

Proposing a Parkinson's Disease–Specific Tremor Scale From the MDS-UPDRS

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ABSTRACT

Background: This article proposes an International Parkinson and Movement Disorder Society (MDS)-UPDRS tremor-based scale and describes its measurement properties, with a view to developing an improved scale for assessing tremor in Parkinson's disease (PD).

Methods: This was a cross-sectional, multicenter study of 435 PD patients. Rasch analysis was performed on the 11 MDS-UPDRS tremor items. Construct validity, precision, and test-retest reliability were also analyzed.

Results: After some modifications, which included removal of an item owing to redundancy, the obtained MDS-UPDRS tremor scale showed moderate reliability, unidimensionality, absence of differential item function-

ing, satisfactory convergent validity with medication, and better precision than the raw sum score. However, the scale displayed a floor effect and a need for more items measuring lower levels of tremor.

Conclusions: The MDS-UPDRS tremor scale provides linear scores that can be used to assess tremor in PD in a valid, reliable way. The scale might benefit from modifications and studies that analyze its responsiveness. © 2015 International Parkinson and Movement Disorder Society

Key Words: Parkinson's disease; MDS-UPDRS; tremor; Rasch analysis

Tremor is the most frequent initial motor symptom of Parkinson's disease (PD): 36% to 49% of patients have tremor-dominant PD or a balance between tremor and gait symptoms.¹ Although efforts have been made to develop valid, reliable scales to quantify tremor in essential tremor,² there is no specific tremor scale for PD.

Several tremor items are included in the UPDRS, the most widely used clinical rating scale in PD recently revised as the International Parkinson and Movement Disorder Society (MDS)-UPDRS.³ A study measured PD tremor using the Tremor Index, using items rating rest, postural, and action tremor.⁴ However, there was no information about its psychometric properties beyond construct validity.

Because the MDS-UPDRS scale is widely used and includes several tremor items, the aim of this study was to propose an improved tremor measure for PD. The measurement properties of the MDS-UPDRS tremor scale were assessed using Rasch analysis.⁵ Its advantages are to capture important aspects of PD tremor, the use of MDS-UPDRS items, and obtaining results in a linear measure.

Patients and Methods

Patients and Measures

A sample of 435 outpatients diagnosed with PD was drawn from an observational, cross-sectional study in five Spanish-speaking countries.⁶ Ethic committees of the participating centers approved the study and patients provided written informed consent. Details about the study are described elsewhere.⁶ In a subsample of 51 stable patients, the MDS-UPDRS was applied again, by the same rater, 7 to 14 days later. Movement disorders specialists applied the Spanish MDS-UPDRS⁶ and Hoehn and Yahr (H & Y) staging.⁷

Statistical Analysis

A Rasch analysis was performed on 11 MDS-UPDRS items that address tremor.⁸ One item belongs

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TABLE 1. Fit of the tremor scale to the Rasch model

| | | Ideal Values | Initial Analysis | Final Analysis |
|----------------------------|---------|----------------|--------------------|---------------------|
| Number of items | | | 11 | 7 |
| Item residual | Mean | 0.0 | -1.005 | -0.858 |
| | SD | <1.4 | 2.035 | 1.219 |
| Person residual | Mean | 0.0 | -0.348 | -0.315 |
| | SD | <1.4 | 0.866 | 0.785 |
| Chi-square | Value | | 150.961 | 91.358 |
| | P level | >0.05/n. items | <0.0001 | 0.011 |
| PSI | | >0.70 | 0.764 | 0.614 |
| Unidimensional test % (CI) | | (LCI <5%) | 8.28 (0.062-0.103) | 1.85 (-0.002-0.039) |

PSI, person separation index; LCI, lower confidence interval.

to Part II (2.10 tremor), and the others to Part III: 3.15a postural tremor-right hand; 3.15b postural tremor-left hand; 3.16a kinetic tremor-right hand; 3.16b kinetic tremor-left hand; 3.17a rest tremor amplitude-RUE; 3.17b rest tremor amplitude-LUE; 3.17c rest tremor amplitude-RLE; 3.17d rest tremor amplitude-LLE; 3.17e rest tremor amplitude-lip/jaw; and 3.18 constancy of rest tremor.

