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BRIEF COMMUNICATION

# Accuracy of MDS-UPDRS section IV for detecting motor fluctuations in Parkinson's disease

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## Abstract

**Background** In a precedent paper, we validated part IV of the Unified Parkinson's Disease Rating Scale (UPDRS) for detecting motor fluctuations in Parkinson's Disease (PD) patients using a 12-h Waking-Day Motor Assessment (WDMA) as gold standard, showing a high sensitivity (> 80%) and a lower specificity (< 45%). The aim of this study was to validate the Movement Disorder Society-UPDRS (MDS-UPDRS) part IV, especially items 4.3 and 4.5, using the same methodology.

**Methods** PD patients attending the Movement Disorders Clinic at the University Hospital in Catania were consecutively enrolled in the study. A diurnal WDMA was performed to detect motor fluctuations. At each time interval, the motor impairment was evaluated using the motor section of the MDS-UPDRS. Presence or absence of motor fluctuations and the type of motor fluctuation were assessed by four blinded expert raters in movement disorders, by evaluating the graphical representations of the WDMA. We evaluated sensitivity and specificity together with 95% Confidence Interval (CI) of items 4.3 and 4.5, using WDMA as gold standard.

**Results** We estimated for item 4.3 of the MDS-UPDRS a sensitivity of 74.3% (95% CI 56.7–87.5) and a specificity of 70.6% (95% CI 44–89.7), while for item 4.5, a sensitivity of 67.9% (95% CI 47.6–84.1) and a specificity of 66.7% (95% CI 44.7–84.4).

**Conclusions** The present showed a higher specificity level for MDS-UPDRS with respect to the UPDRS, while a slightly lower sensitivity mainly for predictable OFF.

**Keywords** MDS-UPDRS validation · 12-h waking-day motor assessment (WDMA) · Motor fluctuations · Wearing-off · Dyskinesia

## Introduction

Motor complications appear in approximately 50% of patients on levodopa therapy for more than 5 years [1]. Motor response and tolerability to dopaminergic drugs in Parkinson's Disease (PD) patients may depend on several factors and there are still few evidences about the role of specific diagnostic instruments, including functional neuroimaging techniques, as support for the clinical judgment when evaluating motor response in PD patients and their pharmacological management [2, 3]. We validated part IV of the Unified Parkinson's Disease Rating Scale (UPDRS) version 3.0 [4] for detecting motor fluctuations using a 12-h Waking-Day Motor Assessment (WDMA) as gold standard, showing a high sensitivity (> 80%) and a lower specificity (< 45%) [5]. The aim of this study was to validate the Movement Disorder Society-UPDRS (MDS-UPDRS) [6] part IV, especially items 4.3 and 4.5, using the same methodology.

## Materials and methods

PD patients attending the Movement Disorders Clinic at the University Hospital in Catania were consecutively enrolled in the study. A diurnal WDMA was performed to detect motor

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**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s10072-019-03745-2) contains supplementary material, which is available to authorized users.

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fluctuation [5]. At each time-interval, the motor impairment was evaluated using the motor section of the MDS-UPDRS [5]. Presence or absence of motor fluctuations and the type of motor fluctuation were assessed by four blinded expert raters in movement disorders, by evaluating the graphical representations of the WDMA. Details on the evaluation of the graphical representations of the WDMA are reported elsewhere [5]. An "excellent" agreement between raters (Cohen's $k > 0.80$) was considered when there was an agreement of at least three out of the four raters. When less than three raters were in agreement, a consensus was reached after a group discussion.

Motor fluctuations were also evaluated by the MDS-UPDRS part IV, computing the hours spent in the OFF state by the item 4.3 and by determining the usual predictability of OFF state by the item 4.5, considered as the wearing off phenomenon (WO) identification item. Presence or absence of motor fluctuation (item 4.3) and predictability of OFF (item 4.5) was analyzed as a dichotomous variable. Item 4.3 ("Time spent in the OFF state") was dichotomized to differentiate fluctuating from stable patients based on patients' score, respectively $\geq 1$ and $< 1$. Item 4.5 ("Complexity of motor fluctuations") was dichotomized to detect the presence of WO if patient's score was $\geq 1$ and lower than four ("OFF episodes are rarely predictable").

We evaluated the sensitivity, specificity, positive and negative predictive values as well as accuracy of items 4.3 and 4.5, using the evaluation on WDMA as gold standard [5]. 95% Confidence Interval (CI) has been also computed. Difference in scalar measures between independent groups has been tested using the *t* test. The study was approved by the local ethics committee.

