Motor Fluctuations Indices in Parkinson's disease

Bonomo R, Raciti L, Mostile G, Contrafatto D, Dibilio V, Luca A, Sciacca G, Cicero C.E, Vasta R, Nicoletti A and Zappia M

Department G.F. Ingrassia, Section of Neurosciences, University of Catania, Italy

1.Introduction:

Motor fluctuations are routinely identified in Parkinson's disease (PD) by clinical scales and self-reported tools[1] whose short-cut and subjective nature of evaluation affects diagnostic accuracy of motor status. Thus, the objective long-term observation by the 12-hours Waking-day Motor Assessment (WDMA) could be considered an appropriate tool for the clinical detection of motor deterioration. WDMA-based indices may be proposed to specifically quantify motor fluctuations.

2. Materials and Methods:

Study samples

Two independent samples of N=51 and N=109 PD subjects were included in the study. All patients satisfied the UK Brain Bank criteria[2] and were being treated with L-Dopa therapy. Demographic and clinical information on all patients were collected. Cognitive abilities were investigated with the Mini Mental State Examination (MMSE) using a cut-off of 24 or lower to define the cognitive impairment [3].

Motor assessment

All patients were evaluated every 2 hours by a WDMA using the motor part of the UPDRS-III[4]. Motor scores were reported as graphs. Six blinded raters, expert in Movement disorders, classified the 51 patients with or without motor fluctuations. To quantify motor fluctuations, a Worsening Index (**WI**), a Mean Fluctuation Index (**MFI**) and a Coefficient of Variation (**CV**) were computed based on variations in UPDRS-ME values *(U).* The optimal cut-off of each index was calculated. Indices cut-off accuracy was then tested in the N=109 sample.

Statistical analysis

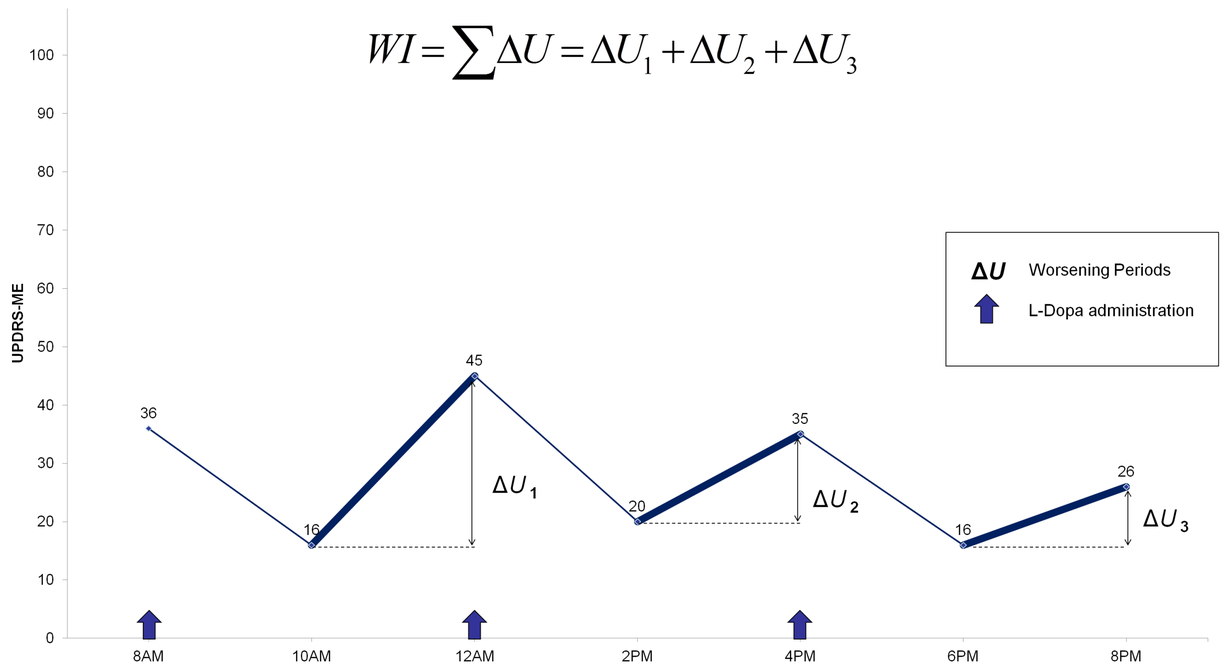
All data were analyzed using STATA 12.1 software. We described all quantitative variables as mean ± standard deviation (SD), besides categorical variables were described using frequency. Difference between means was estimated by the Chi-square test. Cut-offs values were studied by the *Receiver Operating Characteristic* (ROC) using physicians' evaluation of WDMA as *gold standard*. Only those patients with at least 5 out of 6 inter-rater agreement on presence or absence of fluctuation were selected for the analysis.

