REVISTA NEUROCIÊNCIAS

Functional and motor evaluation in a Brazilian Huntington's disease cohort

Avaliação funcional e motora em uma coorte brasileira com doença de Huntington

Evaluación funcional y motora en una cohorte brasileña con enfermedad de Huntington

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Resumo

Introdução. Este estudo avaliou os resultados obtidos na aplicação das escalas clínicas utilizadas para avaliação da progressão da doença de Huntington (DH), tais como a *Functional Independence Measure* (FIM), o *Modified Barthel Index* (MBI), a *Unified Huntington's Disease Rating Scale* (UHDRS), comparando o desempenho motor de participantes brasileiros com DH com o do Grupo de Referência (GR). **Método.** Trata-se de um estudo quantitativo observacional transversal. A sensibilidade e especificidade das escalas MBI e MIF foram calculadas usando a escala UHDRS como escala de referência. **Resultados.** A média de idade de início da DH foi de 41,6±8,3 anos com mediana de duração da doença de 11 anos. O GR teve 22 indivíduos com idade de 51,5±7,6 anos e o grupo DH (n=22) 51,5±8,4 anos. As mulheres do grupo DH foram mais afetadas em suas habilidades funcionais e motoras em relação ao GR (p<0,001). **Conclusões:** Até onde sabemos, esta é a primeira vez que um estudo aplicou a MIF em participantes em DH. A MIF e o MBI podem ser aplicadas para avaliar o desempenho funcional, já que quando comparamos com os resultados das seções funcionais da UHDRS observamos resultados semelhantes (p<0,01). As escalas FIM e MBI são de fácil aplicação e podem ser bons instrumentos para avaliar o desempenho funcional dos pacientes. Sugerimos que podem ser úteis em programas de reabilitação, mas são necessários estudos mais aprofundados para tal.

Unitermos. Avaliação da deficiência; atividades cotidianas; doença de Huntington; Transtornos dos Movimentos; Transtornos das Habilidades Motoras

Abstract

Introduction. This study compared the results of motor performance obtained using three clinical scales for the assessment of Huntington's disease (HD) progression, such as the Functional Independence Measure (FIM), Modified Barthel Index (MBI), and Unified Huntington's Disease Rating Scale (UHDRS), evaluating the motor performances of Brazilian HD participants and Reference Group (RG). **Method.** This was a cross-sectional, observational quantitative study. Sensitivity and specificity of the MBI and FIM scales were calculated using UHDRS as a reference scale. **Results.** The mean age at HD onset was 41.6±8.3 years, with a median value of disease time of 11 years. The mean age of the RG (n=22) was 51.5±7.6 years, and the HD group (n=22) 51.5±8.4 years. Females from the HD group were more

severely affected in their functional and motor capacities as compared to the RG (*p<.001)*. **Conclusions.** To the authors knowledge, this is the first study applying the FIM to participants with HD. Therefore, FIM and MBI can be applied to assess the HD functional performance, since when we compared the UHDRS functional sections we observed similar results (*p*<.01). The FIM and MBI scales are easy to administer and can be used to assess the functional performance of HD patients. Furthermore, they may be effective tools in rehabilitation programs, but further studies of these scales are warranted.
Keywords. Disability evaluation; activities of daily living, Huntington disease; movement disorders; Motor Skills Disorders

Resumen

Introducción. Este estudio evaluó los resultados obtenidos en la aplicación de escalas clínicas utilizadas para evaluar la progresión de la enfermedad de Huntington (EH), tales como la *Functional Independence Measure* (FIM), *Modified Barthel Index* (MBI) el *Unified Huntington's Disease Rating Scale* (UHDRS), comparando el desempeño motor de los participantes brasileños con EH con el del Grupo de Referencia (GR). **Método.** Se trata de un estudio observacional cuantitativo de corte transversal. La sensibilidad y especificidad de las escalas MBI y MIF se calcularon utilizando la escala UHDRS como escala de referencia. **Resultados.** La edad media de inicio de la EH fue de 41,6±8,3 años con una mediana de duración de la enfermedad de 11 años. El GR contó con 22 individuos de 51,5±7,6 años y el grupo EH (n=22) de 51,5±8,4 años. Las mujeres del grupo HD se vieron más afectadas en sus habilidades funcionales y motoras en relación al GR (p<0,001). **Conclusiones.** Hasta donde sabemos, esta es la primera vez que un estudio aplica FIM en participantes de EH. El MIF y el MBI se pueden aplicar para evaluar el desempeño funcional, ya que cuando comparamos los resultados con las secciones funcionales de la UHDRS, observamos resultados similares (p<0,01). Las escalas FIM y MBI son de fácil aplicación y pueden ser buenas herramientas para evaluar el desempeño funcional de los pacientes. Sugerimos que pueden ser útiles en programas de rehabilitación, pero se necesitan más estudios para esto.
Palabras clave. Evaluación de la discapacidad; actividades diarias; Enfermedad de Huntington; Transtornos del Movimiento; Trastornos de la Destreza Motora

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Conflict of interest: no Received in: 04/15/2022 Acept in: 09/29/2022

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INTRODUCTION

Huntington's disease (HD) is an autosomal dominant progressive neurodegenerative disorder. Clinical manifestations, such as behavioral, cognitive and/or motor disturbances, usually occur in the fourth or fifth decade of life[1].

