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The unified Multiple System Atrophy Rating Scale: Intrarater reliability

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Abstract

Background—The unified multiple system atrophy rating scale was developed to provide a surrogate measure of disease progression in multiple system atrophy. In the present study, the intrarater agreement of the motor examination part of the unified multiple system atrophy rating scale was determined.

Methods—All patients were first examined face-to-face, whilst being video-recorded, by two senior and two junior investigators. The patients' videotaped examinations were re-evaluated after 3 months. Intrarater reliability for each item was analyzed by kappa statistics.

Results—Overall weighted κ values were at least substantial or excellent for all unified multiple system atrophy rating scale motor examination items except for ocular motor dysfunction which showed only moderate intrarater agreement. Intrarater reliability was comparable between senior and junior raters with all κ differences being ≥ 0.22 .

Conclusions—The motor examination part of the unified multiple system atrophy rating scale was found to have satisfactory intrarater reliability in the present cohort.

Keywords

Multiple system atrophy; MSA; UMSARS; rating scale; EMSA-SG

Introduction

Multiple system atrophy (MSA) is a relentlessly progressive and ultimately fatal neurodegenerative disease characterized clinically by autonomic failure accompanied by characteristic motor features.^{1, 2} According to applicable diagnostic criteria two motor variants may be distinguished; patients with predominant parkinsonism are designated MSA-P, whereas MSA-C applies to patients having a prominent cerebellar phenotype.³ In addition, three diagnostic categories of increasing certainty were specified: possible, probable, and definite MSA. While definite MSA requires pathological confirmation of widespread glial cytoplasmic inclusions accompanied by a distinct pattern of neurodegeneration,⁴ possible and probable MSA rely on clinical and neuroimaging findings.³ Patient care is currently restricted to symptom-based therapy because of the current absence of disease-modifying agents.⁵ The European MSA Study Group (EMSA-SG) recognized the need for a disease-specific rating instrument which may serve as an outcome measure in clinical trials, and thus reliably determine the efficacy of given interventions. We therefore developed and validated the Unified MSA Rating Scale (UMSARS).⁶ During the validation process, the UMSARS was shown to be a reasonably short, multidimensional, reliable, and valid scale for semiquantitative assessment of Caucasian MSA patients with high internal consistency and substantial-to-excellent interrater agreement.⁶ Subsequently, two independent groups confirmed the instrument's sensitivity to change^{7, 8} which allowed the conduct of multicenter clinical trials exploiting UMSARS as surrogate measure of disease progression.^{9, 10} We here report the intrarater reliability of the motor examination part of UMSARS as determined in a multicenter validation study.

Methods

A total of 40 patients with a clinical diagnosis of MSA according to the initial Gilman criteria¹¹ were recruited in four EMSA-SG centers (Bordeaux, Innsbruck, London, Toulouse) and assessed on their regular medication. Global disease severity was determined by Hoehn & Yahr staging (H&Y) and a 3-point disease severity scale (SS-3).⁶ Intrarater validation was performed in a two-step approach. First, all patients were examined face-to-

face (live rating) by one senior investigator travelling to the centers (GKW) as well as an additional senior and two junior investigators from each local center (Local rater teams were Bordeaux: FT [senior], IG [junior], FY [junior]; Innsbruck: WP [senior], KS [junior], ADZ [junior]; London: NPQ [senior], MB [junior], TS [junior]; Toulouse: OR [senior], MG [junior], FO [junior]). Board-certified neurologists with long-lasting experience in movement disorders were considered senior investigators whereas the term junior investigators applied to residents in neurology. Each face-to-face examination was recorded on videotape. In a second step, three months after the initial examination, the same investigators re-rated the motor part of the UMSARS examination from the original video recordings. In order to obtain independent assessments, the examiners were not allowed to exchange opinions during evaluations. Finally, as rigidity cannot be judged by inspection, item 6 of the UMSARS motor examination subscale (“Increased tone”) was excluded from the present analysis.

Statistical Analysis

Data were analysed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA) and Excel (Microsoft, Redmond, WA, USA). Intrarater reliability among individual junior and senior raters as well as overall agreement for each UMSARS motor examination item were determined by kappa (κ) statistics.^{12, 13} Weighted κ values were calculated by means of quadratic disagreement weights¹⁴ and interpreted as follows according to recommendations published previously:¹⁵ 0 to 0.20 slight agreement; 0.21 to 0.40 fair agreement; 0.41 to 0.60 moderate agreement; 0.61 to 0.80 substantial agreement; 0.81 to 1.00 excellent agreement. Intrarater agreement of UMSARS motor examination subscore of live examination and video rating was determined using intraclass correlation coefficients (ICC) derived from a one-way random effects analysis of variance model.¹⁶

Results

In the present cohort, MSA-P was more frequent than MSA-C (MSA-P:MSA-C 1.8:1) with diagnostic certainty being considered probable in 32 and possible in 8 out of 40 cases. Mean (standard deviation) age at symptom-onset and disease duration were 57.0 (8.5) and 6.0 (4.2) years, respectively. Further demographic and clinical data are given in Table 1.

