

# SLEEP DISTURBANCES ARE CORRELATED TO THE ONSET OF WEARING OFF IN MODERATE PARKINSON'S DISEASE

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**INTRODUCTION:** sleep disturbances reach up to 90% of prevalence in Parkinson's disease (PD) and may deteriorate quality of life, limiting activities of daily living independence, but their pathophysiology is not fully clear. Several studies have reported sleep issues across all stages of the disease and also relevant in early untreated patients [1], but their severity seems related to disease duration [2].

Furthermore, while some authors found that sleep derangement is not dependent on homeostatic mechanisms and resides on extrastriatal circuits, at least some problems, such as sleep-maintenance insomnia, are probably related to nocturnal akinesia [3] and therefore to motor complications of the disease.

**OBJECTIVE:** To assess the correlation between sleep disturbances and diurnal ON-OFF fluctuations in a cohort of PD patients within H&Y 2 disease stage.

**MATERIALS AND METHODS:** we analyzed the data of 40 patients with bilateral PD without postural instability in a stable dose of L-DOPA. Sleep was assessed using the Parkinson's Disease Sleep Scale (PDSS) and ON-OFF fluctuations by means of the Wearing-OFF Questionnaire (WOQ-19). Motor conditions and motor complications were evaluated with the MDS-UPDRS parts III and IV. We also screened for mood levels with the Beck Depression Inventory (BDI) and cognitive performances using the Montreal Cognitive Assessment (MOCA).

**RESULTS:** we recruited 19 patients with ON-OFF fluctuations (defined by a WOQ-19  $\geq 2$  score) and 21 non fluctuating age-matched PD patients. Analysis of variance of the total PDSS scores between the two groups showed a significant difference ( $p=0.027$ ), while we found equal respective scores at the MOCA (26.75 vs 26.82) and no patients exhibited BDI scores above the cut-off value of minimal depression.

Variables (mean values $\pm$ SD)	Non-fluctuating patients (WOQ-19 < 2)	Fluctuating patients (WOQ-19 $\geq 2$ )	P values
Age	69.29 $\pm$ 7.42	67.32 $\pm$ 8.97	0.23
Disease duration	4.14 $\pm$ 3.47	5.72 $\pm$ 3.34	0.079
LEDD	490.24 $\pm$ 294.15	655.00 $\pm$ 409.99	0.075
PDSS	119.29 $\pm$ 15.73	107.47 $\pm$ 21.86	0.027
MDS-UPDRS III	21.86 $\pm$ 6.98	27.95 $\pm$ 12.43	0.030
BDI	5.43 $\pm$ 4.49	8.56 $\pm$ 3.50	0.011
MOCA corrected	26.75 $\pm$ 1.82	26.82 $\pm$ 1.75	0.68
PDQ-8 score	17.11 $\pm$ 16.01	33.39 $\pm$ 13.78	<0.001