The global prevalence of HD is 2.7 per 100,000 inhabitants[2]. In the first semester of 2022, 3.671 families with HD were registered in the Brazil Huntington Association.

In Brazil, there are some HD clusters, such as: one in Feira Grande town - AL, with a prevalence of 10.4/10,000 inhabitants[3]; one in Senador Sá - CE with a prevalence of 23.3/10,000 inhabitants[4] and one in Ervália town - MG with a prevalence of 7.2/10.000 inhabitants[5]. The minimal prevalence in Rio Grande do Sul state was estimated at 1.85:100,000 inhabitants[6].

The incidence and prevalence of HD are the same for both sexes. HD alleles when inherited from the father are more likely to be more expanded and can cause the HD juvenile form[7,8]. Expanded alleles transmitted by the mother to her offspring rarely show an increase of more than 20 CAG repeats[9,10].

The motor symptoms in HD are chorea, dystonia, dyskinesia, akinesia, hypokinesia and bradykinesia, as well as motor impersistence and rigidity. Other symptoms of HD including inquietude and the presence of movements that simulate throwing (ballism), become more evident throughout the disease progression[11–14].

Motor impairments negatively affect the upper limbs and limit the ability to perform reaching, grasping and fine motor activities in individuals with HD. On the other hand, cognitive symptoms (psychiatric and behavioral) contribute to decreased performance on the Activities of Daily Living (ADLs) and reduced quality of life in patients with HD[13,15]. Motor impairments contribute to the functional decline as measured by the Instrumental Activities of Daily Living (IADLs), such as feeding and hygienic practices; especially

those ADLs and social activities that require a higher level of discernment and mental skills, such as finance management and cooking[16].

Some functional activities assessment tools including the UHDRS, six-minute walk test, 10m walk, the Timed Up & Go (TUG test), Physical Performance Test (PTT) and Barthel Index have been used clinically to determine the effect of interventions and to measure disease progression in individuals with HD. Efficient, low-cost, easy-to-use tools to assess patients with HD are important to identify the current impact of motor impairment on daily activities and the quality of life in HD different stages[17–20].

The aim of this study was to compare the results of the clinical scales for the assessment of disease severity and progression, such as the Functional Independence Measure (FIM), Modified Barthel Index (MBI) and the Unified Huntington's Disease Rating Scale (UHDRS), applied to Brazilian participants with HD and to a reference group (RG); and to examine their relationship with motor performance. It is worth mentioning that the originality of this work resides in the fact that FIM and MBI scales were used for the first time to assess patients with HD, and very little work has been done examining Brazilian HD cohorts.

In Brazil, rare diseases such as HD suffer from being unknown to most health professionals, thus, few professionals have experience in assisting patients with HD. In addition, UHDRS is rarely used for the functional evaluation of Brazilian individuals with HD by

physiotherapists. This is due to a lack of knowledge about HD and low training of assessment instruments. For this reason, to our knowledge, no HD specific and easy-to-use scales have been tested in Brazil. Our study investigated the applicability of two easy-to-use scales such as FIM and MBI to assess the clinical evolution of HD comparing their results with those obtained with UHDRS.

METHOD

Study Design

This was a cross-sectional, observational quantitative study with a reference group.

Participants

Brazilian individuals with HD were recruited in the Genetics Out-patient Clinic of the Gaffrée and Guinle University Hospital (HUGG) of the Universidade Federal do Estado do Rio de Janeiro (UNIRIO) and all of them were resident in Rio de Janeiro city. The reference group had three individuals from the city of *Rio de Janeiro* and 19 individuals from the Ariquemes small town in Rondônia state. To make sample more homogeneous, the UHDRS TFC section was used to categorize individuals according to their functional performance at different stages of the disease. HD participants and the reference group were compared by age, gender and educational level.

This project was approved by the Research Ethics Committee (CAAE number 26387113.1.0000.5258).

Individuals with HD familial history and with a positive genetic diagnosis for HD with expanded alleles bearing more than 39 CAG repetitions were recruited. Reference group participants did not have familial history of HD or any movement disorder or neurological disease (sample without normal distribution). All participants were over 18 years old and resided in *Rio de Janeiro* city, Brazil, at the time of the study.