Intrarater agreement

The results of the intrarater reliability analysis are summarized in Table 2. Overall weighted κ values were at least substantial (κ (w) = 0.6–0.8) or excellent (κ (w) = 0.8) for all UMSARS motor examination items except for ocular motor dysfunction which showed moderate intrarater agreement. Intrarater reliability was comparable between senior and junior raters with all κ discrepancies being ≤ 0.22 . Finally, intraclass correlation coefficients proved the UMSARS motor examination subscore to be reliable.

Discussion

It was previously demonstrated that the UMSARS is a MSA-specific semi-quantitative assessment instrument showing high internal consistency as well as substantial to excellent

interrater reliability⁶. Moreover, two independent groups have shown that UMSARS scores are sensitive to change.^{7, 8} To complete the validation process of the scale, we here report the results of an intrarater validation study.

The motor examination part of the UMSARS underwent intrarater reliability testing by comparison of live rating to subsequent video analysis of the initial examination 3 months later. Our results revealed that all but one item (ocular motor dysfunction) had substantial to excellent intrarater agreement. Ocular motor dysfunction showed moderate agreement which might be explained by the challenge of scoring eye movement using video analysis. As expected, κ values were higher in the intrarater reliability study compared to the interrater reliability study published previously.⁶ Moreover, intrarater agreement was comparable among senior and junior examiners with differences in κ values being below or equal to 0.20 except for item 3 (ocular motor dysfunction) which had a κ of 0.22. The latter observation confirms the previous finding that junior investigators can use the UMSARS reliably once they are trained in applying the UMSARS and provided they receive detailed instructions.⁶

The present study further underscores that the UMSARS has satisfactory intrarater reliability as a disease-specific and multidimensional rating instrument for semi-quantitative assessment of MSA patients. However, some limitations have to be acknowledged. Video analysis may not perfectly replicate a face-to-face examination. An intrarater study with two live examinations separated by a certain time interval is difficult to perform in MSA. Choosing an appropriate time interval between two live examinations is limited by the rapidly progressive disease course of MSA. Thus, as demonstrated by two studies with the serial application of the UMSARS at patients with MSA,^{7, 8} the progressive nature of the disease would have led to a deterioration of the UMSARS score and several of the UMSARS items at follow-up. On the other hand, a short follow-up between two potential live examinations might have introduced a bias towards overestimation of the intrarater reliability values. Therefore, we chose this study design of a videotaped face-to-face examination of the patients followed by a re-evaluation using the same video 3 months later. Furthermore, since the scale was validated in European Caucasians, its validity and applicability in a different racial or ethnic context remains to be established. Finally, UMSARS does not cover every aspect of the complex phenomenology of MSA, so that other validated scales may need to be developed to document a more comprehensive picture of the disease.

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Table 1

Demographics and clinical characteristics

Patients (n)	40
Gender (male/female, n)	16/24
MSA-P/C (n)	26/14
MSA-possible/probable (n)	8/32
Age at onset, years (mean \pm SD)	57.0 \pm 8.5
Disease duration, years (mean \pm SD)	6.0 \pm 4.2
H & Y stage, median (range)	4 (2 – 5)
3-point severity scale (n)	5 / 13 / 22
UMSARS (mean \pm SD, median, IQR)	52.3 \pm 18.3, 53.5, 31.0
UMSARS ADL (mean \pm SD, median, IQR)	25.8 \pm 9.6, 25.0, 16.0
UMSARS ME (mean \pm SD, median, IQR)	26.5 \pm 9.6, 25.5, 13.5

MSA-P/C ... multiple system atrophy-parkinsonian subtype/cerebellar subtype; H & Y stage ... Hoehn & Yahr staging (0 – 5); 3-point severity scale ... mild / moderate / severe; UMSARS ... Unified MSA rating scale (0 – 104); UMSARS ADL ... UMSARS subscale “Activities of daily living” (0 – 48); UMSARS ME ... UMSARS subscale “Motor examination” (0 – 56)

Table 2

UMSARS motor examination: Intrarater reliability. κ (w) over all centres; 0– 0.20, slight agreement; 0.21– 0.40, fair agreement; 0.41– 0.60, moderate agreement; 0.61– 0.80, substantial agreement; 0.81–1.00, excellent agreement.

Item	κ (w)		
	SR	JR	Overall
1 Facial expression	0.75	0.71	0.74
2 Speech	0.84	0.75	0.79
3 Ocular motor dysfunction	0.57	0.44	0.50
4 Tremor at rest	0.73	0.73	0.73
5 Action tremor	0.82	0.69	0.76
6 Increased tone	Not applicable		
7 Rapid alternating movement of hands	0.68	0.60	0.64
8 Finger tapping	0.78	0.74	0.76
9 Leg agility	0.80	0.60	0.71
10 Heel-Shin test	0.84	0.82	0.83
11 Arising from chair	0.96	0.97	0.96
12 Posture	0.86	0.84	0.85
13 Body sway	0.90	0.91	0.91
14 Gait	0.89	0.90	0.89
ICC of UMSARS II score - 1st examination	0.98	0.97	0.98

Abbreviations: ICC ... intraclass coefficient; κ (w) ... weighted kappa; SR ... senior rater; JR ... junior rater; UMSARS ... unified MSA rating scale.