Cohen's kappa was also calculated to measure the inter-rater agreement. 95% Confidence Intervals (CI) of sensitivity and specificity were as well computed.

WORSENING INDEX (WI):

Overall motor deterioration during the day

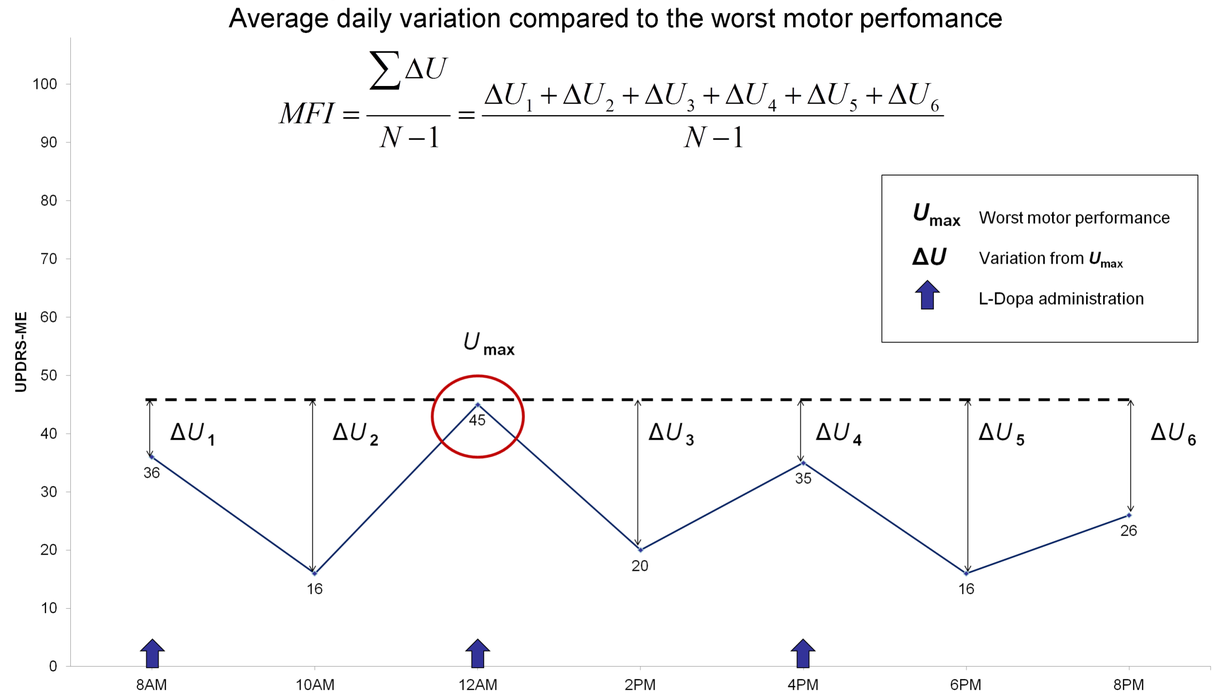
$$WI = \sum \Delta U = \Delta U_1 + \Delta U_2 + \Delta U_3$$



MEAN FLUCTUATION INDEX (MFI):