Procedure

The UHDRS, developed by the Huntington Study Group, is the most commonly used scale in Europe and United States to assess the clinical evaluation of individuals with HD[12] (Huntington Study Group, 1996) but it is not commonly used in Brazil. The UHDRS was translated and validated in Brazilian Portuguese as *Escala Unificada de Avaliação da Doença de Huntington* (EUADH)[1]. The UHDRS evaluates four clinical aspects: motor performance, cognitive, functional and behavioral abnormalities; and its sections are as follows: Functional and motor sections are composed by the Functional Assessment Scale (FAS), Total Functional Capacity (TFC), Independence Scale (IS) and Total Motor Assessment Scale (TMS)[1,12]. FAS section assesses functional skills consisting of 25 specific questions. FAS score ranges from 0 to 25; the higher the score, the better the functional performance. FAS is the most used section for assessing ADL, evaluating whether the individual is able or unable to perform certain tasks[1,12]. The IS is a checklist regarding the

HD patient independence to perform daily activities; this section is completed with caregiver's reports. The result ranges from 0 to 100% in intervals of 10; the higher score indicates greater independence[1,12,21]. The TFC categorizes individuals into different stages of the disease and detects the degree of independence in performing activities related to occupation, finances, household chores, and ADL. TFC also measures the level of care provided by the caregiver[12]. Higher TFC score indicates better functional performance; it means greater integrity and preservation of functions. TFC was used to categorize stages of functional impairment of individuals with HD[22].

The median value obtained from the reference group (sample without normal distribution) assessed by UHDRS scale, was used as the cutoff value applied to the HD group. This approach categorized the functional and cognitive aspects into normal or impaired. The MBI and FIM scales have been widely used in routine physiotherapy and clinical trials to assess functionality and to support further interventions. In addition, MBI and FIM are easy to administer and apply to individuals with neurodegenerative diseases. Both scales have a score for each activity and can assess the degree of functional independence. These scales' forms can be completed by the individual or his/her family[1,12,23,24].

The MBI scale assesses functional performance of daily activities with scores ranging from 0 to 100. The higher the score, more independent the individual is. The scores classify

the individual as totally independent (100 points), mild dependent (99 to 76 points), moderately dependent (75 to 51 points), severely dependent (50 to 26 points) or totally dependent (25 or less points)[25].

The FIM scale assesses the level of functional dependence with scores ranging from 1 to 7 points, 1 point indicates the patient total dependence and 7 indicates complete independence. The total score ranges from 18 to 126; higher score indicates greater individual independence[23].

Statistical analysis

Data was analyzed using SPSS version 17.0 software. Descriptive statistics were calculated. The Shapiro-Wilk normality test was used to assess normality. Correlation analyses were conducted using the Spearman *rho* test. The Wilcoxon-Mann-Whitney test was used to compare the medians of the analyzed groups (independent sample test).

For the association analysis, simple regression was used with the aim of investigating the similarities among the scales. The R-squared (R^2) was calculated. It is a statistical measure in a regression model that determines the proportion of variance in the dependent variable that can be explained by the independent variable.

Multiple regressions were used for investigating the association of a dependent variable with independent ones. Statistical significance was considered when $p<0.05$.

RESULTS

Among the 22 patients with HD, 54.5% were male and 45.4% were female. The mean age was 51.5±8.4yr and approximately 86% of them manifested symptoms of the disease before 51 years of age. The male (n=12) mean age was 50.8±6yr and the female (n=10) mean age was 52.5±11yr. The mean age at onset of HD in the male group was 41.3±8.2yr and in the female group 42.1±9yr (Table 1). In the total, the mean age at HD onset was 41.6±8.3yr. The smallest number of CAG repeats in the *HTT* gene was 41 units, and the largest 56 (median=45.3). The time since onset of the disease had a median of 11 years (minimum 1yr and maximum 17yr) and the mean of 10±4.4yr.

The reference group was comprised of 22 individuals, 10 females (45.5%) and 12 males (54.5%). Their mean age was 51.6±10.6yr for females and 51.6±4.4yr for males (Table 1).

In the present study, the TFC score was used to categorize individuals according to their functional performances at different stages of the disease[22]. Those classified as pre-symptomatic were asymptomatic on the date of the study, and the other symptomatic patients were categorized into early, middle, or late phase of disease (Table 2); as follows in additional Supplementary Table (ST01) for each patient and its respective individual and cumulative percentages according to the TFC score (ST02).

The scores for the MBI, FIM and FAS are shown in Table 3 and in the additional Supplementary Tables (ST02, ST03

and ST04) for each patient, and respective individual and cumulative percentages according to the MBI, FIM and FAS score.

Table 1. Categorization of reference group and HD group (male and female), comparison of the scale between reference group and HD groups.