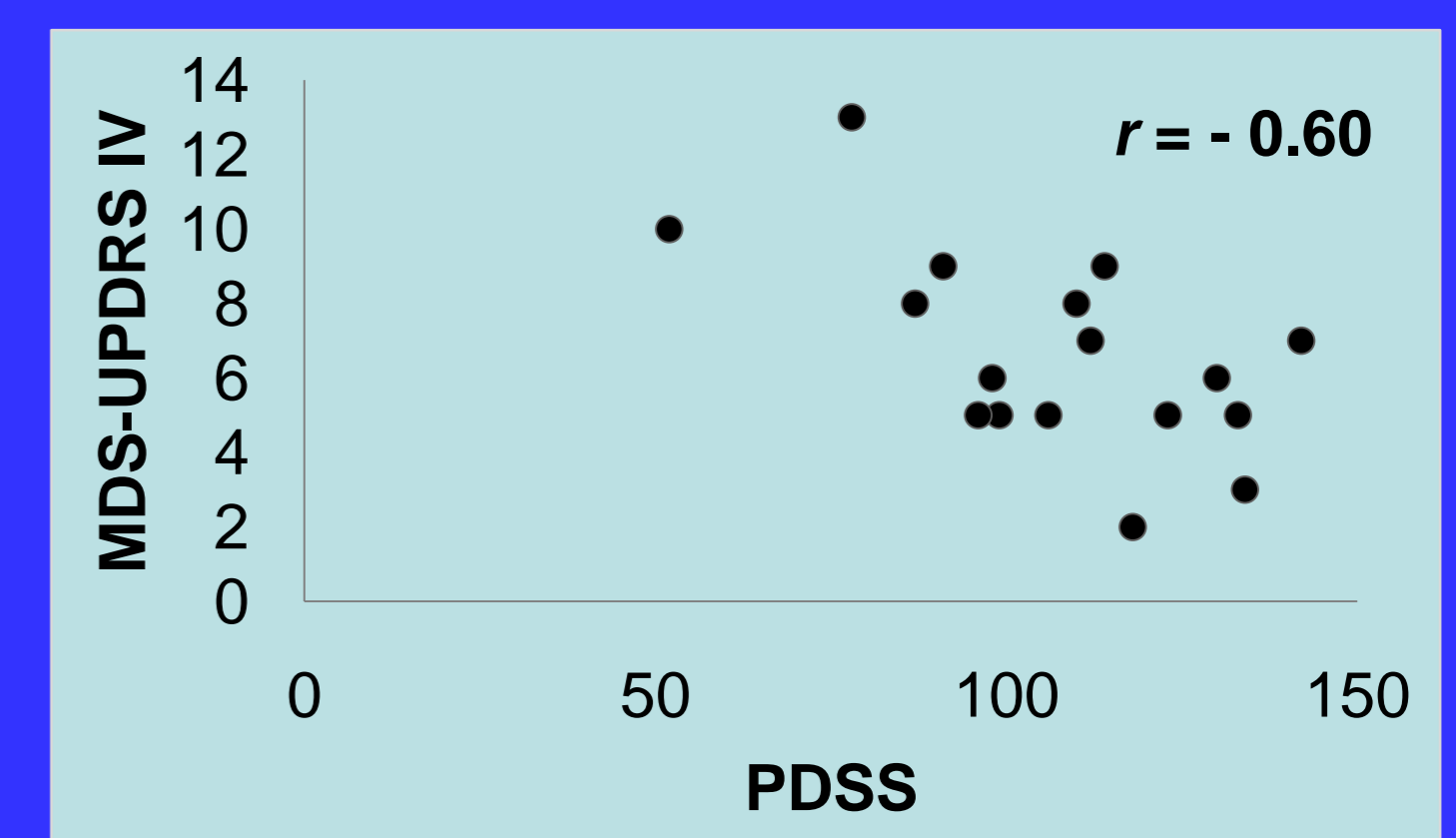
Comparison between patients without and with ON-OFF fluctuations using the Mann-Whitney test

The comparison between the total scores of each group at each individual item of the PDSS showed a significant difference for items 1 (overall quality of sleep,  $p=0.01$ ), 3 (sleep maintenance insomnia,  $p=0.025$ ), 9 (nocturnal akinesia,  $p=0.032$ ), 12 (nocturnal cramps,  $p=0.01$ ), 14 and 15 (sleep refreshment and daytime dozing,  $p=0.04$  both).

Among fluctuating patients the PDSS resulted significantly correlated with the severity of motor fluctuations (MDS-UPDRS IV score) ( $r=-0.60$ ).

Item	Comparison	P value
1	NFI vs FI	0.01
2	NFI vs FI	0.39
3	NFI vs FI	0.025
4	NFI vs FI	0.33
5	NFI vs FI	0.27
6	NFI vs FI	0.13
7	NFI vs FI	0.10
8	NFI vs FI	0.28
9	NFI vs FI	0.032
10	NFI vs FI	0.13
11	NFI vs FI	0.21
12	NFI vs FI	0.010
13	NFI vs FI	0.14
14	NFI vs FI	0.039
15	NFI vs FI	0.040

Comparison between non-fluctuating patients (NFI) and fluctuating patients (FI) scores at each item of the PDSS using a t test for unpaired data



Correlation between the scores at the PDSS and the MDS-UPDRS IV of fluctuating patients

**DISCUSSION AND CONCLUSION:** we showed that the onset of the Wearing Off phenomenon is associated with a reduced quality of sleep in PD, that appears limited to nocturnal akinesia aspects, and independent of disease duration and mood and cognitive levels. We can suggest that the reduction of nocturnal dopaminergic levels could be a major determinant of sleep disturbances in moderate PD, apparently sufficient to induce a trend towards more perceived daytime sleepiness.

- [1] Aarsland DI, Brønnick K, Alves G, Tysnes OB, Pedersen KF, Ehrt U, Larsen JP. The spectrum of neuropsychiatric symptoms in patients with early untreated Parkinson's disease. J Neurol Neurosurg Psychiatry. 2009 Aug;80(8):928-30

- [2] Chaudhuri KRI, Pal S, DiMarco A, Whately-Smith C, Bridgman K, Mathew R, Pezzela FR, Forbes A, Högl B, Trenkwalder C. The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. J Neurol Neurosurg Psychiatry. 2002 Dec;73(6):629-35.

- [3] Maass A, Reichmann H. Sleep and non-motor symptoms in Parkinson's disease. J Neural Transm. 2013 Apr;120(4):565-9