## Results

Fifty-two PD patients were enrolled in the study. Baseline characteristics of PD patients are shown in Table 1. Item 4.3 score was in average 1 ± 1, with 21 (40.4%) patients having a score equal to 0, 14 (26.9%) equal to 1, 13 (25%) equal to 2, and 4 (7.7%) equal to 3. Item 4.5 score was in average 0.8 ± 0.9, with 25 (48.1%) patients having a score equal to 0, 16 (30.8%) equal to 1, 8 (15.4%) equal to 2, and 3 (5.8%) equal to 3. No patient presented a 4.5 item score equal to 4. According to the raters' evaluation, 35 (67.3%) out of the 52 patients were classified as having motor fluctuation during the WDMA. On the contrary, according to the item 4.3 of the MDS-UPDRS section IV, 31 PD patients (59.6%) reported to spend some time in the OFF state giving a sensitivity of 74.3% (95% CI 56.7–87.5), a specificity of 70.6% (95% CI 44–89.7), and an accuracy of 73.1% (95% CI 59–84.4). Details are reported in Table 2. Taking into account only the predictability of OFF time (WO), based on the raters evaluation, 28 PD patients (53.8%) were classified as having WO.

**Table 1** Clinical characteristics of PD study patients

| Clinical characteristics | 52 pts |
|---|---|
| Age (years) | 66 ± 8.17 |
| Age at onset (years) | 58.9 ± 8.9 |
| Age at diagnosis (years) | 60.3 ± 9.1 |
| Disease duration (years) | 7.21 ± 4.84 |
| LEDD (mg) | 774.4 ± 444.1 |
| MMSE score | 26.6 ± 3.21 |
| H-Y (OFF) stage | 2.53 ± 0.65 |
| MDS-I score | 9.13 ± 4.26 |
| MDS-II score | 11.9 ± 6.45 |
| MDS-III OFF score | 40.4 ± 15.9 |
| MDS-III ON score | 33.4 ± 13.7 |
| MDS-IV score | 4.13 ± 4.17 |

Values are mean ± standard deviation

*LEDD* levodopa equivalent daily dose, *MMSE* Mini Mental State Examination, *H-Y* Hoehn-Yahr, *MDS-UPDRS* Movement Disorders Society—Unified Parkinson's Disease Rating Scale

On the other hand, according to item 4.5 of the MDS-UPDRS, 27 PD patients (51.9%) reported a predictability motor fluctuation giving a sensitivity of 67.9% (95% CI 47.6–84.1), a specificity of 66.7% (95% CI 44.7–84.4), and an accuracy of 67.3% (95% CI 52.9–79.7) — see Table 2. Differences in clinical characteristics between stable and fluctuating patients as well as between patients with and without WO detected at the WDMA are reported in the Supplementary Table.

**Table 2** Sensitivity and specificity of MDS-UPDRS items 4.3 and 4.5

| 52 pts | WDMA | | | Item 4.3 | |
|---|---|---|---|---|---|
| Item 4.3 | + | – | Tot | Sensitivity | Specificity |
| + | 26 | 5 | 31 | 74.3% (95% CI 56.7–87.5%) | 70.6% (95% CI 44–89.7) |
| – | 9 | 12 | 21 | | |
| Tot | 35 | 17 | 52 | Positive predictive value | Negative predictive value |
| | | | | 83.9% (95% CI 70.8–91.8) | 57.1% (95% CI 41.2–71.7) |
| 52 pts | WDMA | | | Item 4.5 | |
| Item 4.5 | + | – | Tot | Sensitivity | Specificity |
| + | 19 | 8 | 27 | 67.9% (95% CI 47.6–84.1) | 66.7% (95% CI 44.7–84.4) |
| – | 9 | 16 | 25 | | |
| Tot | 28 | 24 | 52 | Positive predictive value | Negative predictive value |
| | | | | 70.4% (95%CI 56.1–81.5) | 64% (95%CI 49.2–76.6) |

*WDMA* 12-h Waking-Day Motor Assessment, *CI* confidence interval

## Discussion

This is the first validation study of the MDS-UPDRS part IV, items 4.3 and 4.5. The present findings compared to the previous study on validation of UPDRS-IV version 3.0 [5] showed a higher specificity level for MDS-UPDRS with respect to the UPDRS 3.0. (item 4.3 vs items 36–38, 70.6% vs 43.5%; item 4.5 vs item 36, 66.7% vs 40%), but with a consequent slightly lower sensitivity mainly for predictable OFF (item 4.3 vs items 36–38, 74.3% vs 87.2%; item 4.5 vs item 36, 67.9% vs 86.5%) [5]. The higher specificity with slightly lower sensitivity we found for the MDS-UPDRS in detecting motor fluctuations could be due to the greater information and more complexity provided by items 4.3 and 4.5. False positive and negative rates detected using the two items of the MDS-UPDRS could be instead partially explained by possible inaccurate information reported by the patients regarding their motor status. In conclusion, our data suggest an improved specificity of part IV of the MDS UPDRS with respect to the old version in detecting motor fluctuations.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The study has been approved by the local ethics committee and it has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.



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