	HD group	Reference group	
Sex	Female (n=12)	Male (n=10)	
Age (yr)	52.5±11	50.8±6	
Age at onset (yr)	42.1±9	41.3±8.2	
	Reference Group (0) HD Group (1)	**Sample (N)**	**Mean / SD**
Current Age (yr)	0	22	51.5±7.6
	1	22	51.5±8.4
		Total 44	
Age at onset (yr)	0	0	0
	1	22	41.8±8.3
		Total 22	
Time since onset (yr)	0	0	0
	1	22	10.0±4.4
		Total 22	
Disease Stage	0	0	0
	1	22	2.7±1.2
		Total 22	
Years of Education	0	22	8.4±5.5
	1	21	10.1±4.6
		Total 43	
Highest CAG	0	0	0
	1	22	45.3±3.9
		Total 22	
MBI	0	22	100
	1	22	71.7±39.8
		Total 44	
FIM	0	22	126
	1	22	92.6±41.1
		Total 44	
UHDRS- FAS	0	22	24.7
	1	22	12.5±7.9
		Total 44	
UHDRS- TFC	0	22	13.0
	1	22	6.1±4.1
		Total 44	
UHDRS- IS	0	22	100
	1	22	66.8±27.8
		Total 44	
UHDRS- TMS	0	22	2.1±5.1
	1	22	52.8±29.6
		Total 44	

0= Reference Group, 1= HD Group. SD=Standard Deviation. MBI= Modified Barthel Index. FIM= Functional Independence Measure. UHDRS- FAS= Unified Huntington Disease Rating Scale- Functional Assessment Scale. UHDRS-TFC= Unified Huntington Disease Rating Scale- Total Functional Capacity. UHDRS- IS= Unified Huntington Disease Rating Scale- Independence Scale. UHDRS TMS=Unified Huntington Disease Rating Scale- Total Motor Score.

Table 2. Categorization of individuals into the stages of the disease and TFC scores, according to Shoulson and Fahn (1979)[22].

HD Stage	Score TFC	Disease Stage	Absolute Frequency	Relative Frequency (%)
Early	TFC 11 – 13	I	3	13.6
Middle	TFC 7 – 10	II	8	36.4
	TFC 3 – 6	III	6	27.3
Late	TFC 1 – 2	IV	2	9.1
	TFC 0	V	3	13.6
Total			22	100

TFC= Total Functional Capacity.

Table 3. Classification of the disease stages and the scores of the functional scales. The disease progression categories use the Shoulson and Fahn (1979)[22] TFC scores.

HD Stage	MBI (n=22)			FIM (n=22)			FAS (n=22)		
	Med.	**Min.**	**Max.**	**Med.**	**Min.**	**Max.**	**Med.**	**Min.**	**Max.**
Early (TFC 11-13)	100	100	100	125	124	125	24	20	24
Middle (TFC 3-10)	96	38	100	115	53	126	15.5	4	22
Late (TFC 0-2)	0	0	27	19	18	50	1	0	6

Subtitle: Med. - Median, Min. - Minimum, Max. - Maximum. TFC= Total Functional Capacity. MBI= Modified Barthel Index. FIM= Functional Independence Measure. FAS= Functional Assessment Scale. IS= Independence Scale.

HD individuals were categorized using disease progression according to the Shoulson and Fahn (1979)[22]. TFC scores and all scales are shown in Table 4. As well as in the additional Supplementary Tables (ST05 and ST06), for each patient and the respective individual and cumulative percentages according to the IS and TMS score.

Table 4. HD stages and the results of the UHDRS functional and motor sections (TFC, IS and TMS) application.

HD Stage	TFC (n=22)			IS (n=22)			TMS (n=22)		
	Med.	Min.	Max.	Med.	Min.	Max.	Med.	Min.	Max.
Early	12	11	13	90	90	90	14	5	21
Middle	8	3	10	80	50	90	50	6	88
Late	0	0	2	20	10	60	80	73	110

Subtitle: Med. - Median, Min. - Minimum, Max. - Maximum. TFC= Total Functional Capacity. IS= Independence Scale. TMS= Total Motor Score.

Correlation between functional and motor performance in HD individuals

We observed a strong negative correlation between functional performance as measured by the MBI, and motor performance as measured by TMS-UHDRS (***r***=-0.75 and $p<0.01$), meaning that the lower the TMS score the better the motor performance on the MBI. Functional impairment, measured using the FIM scale, showed a moderate negative correlation (***r***=-0.64 and $p=0.01$), with the motor performance obtained by TMS-UHDRS. Lower TMS score indicates greater motor impairment (Table 5).

Table 5. Correlation between each pair of functional scales (p<0.01).