Rasch analysis models the probability of a specific response as a function of person and items parameters and allows ordering persons and items in the same logit scale.⁵ Details are presented in Appendix 1 and excellent Rasch analysis tutorials are available.⁹⁻¹¹ Rasch analysis has several advantages over classical methods: robustness against missing data; continuous interval linear measure; known precision and accuracy; and using parametric statistics in lineal analysis.¹² After obtaining fit to the Rasch model, the person locations were imported to the statistical software IBM SPSS Statistics 19 (IBM Corp. Armonk, NY). Test-retest reliability was calculated through bidirectional random effects intraclass correlation coefficient (ICC > 0.7).¹³

For discriminant validity, we expected to find low Pearson's correlation coefficients ($r < 0.30$) between the tremor linear measure and each of the MDS-UPDRS sections (Parts I-IV), corrected for item overlap.^{21,22} Coefficients of 0.30 to 0.59 were considered as of moderate magnitude.¹⁴

For construct validity, patients on levodopa were expected to have lower tremor values than the others (independent t test).⁴ We also performed a post-hoc comparison by disease duration (cutoff by the median, 7 years) and phenotype groups: tremor dominant or postural instability/gait difficulty (PIGD).¹ The mean of MDS-UPDRS items 2.10, 3.15a-b, 3.16a-b, 3.17a-e, and 3.18a was divided by the mean of the MDS-UPDRS items 2.12, 2.13, 3.10-12. A ratio ≥ 1.15 indicated tremor dominant and ≤ 0.90 PIGD.¹

For precision, the standard error of measurement [SEM = $SD\sqrt{(1-ICC)}$] was calculated.¹⁵ The SEM should be < 0.5 SD and the upper level of the 95%

confidence interval (CI) approaches the minimal detectable change.¹⁵ For relative precision, we compared the linear measure with the sum of item raw scores in their ability in discriminating among groups by medication and disease duration.¹⁷

Results

Mean \pm standard deviation (M \pm SD) age was 66.71 \pm 10.32 years, 51.49% were males, with 11.14 \pm 4.70 years of education. Disease duration was 8.52 \pm 6.14 years, 80.5% of patients were treated with L-dopa as monotherapy, and 61.8% were in H & Y stage 2. Only one item had a missing value (0.2%).

To reach fit to the Rasch model, the following modifications were performed: response scale rescoring; creation of super-items; and deletion of one item (Appendices 1-4). The final model was satisfactory, with no item bias (Table 1).

Given model fit to the Rasch, raw scores were converted into an interval scale measure using a transformation table (Appendix 3). The tremor scale had a M \pm SD = 11.131 \pm 5.390, range of 0 to 22.909, skewness = -0.830, and SEM = 2.156 (upper 95% CI = 4.222). For the rawscores: SEM = 2.176; SD = 5.736). For test-retest reliability, ICC = 0.856.

For the total group (Table 2), tremor scores were significantly lower for patients taking L-dopa and with higher disease duration (t test, $p < 0.005$). These differences were not significant when using raw sum scores, and the relative precision (3.218 and 6.627 for medication and disease duration, respectively) favored the linear measure. The correlation coefficients between the tremor measure and the MDS-UPDRS sections were close to zero ($r = -0.091-0.038$). The correlation between the item 3.18 "constancy of rest tremor" and the linear tremor measure scores was 0.674.

Approximately one third of patients (34.3%) were tremor dominant (Table 2). In this group, the tremor scale showed a low correlation with Parts I and II ($r = 0.27-0.29$; $P \leq 0.001$) and moderate with Part III

TABLE 2. MDS-UPDRS tremor linear scores by sociodemographic and clinical variables, for the total sample, and tremor-dominant and postural instability/gait difficulty groups

| | Total Sample | | | Tremor Dominant ^a | | | PGID ^a | | |
|-------------------------------------|--------------|-------|---------|------------------------------|-------|---------|-------------------|-------|---------|
| | (n = 435) | | | (n = 149) | | | (n = 239) | | |
| | Mean | SD | P Value | Mean | SD | p-value | Mean | SD | P Value |
| Sex | | | 0.729 | | | 0.718 | | | 0.475 |
| Male | 11.126 | 5.053 | | 14.252 | 2.518 | | 9.017 | 5.244 | |
| Female | 10.633 | 5.807 | | 14.414 | 2.912 | | 8.496 | 5.953 | |
| Age, years | | | 0.430 | | | 0.625 | | | 0.222 |
| ≤68 | 11.258 | 5.095 | | 14.227 | 2.782 | | 9.205 | 5.322 | |
| >68 | 10.495 | 5.739 | | 14.446 | 2.585 | | 8.318 | 5.842 | |
| Education level, years | | | 0.446 | | | 0.761 | | | 0.945 |
| ≤11 | 11.028 | 5.511 | | 14.386 | 2.541 | | 8.790 | 5.820 | |
| >11 | 10.754 | 5.323 | | 14.250 | 2.873 | | 8.740 | 5.375 | |
| Medication (L-dopa) | | | 0.003 | | | 0.629 | | | 0.976 |
| No | 12.446 | 4.252 | | 14.196 | 2.010 | | 8.796 | 5.434 | |
| Yes | 10.808 | 5.592 | | 14.396 | 3.020 | | 8.761 | 5.623 | |
| Disease duration, years | | | 0.004 | | | 0.206 | | | 0.500 |
| ≤7 | 11.633 | 4.635 | | 14.106 | 2.395 | | 9.056 | 4.997 | |
| >7 | 10.152 | 6.026 | | 14.763 | 3.187 | | 8.572 | 5.963 | |
| H & Y stage | | | 0.277 | | | 0.002 | | | 0.001 |
| 1 | 11.658 | 3.906 | | 12.942 | 2.635 | | 8.388 | 4.782 | |
| 2 | 10.915 | 5.361 | | 14.544 | 2.595 | | 7.632 | 5.099 | |
| 3 | 9.741 | 5.990 | | 16.574 | 2.288 | | 9.090 | 5.830 | |
| 4 | 11.931 | 5.916 | | — | — | | 11.931 | 5.916 | |
| 5 | 13.151 | 5.201 | | — | — | | 13.151 | 5.201 | |
| Pearson correlations with MDS-UPDRS | r | | P Value | r | | P Value | r | | P Value |
| Part I | 0.022 | | 0.650 | 0.267 | | 0.001 | 0.170 | | 0.008 |
| Part II (without tremor item) | 0.011 | | 0.814 | 0.288 | | <0.001 | 0.304 | | <0.001 |
| Part III (without tremor items) | 0.038 | | 0.432 | 0.437 | | <0.001 | 0.187 | | 0.004 |
| Part IV | -0.091 | | 0.060 | 0.049 | | 0.555 | 0.145 | | 0.025 |

