers that are reported both by professionals and patients when addressing sexual issues. The use of questionnaires would increase the provision of proper diagnoses

in 2% to 42% of women with MS (Cordeau and Courtois, 2014).

In a recent systematic review evaluating available PROMs for SD in neurological patients, strong evidence was only found for the MSISQ-19 and it's shorter version the MSISQ-15 for PwMS (Hoen et al., 2017). The synthesis of the level of evidence was performed based on the assessment of internal consistency, reliability, measurement error, content validity, structural validity, hypotheses testing, cross-cultural validity/translation, criterion validity, and responsiveness, with the following possible levels of evidence: strong, moderate, limited, conflicting, and unknown. Even though strong evidence was found for the MSISQ-19, the authors concluded that none of the PROMs identified were found to be adequate to evaluate change in sexual function in neurological patients over time because responsiveness has not been established and no assessment has been made of the measurement error.

The results of our study confirmed construct validity for primary, secondary, and tertiary sexual dysfunction, in line with the original validation study.

The reliability of the French MSISQ-19 was confirmed by a good internal consistency for the overall score, and all subscales scores with Cronbach's alpha ranging from 0.71 to 0.89 which is comparable with that of the original MSISQ-19 and other validated version of MSISQ-19 (Mohammadi et al., 2014; da Silva et al., 2015; Nehrych et al., 2019; Carotenuto et al., 2021). The reproducibility for the French MSISQ-19 in terms of test-retest score was excellent with a mean change between test and retest of 0.4 point. MSISQ-19 test and retest total scores highly and significantly correlated between each other ($r = 0.93$, $p<0.001$) just like in the Brazilian version ($r = 0.90$, $p<0.001$)(15), whilst it was reported to be moderately correlated ($r = 0.48$, $p = 0.01$) in the Italian validation study (Carotenuto et al., 2021). We found an ICC of 0.90 for the 19 items of the French translation of the MSISQ-19, indicating also an excellent reliability similarly as in the Ukrainian version (ICC=0.99) (Nehrych et al., 2019). Comparison with the original study and the Persian validation study (Mohammadi et al., 2014)was not possible because a test-retest had not been performed.

In order to address concurrent validity, we assessed the association between the French MSISQ-19 version and FSFI for female patients with MS and MSHQ for male patients with MS. The FSFI was also used in the Italian (Carotenuto et al., 2021) and Persian (Mohammadi et al., 2014) validation study, whilst the Urinary Incontinence Sexual Questionnaire (PISQ-12) was used in the Dutch (Noordhoff et al., 2018) validation study to assess concurrent validity for female subjects. The Italian(17) and Dutch (Noordhoff et al., 2018) validation study made use of the International Index of Erectile Function (IIEF) to assess concurrent validity in male subjects. The IIEF's focus on erection is its main limitation. IIEF's ability to assess desire, orgasm and ejaculation is limited, which is why we decided to use the MSHQ instead. It was hypothesized that the FSFI score and MSHQ score would be significantly correlated with scores on the MSISQ-19 and its subscales. Our results showed a significant, moderate to high, negative correlation between them confirming the validity of the French MSISQ-19 questionnaire for patients with MS, just like in the other validations studies with their respective questionnaires. Indeed, the Italian validation study (Carotenuto et al., 2021) showed a significant, weak to moderate, negative correlation between FSFI, IIEF and MSISQ-19 total and subscales score except for FSFI and MSISQ19 secondary subscale score (significant, weak, positive correlation). The Persian validation study (Mohammadi et al., 2014) found a significant, moderate, negative correlation between FSFI and MSISQ19 total score and subscales scores. A significant, moderate, negative correlation between IIEF, PSISQ-12 and total MSISQ-15 score was also found in the Dutch validation study (Noordhoff et al., 2018). The Ukrainian (Nehrych et al., 2019) and Brazilian (da Silva et al., 2015) validation study did not use another sexual questionnaire to assess concurrent validity, both made use of the EDSS score only.

It was expected that the MusiQoL total score would correlate with scores of the MSISQ-19 and its subscales because SD is known to impact quality of life (Tepavcevic et al., 2008; Schairer et al., 2014; Nazari et al., 2020), which was confirmed with our results.