Scales	TFC	FAS	IS	FIM	MBI
MBI	***r***=0.90** $p<0.01$	***r***=0.90** $p<0.01$	***r***=0.82** $p<0.01$	***r***=0.85** $p<0.01$	____
FIM	***r***=0.85** $p<0.01$	***r***=0.90** $p<0.01$	***r***=0.88** $p<0.01$	____	____
UHDRS TMS	***r***=-0.86** $p<0.01$	***r***=-0.82** $p<0.01$	***r***=-0.72** $p<0.01$	***r***=-0.64** $p=0.01$	***r***=-0.75** $p<0.01$

**the strong negative correlations that were significant. TFC= Total Functional Capacity. FAS= Functional Assessment Scale. IS= Independence Scale. TMS= Total Motor Score. FIM= Functional Independence Measure. MBI= Modified Barthel Index. UHDRS TMS=Unified Huntington Disease Rating Scale Total Motor Score.

There was a strong negative correlation of the functional performances, determined by the UHDRS sections TFC, FAS and IS with the TMS (***r***=-0.86, ***r***=-0.82; and ***r***=-0.72 respectively, $p<0.01$), indicating that motor and functional impairments assessed by UHDRS sections correspond each other (Table 5).

Comparison of the functional scales (UHDRS, FIM AND MBI) with regard to their similarities

The FIM and MBI scales were 97.3% similar considering the variability of their scores (R^2=0.973 and $p<.05$). A similarity of 73% was observed considering MBI scale and the TFC section (R^2=0.73 and $p<.05$). Furthermore, a similarity of 78% was observed for the functional scales UHDRS- TFC and FIM (R^2=0.78 and $p<.05$).

There was a strong association between each score obtained by UHDRS functional sections (FAS, TFC and IS) and the disease stage (score measured by TFC section) in individuals with HD (R^2= 0.97 and $p<.05$); which means that 97% similarity was observed between each functional section; therefore, they were able to identify the functional impairment of normal or abnormal individuals.

Descriptive statistical analysis and comparison of the functional and motor scales between the reference and the HD groups

In the reference group (n=22) and HD group (n=22), the median value, obtained after the application of each

functional scale, was used as a cutoff point for the evaluation of normal or abnormal functional performances. Table 6 shows the median, minimum and maximum values.

The scores obtained with each scale applied to the reference group were: 1) for FAS, the mean was 24.7±0.4. In 72.7% of the individuals, the FAS score was equal or lower than 18; 2) for TFC, 100% of the individuals obtained the maximum score 13; 3) for the IS section, all subjects obtained the maximum score 100; and 4) for TMS, 90.9% of the cases had a score equal or lower than three (the higher the score, the worse the motor performance).

The results obtained from the two groups were statistically significant different on the MBI functional scale (p=.002); the reference group score was 3.3 times higher than the HD group. The HD and reference group average scores were 71.7±8.5 and 100 (all the reference group individuals had the same score), respectively. There was no difference on the IBM score between males from the HD and reference groups (p=.11). There was a statistically significant difference when comparing the IBM score between females from the HD and reference groups (t=3.1, p=.006). The FIM scale detected that the performance of the reference group was 3.8 times higher (p<.05) than the performance of participants with HD, the average score for the reference group was 126 and 92.7±8.7 for the HD group. It is important to investigate and compare impairment between males and females with the aim of identifying whether females are more impaired. This may be due since

some neurological diseases (Parkinson's disease, ataxia and among other disease with movement disorder) in females present greater impairment when compared to males. In this study the reference group was compared with the HD group. The comparison of FIM scores between males from the HD and the reference groups was statistically different (t=2.2; p=.04) which means that the FIM scores of the affected group are lower or worse than the reference group. Similarly, the FIM scores of females from the HD group and reference group were also statistically different (t= 3.3; p=.004).

Furthermore, the reference group performed 7.2 times more functional independence as detected by UHDRS-FAS (p<.05) than the HD group: the average score of the reference group was 24.7±0.1 and the average score of the HD group 12.5±1.7. The HD group showed decreased functional performance when compared to the reference group as measured by both scales MBI and FIM, and even lower when the functional performance was measured by UHDRS-FAS.

In addition, the functional performance of the reference group using the UHDRS-TFC was 7.7 times higher (p<.05) than that of the HD group. There was a statistical difference on TFC score between males (t=4.6; p<.05) and females, as well as between the reference and the HD group (t=7.1; p<.05). All scales detected a greater deficiency in female functional capacity, when females from the HD and reference groups were compared, than the male counterpart. Concerning the IS, there was a difference when comparing

scores between males (t=3.3; p=.003) and females (t=5.1; p<.05) indicating that the IS was sensitive enough to distinguish between group differences and determine differences in functional capacity.

The UHDRS-TMS score was 7.9 times higher (p<.05) in HD group when compared with the reference group (higher score reflects greater disability). It is important to mention that the reference group was chosen to eliminate the bias of motor and functional impairment of the general population that usually increases according to age, since the individuals of both groups had similar ages. Normal results were found in the reference group as expected (Table 6).