For all group comparisons, *t* tests were used except for comparisons by H & Y (ANOVA).

^a“Indeterminate” type patients were not included in the analyses because of its low frequency (n = 46).

($r = 0.44$; $P < 0.001$). There was a significant trend (analysis of variance [ANOVA]: $P = 0.002$) with tremor scores increasing with H & Y stages 1-3.

Discussion

Rest tremor is one of the cardinal signs of PD, and most motor examination scales in PD include items addressing tremor. This article aimed at proposing a scale based on the MDS-UPDRS tremor items and assessing its measurement properties using Rasch analysis.

The obtained scale was unidimensional, supporting the use of sum scores as a global PD tremor measure. The correlation between the item “constancy of rest tremor” and the linear tremor measure scores indicates a high convergent validity. A previous study also showed that constancy of tremor, as measured with an actigraph, was a good indicator of tremor severity.¹⁸

The MDS-UPDRS tremor scale presented a satisfactory, but moderate, reliability, probably owing to a small number of items and floor effect. However, this instrument is useful to measure patients with higher levels of tremor in PD. A floor effect for rest, postural,

and kinetic tremor has been documented for the previous version of the UPDRS.¹⁹ The person-item distribution suggests that more items are needed, especially measuring lower tremor levels. In addition, the impact of tremor on social functioning, a clinically important problem in PD, is not captured by the MDS-UPDRS scale. Given that almost all items of this scale are rated by the clinician, the scale might benefit from the addition of items centered on the patient’s perspective. Items to be added, which could be drawn from other tremor scales, should be assessed according to content and overall purpose of the tool: assessing tremor in PD patients.

Our study found evidence that, for each hand, the scores of kinetic and postural tremor should be considered as a single item. This was also observed for rest tremor amplitude of left and lower extremities. A confirmatory factor analysis of the UPDRS motor section also showed a high unexplained residual correlation between these items.²⁰ In addition, the items’ hierarchy reflects the initial unilateral involvement, which supports the content validity of the scale.

Our results support the measure's construct validity with other variables. As hypothesized, the tremor measure showed good discriminant validity with the MDS-UPDRS sections. Tremor in PD is a relatively independent sign/symptom, with a loose relationship with other features.^{21,22} Another study, using the UPDRS, revealed that tremor is significantly influenced by age, but not gender.²³ These results are partially concordant with ours. Tremor scores were significantly lower in patients taking L-dopa, which is congruent with the tremor-beneficial medication effect.⁴

As in other studies, the linear measure showed a lower SEM and better relative precision than the raw scores.²⁴ Thus, the use of the linear measure instead of sum scores is recommended. More studies are needed to fully evaluate the scale's responsiveness.

Some limitations must be acknowledged. We did not include an objective tremor measure, because our study is based on secondary data analysis. Previous studies show a significant, high-magnitude correlation between the UPDRS 3.0 tremor items and objective measures [19,23,25].^{19,23,25} In addition, information about L-dopa equivalent daily dose was not available. Although the scale's responsiveness has not been formally tested and longitudinal studies are needed, its precision was adequate.¹⁵

In summary, the MDS-UPDRS tremor scale has several strengths, but also some weaknesses. On one hand, the MDS-UPDRS tremor scale is a short instrument specific for PD tremor, using items already available, that provides a linear measure unbiased that is by age, sex, and education. It is strictly unidimensional, its reliability is moderate, it captures the lateralization of tremor symptoms, has good construct validity, and is a more precise measure than the raw sum scores. On the other hand, the scale shows potential for improvement. The addition of more items targeting low tremor levels would probably resolve its floor effect and improve reliability. Modifications of the scale would require further validation studies. More research is needed to further evaluate the scale's validity and sensitivity to change. ■

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.