Furthermore, satisfaction with sexual function on the MusiQoL significantly correlated with MSISQ-19 total score, and with primary, secondary, and tertiary SD subscale scores. If the patient with MS becomes unable to engage in sexual activity, their partners also show less satisfaction with their sex lives which could have repercussion on relationships and satisfaction with their sentimental life. In addition, we also found a direct correlation between MSISQ-19 total score and subscales scores and psychological well-being score on the MusiQoL. The relations between psychic distress and sexual function were already reported in the original validation study (Sanders et al., 2000), as well as in Italian (Carotenuto et al., 2021) and Persian (Mohammadi et al., 2014) versions. Authors found correlations between the MSISQ-19 and its subscales and (a) the Mental Health Inventory score (Sanders et al., 2000) and (b) the Beck Depression Inventory-II (Mohammadi et al., 2014; Carotenuto et al., 2021). As depressive disorders are more prevalent in MS than in other chronic neurological diseases (Schubert and Foliart, 1993), it would be helpful for clinicians to assess psychological symptoms together with sexual function in order to have a global vision of the symptoms and to better adjust sexual dysfunction treatment.

The EDSS is the gold standard for assessment of disability in people with MS. Considering SD may result from MS-related symptoms that interfere with sexual function and considering that those symptoms are assessed by the EDSS, our hypothesis was that EDSS would be correlated with the MSISQ-19 total scores and it's subscales, especially secondary dysfunction subscale as it is a measure of the impact of physical disability on sexual functioning. Although Dastoorpoor et al. (2021) showed no significant relationship between the prevalence of SD in men with MS and the degree of disability evaluated by EDSS in their meta-analysis and although the Brazilian version of MSISQ-19 (da Silva et al., 2015) did not observe a significant correlation between EDSS score and SD, the Persian (Mohammadi et al., 2014), Ukrainian (Nehrych et al., 2019), and Italian (Monti et al., 2020) MSISQ-19 have demonstrated a significant association between the EDSS score and SD. Since expected, our study showed that disability level, measured by the EDSS, significantly and moderately correlated with the MSISQ-19 total score and subscale scores, especially the secondary SD subscale score. As mentioned in previous studies, because of the progressive nature of MS or medication adverse effects, longer disease duration is considered a related factor of SD in patients with MS (Azimi et al., 2019). However, although EDSS correlated significantly and moderately with MSISQ-19 scores, in our study, we found no significant relationship between duration of the disease and prevalence of SD, which is consistent with the results of the meta-analysis by Dastoorpoor et al. (2021). Further studies are needed to better understand the association between the MSISQ-19, the degree of disability and the duration of disease.

4.1. Limitations

Several limitations of our study should be acknowledged. First, our small sample size was conveniently determined, and not based on a statistical calculation. Furthermore, the study cohort is not fully representative of the wider MS population, since the proportion of patients with progressive forms of MS is low (4% of subjects with secondary progressive MS and 6% with primary progressive MS) compared to the general MS population (Holland et al., 2011; Boyko et al., 2021). However, this low rate is in line with the proportion of outpatients with progressive forms at the Department of Neurology in our clinics.

Another limitation is the lack of a French golden standard evaluating SD in neurological patients to which we could correlate the French MSISQ-19. Indeed, 't Hoen et al. have highlighted in their systematic review that the IIEF and FSFI which are commonly used, have actually not or not adequately been validated in neurological patients (Hoen et al., 2017). We found no validation of the MSHQ in neurological patients neither.

5. Conclusions

The present study assessed content validity, construct validity, concurrent validity, internal consistency, reproducibility, and responsiveness of the French MSISQ-19. All measurement properties obtained significant, moderate to high scores. This study provides thus a preliminary validation of the French version of the MSISQ-19 which seems to be a reliable, reproducible, and responsive instrument for evaluation of sexual dysfunction in French-speaking PwMS. These results need to be confirmed in a larger cohort which will be more representative of the general MS population.

This questionnaire could be a rapid and easy to use assessment tool in the daily care of MS patients. The administration of this self-reported, standardized tool might help the initial approach of this sensitive topic by encouraging healthcare professionals to initiate discussion about sexual concerns and provide appropriate and multidimensional management, thus improving the quality of life of PwMS. Similarly, this tool may be considered as an outcome measure of sexual functioning in research trials.

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CRediT authorship contribution statement

Marine Devis: Conceptualization, Visualization, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **Gaëtan Stoquart:** Formal analysis, Data curation, Writing – review & editing. **Marie Géonet:** Conceptualization, Visualization, Writing – review & editing. **Frédéric London:** Funding acquisition, Data curation, Writing – review & editing. **Vincent van Pesch:** Conceptualization, Visualization, Funding acquisition, Data curation, Writing – review & editing.

Declaration of Competing Interest

The authors report no conflicts of interest.

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