Functional performance diagnostic testing with the FIM and MBI versus UHDRS (FAS, TFC AND IS)

The FIM and MBI were compared, about their testing properties, with the functional sections of the UHDRS (Table 7). Affected individuals were categorized as follows: values below the median as having abnormal functional performance; and above the median, as having a normal functional performance. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated for FIM and MBI using the UHDRS as reference (ST 07). Therefore, FIM and MBI can be applied to assess the functional performance because when we compared these scales with the UHDRS sections FAS, TFC and IS we observed similar results (p<.05) associated with the activities of daily living of HD patients.

Table 6. Reference group and HD group median, minimum and maximum scores.

		Reference Group			HD Group		
	Scales	**Median**	**Minimum Score**	**Maximum Score**	**Median**	**Minimum Score**	**Maximum Score**
Percentile Median	**MBI**	100	100	100	94	0	100
	25%	100			35.5		
	50%	100			94		
	75%	100			100		
	FIM	126	126	126	112	18	126
	25%	126			52.25		
	50%	126			112		
	75%	126			125		
	UHDRS FAS	25	24	25	14,5	0	24
	25%	24			5.50		
	50%	25			14.50		
	75%	25			19.25		
	UHDRS TFC	13	13	13	6,5	0	13
	25%	13			2.75		
	50%	13			6.50		
	75%	13			10		
	UHDRS IS	100	100	100	80	10	90
	25%	100			57.50		
	50%	100			80		
	75%	100			90		
	UHDRS TMS	0	0	20	55	5	110
	25%	0			22.50		
	50%	0			55		
	75%	2.25			74		

MBI= Modified Barthel Index. FIM= Functional Independence Measure. UHDRS- FAS= Unified Huntington Disease Rating Scale- Functional Assessment Scale. UHDRS- TFC= Unified Huntington Disease Rating Scale- Total Functional Capacity. UHDRS- IS= Unified Huntington Disease Rating Scale- Independence Scale. UHDRS TMS=Unified Huntington Disease Rating Scale- Total Motor Score.

Table 7. Comparison of two scales concerning Sensitivity, Specificity, PPV and NPV.

Compared Scales	Sensitivity	Specificity	PPV	NPV
FIM and FAS	100%	*	91%	**
FIM and TFC	100%	50%	95%	100%
FIM and IS	100%	91%	**	**
MBI and FAS	100%	*	59%	**
MBI and TFC	100%	11%	62%	100%
MBI and IS	100%	*	59%	**

*Specificity could not be calculated, because there was no negative case. **No significant result. FIM=Functional Independence Measure. MBI= Modified Barthel Index FAS= Functional Assessment Scale. TFC= Total Functional Capacity. IS= Independence Scale.

DISCUSSION

In this study, the females from the HD cohort showed a higher score on the functional scales FIM, IBM, FAS, TFC, IS and UHDRS-TMS, that means greater motor and functional impairment compared to men. Unlike our findings[26], other authors observed greater female impairment, when compared to males (37.1±21), only with UHDRS-TMS (39.4±21.2). The mean female age was 50.5±12.1yr (n= 636) and the mean male age was 51.1±12.0yr (n= 631)[26].

In this study, most participants with HD were in the middle stage of the disease, presenting with involuntary movements such as chorea, abnormal postures, balance deficit, abnormal gait steps, frequent falls, and difficulties in performing ADL and motor impairment. The early manifestations are generally mild; however, the disease progresses inexorably, and the individual develops severe

functional disabilities and difficulty in learning new tasks and also requires home care or comprehensive nursing home care[27–30].

We determined the cutoff value to classify individuals with HD as having normal functional performance or not. When individuals scored less than 90, with the IS section of the UHDRS, the functional performance was classified as abnormal, although the patients would not need physical care if difficult tasks were avoided. Peavy *et al*. (2009) used a different cutoff of 80 points[31]. They obtained this value by IS and applied to individuals with early disease (mean age of 41.6yr). At this point the patient could not develop tasks at his/her previous employment as before the disease, could not perform complex domestic tasks and needed help managing the finances[31].

Since the onset of symptoms, functional impairment can be observed and may interfere with daily work activities. This can be a target point to improve the development of functional instruments, in order to make such instruments more sensitive and reliable for the patient occupational assessment[19,28,32,33]. Among our participants, only 4.5% of the individuals had the maximum TFC score. This value was lower when compared to other study, who found 31.8%; furthermore, in our investigation, FAS classified 90% of individuals with a score lower than 24 points; on the other hand, it showed that 50% of individuals had minimal functional impairment and a score between 23 and 25[18].