Average daily variation compared to the worst motor perfomance

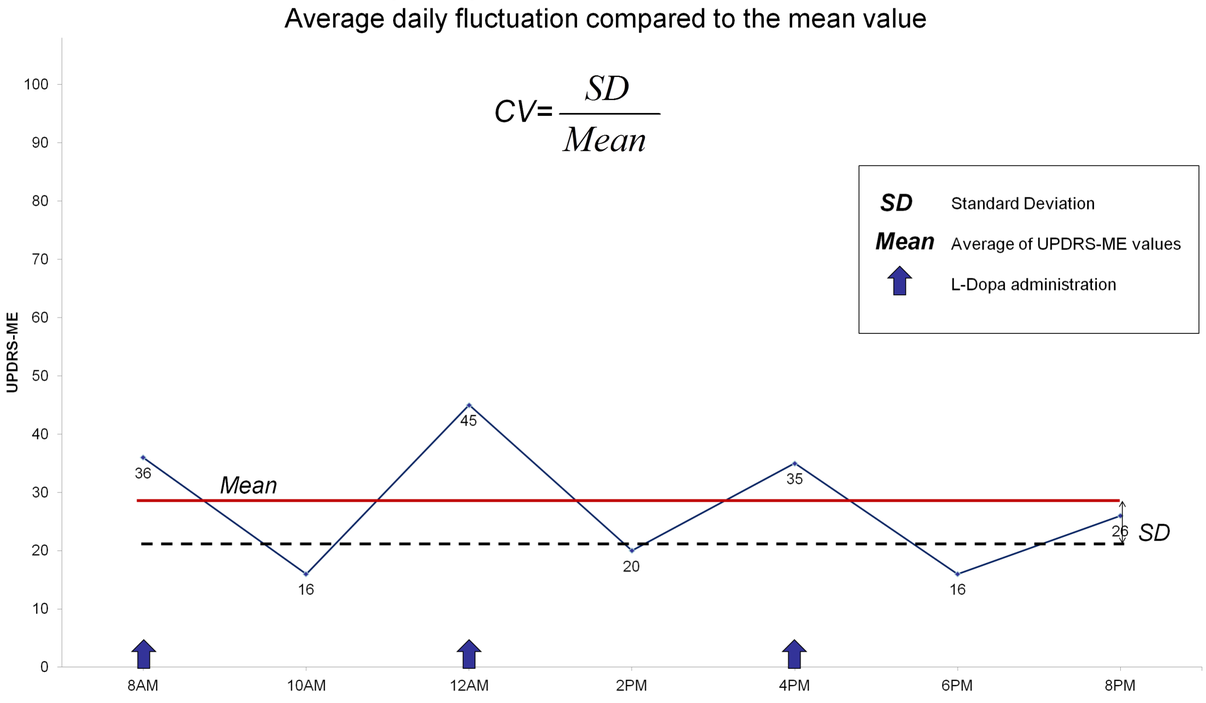
$$MFI = \frac{\sum \Delta U}{N-1} = \frac{\Delta U_1 + \Delta U_2 + \Delta U_3 + \Delta U_4 + \Delta U_5 + \Delta U_6}{N-1}$$



COEFFICIENT OF VARIATION (CV):

Average daily fluctuation compared to the mean value

$$CV = \frac{SD}{Mean}$$



3.Results

Cut-offs' identification

In 51 PD patients sample, indices' optimal cut-offs calculated by using the ROC curve analysis were **8.3** for the WI, **5** for the MFI and **12.9** for the CV. The cut-offs were selected by identifying the values with the highest efficiency.

Indices' validation

Accuracy of the cut-offs verified in the 109-study population showed a sensitivity and a specificity of **97.9%** (95%CI: 94.8 to 100) and **94.3%** (95%CI: 81.4 to 97.5) for the WI, **87.5%** (95%CI: 80.4 to 94.6) and **94.3%** (95%CI: 89.3 to 99.3) for the MFI, **81.3%** (95%CI: 72.9 to 89.6) and **100%** (95%CI: 99.9 to 100) for the CV.

4.Conclusions

Our study proved that the WI, the MFI and the CV represent sensitive and reliable indices of motor status giving a specific and quantitative estimation of motor fluctuations in complicated PD.

References

1. Antonini A et al. Wearing-Off Scales in Parkinson's Disease: Critique and Recommendations. Mov Disord, Vol 26, n °12, 2011.
2.Gibb WR et al. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. JNeurol Neurosurg Psychiatry. 1988;51(6):745-52.
3.Stacy M et al. End-of-dose wearing off in Parkinson disease: a 9-question survey assessment. Clin Neuropharmacol. 2006 Nov-Dec;29(6):312-21.
4.Fahn S, Elton RL and the Members of the UPDRS Development Committee. Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden CD, Calne DB, eds. Recent developments in Parkinson's disease. London: Macmillan 1987: 153-163.

Sin

XLVI CONGRESSO NAZIONALE
10-13 OTTOBRE 2015 – GENOVA