In this investigation, the low value of maximum TFC score can be justified by the greater number of CAG repeats and the earlier motor symptoms of HD patients when compared with those patients of Beglinger *et al*. (2010)[18]. The duration of the disease favors longer impairment of the individual's functionality; therefore, the longer the disease duration, the lower can be the TFC score. In that study, 55% of the participants had a TFC score between 11 and 13, which corresponds to stage I of HD; in our study it was 13.6% of the participants[18].

We applied the UHDRS to a sample of 21 Brazilian HD patients, and correlated the results obtained by the TMS with the results of the functional sections FAS, TFC and IS. It was demonstrated that the motor performance shows a strong negative correlation with the functional performance, a result that corroborates those of our study[1]. When comparing the results obtained with the MBI functional performance scale with those using BI[34], it was observed that both results were similar: ours with an average score of 71.7±39.8 and theirs 76.9±22.9[1,34].

This present study showed that the average score for functional performance obtained with TFC was 6.1±4.1. Another investigation obtained 5.6±4.0 (n= 21 patients with HD)[1]. Investigating the influence of a certain medication, before and after the intervention, the authors did not determine the different stages of the disease. They found that the mean TFC score before the intervention was 5.6±1.8 in 34 people with HD[34].

MBI has been cited as an useful tool to assess the ability to perform the ADL, the level of functional dependence and also the effectiveness of a proposed rehabilitation intervention[22]. Individuals with HD, classified as having moderate dependence according to MBI, showed their functional performance by FAS with an mean of 12.5±7.9[35]. Individuals with HD were also assessed according to their functional performance using the BI, showing an average score of 19.2±1.2; that means total dependence; as well as FAS mean of 20.3±11.1[35].

In a one-year rehabilitation program the individuals were submitted to rehabilitation activities for a period of 9 weeks (3 weeks at 3 times a year for 12 months) and after that they were reassessed. It is worth mentioning that the individuals maintained the functions related to the ADL stable, without significant decline in the BI score (mean 19.3±1.6) and FAS (mean 21.2±12.1)[35]. The present study (a two-year program) showed that the average score for motor performance obtained with TMS was 52.8±29.6 (n=22 HD patients), and the mean duration of HD symptoms was 10.0±2.7yr. Another investigation obtained 47.4±9.8 points (n=10 HD patients) and the HD symptoms mean duration was 6.6±4.3yr[35].

Even if the individual, bearing the HD mutation, had not started the clinical manifestations (pre-symptomatic stage), it would be interesting to develop sensitive tools to the point of being able to detect minimal functional changes related to the onset of the disease and disturbance of his/her usual

occupational activities. This sensitivity could not be determined in this study, because the individuals were mostly in the early and middle stages of the disease, and none were in the pre-symptomatic stage. Furthermore, pre-symptomatic subjects were not selected according to the inclusion criteria because we could not offer predictive test for ethical reasons.

CONCLUSION

This study was the first one that reported the application of MIF and MBI scales in HD patients. FIM and MBI scales were sensitive in detecting functional dependence on ADL in individuals with HD and, we concluded that, comparing the results with UHDRS scale, there was no significant difference among the results of the three scales. In addition, the MBI and MIF can be good alternatives to be used by physical therapists to assess the functional performance of HD individuals and, consequently, can be effective in the strategy of rehabilitation programs, as well as to measure the progression of the disease, considering that these scales are already used in the clinical practice of physical therapists.

ACKNOWLEDGEMENTS

The investigators are very grateful to all the patients and their families that kindly agreed to participate in this study. The authors would like to thank CAPES (Coordenação

de Aperfeiçoamento de Pessoal de Nível Superior-Brazil) for the scholarship granted to D.R during his M.Sc. course.

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SUPPLEMENTARY TABLES (ST)

ST 01. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late) for each patient and the individual and cumulative percentage according to the TFC scores.

Disease Stage	Sample (N)	TFC Score	Individual Percentage	Cumulative Percentage
Early Stage	1	13	33.3	33.3
	1	12	33.3	66.7
	1	11	33.3	100
Total	3		100	
Middle Stage	1	3	7.1	7.1
	3	10	21.4	28.6
	2	9	14.3	42.9
	3	4	21.4	64.3
	2	2	14.3	78.6
	3	8	21.4	100
Total	14		100	
Late Stage	3	0	60	60
	1	1	20	80
	1	2	20	100
Total	5		100	

ST 02. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late) for each patient and the individual and cumulative percentage according to the MBI scores.

Disease Stage	Sample (N)	MBI Score	Individual Percentage	Cumulative Percentage
Early Stage	3	100	100	100
Total				
Middle Stage	1	38	7.1	7.1
	1	68	7.1	14.3
	1	79	7.1	21.4
	1	90	7.1	28.6
	1	91	7.1	35.7
	1	93	7.1	42.9
	1	95	7.1	50
	1	97	7.1	57.1
	6	100	42.9	100
Total	14		100	
Late Stage	4	0	80%	80%
	1	27	20%	100%
Total	5		100%	

ST 03. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late stages) for each patient and the individual and cumulative percentage according to the FIM score.

Disease Stage	Sample (N)	FIM Score	Individual Percentage	Cumulative Percentage
Early Stage	1	124	33.3	33.3
	2	125	66.7	100
Total	3		100	
Middle Stage	1	53	7.1	7.1
	1	98	7.1	14.3
	1	100	7.1	21.4
	1	103	7.1	28.6
	1	104	7.1	35.7
	1	110	7.1	42.9
	1	114	7.1	50
	1	116	7.1	57.1
	1	119	7.1	64.3
	1	120	7.1	71.4
	2	125	14.3	85.7
	2	126	14.3	100
Total	14		100	
Late Stage	1	18	20	20
	2	19	40	60
	1	20	20	80
	1	50	20	100
Total	5		100	

ST 04. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late stages) for each patient and the individual and cumulative percentage according to the FAS.

Disease Stage	Sample (N)	FAS Score	Individual Percentage	Cumulative Percentage
Early Stage	1	20	33.3	33.3
	2	24	66.7	100
Total	3		100	
	1	4	7.1	7.1
	3	8	2.4	28.6
	1	12	7.1	35.7
Middle Stage	1	14	7.1	42.9
	1	15	7.1	50
	1	16	7.1	57.1
	2	17	14.3	71.4
	1	18	7.1	78.6
	1	19	7.1	85.7
	1	20	7.1	92.2
	1	22	7.1	100
Total	14		100	
	1	0	20	20
Late Stage	3	1	60	80
	1	6	20	100
Total	5		100	

ST 05. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late stages) for each patient and the individual and cumulative percentage according to the IS.

Disease Stage	Sample (N)	IS Score	IndividualPercentage	Cumulative Percentage
Early Stage	3	90	100	100
Total	3			
Middle Stage	1	50	7.1	7.1
	2	60	14.3	21.4
	2	70	14.3	35.7
	4	80	28.6	64.3
	5	90	35.7	100
Total	14		100	
Late Stage	2	10	40	40
	2	20	40	80
	1	60	20	100
Total	5		100	

ST 06. Stages of the disease according to Shoulson and Fahn (1979)[22] (early, middle and late stages) for each patient and the individual and cumulative percentage according to the TMS.

Disease Stage	Sample (N)	TMS Score	Individual Percentage	Cumilative Percentage
Early Stage	1	5	33.3	33.3
	1	14	33.3	66.7
	1	21	33.3	100
Total	3		100	
Middle Stage	1	6	7.1	7.1
	1	21	7.1	14.3
	1	23	7.1	21.4
	1	39	7.1	28.6
	1	43	7.1	35.7
	1	44	7.1	42.9
	1	46	7.1	50
	1	54	7.1	57.1
	1	56	7.1	64.3
	1	57	7.1	71.4
	1	67	7.1	78.6
	1	69	7.1	85.7
	1	71	7.1	92.9
	1	88	7.1	100
Total	14		100	
Late Stage	1	73	20	20
	1	77	20	40
	1	80	20	60
	1	98	20	80
	1	110	20	100
Total	5		100	

ST 07. The number of individuals evaluated as normal (-) or abnormal (+) was according to the UHDR results (FAS, TFC and IS sections).

Number of patients with abnormal or normal performance, assessed by UHDRS sections FAS and FIM

		FAS +	FAS -	
FIM	+	20 (a)	2 (b)	22
	-	0 (c)	0 (d)	0
	Total	20	2	22

Number of patients with abnormal or normal performance assessed by UHDRS sections FAS and MBI

		FAS +	FAS -	
MBI	+	13 (a)	9 (b)	22
	-	0 (c)	0 (d)	0
	Total	13	9	22

Number of patients with abnormal or normal performance assessed by UHDRS sections TFC and FIM

		TFC +	TFC -	
FIM	+	20 (a)	1 (b)	21
	-	0 (c)	1 (d)	1
	Total	20	2	22

Number of patients with abnormal or normal performance assessed by UHDRS sections TFC and MBI

		TFC +	TFC -	
MBI	+	13 (a)	8 (b)	21
	-	0 (c)	1 (d)	1
	Total	13	9	22

Number of patients with abnormal or normal performance assessed by UHDRS sections IS and FIM

		IS +	IS -	
FIM	+	20 (a)	2 (b)	22
	-	0 (c)	0 (d)	0
	Total	20	2	22

Number of patients with abnormal or normal performance assessed by UHDRS sections IS and MBI

		IS +	IS -	
MBI	+	13 (a)	9 (b)	22
	-	0 (c)	0 (d)	0
	Total	13	9	22

MBI= Modified Barthel Index. FIM= Functional Independence Measure. FAS= Functional Assessment Scale. TFC= Total Functional Capacity. IS= Independence Scale.