Prevalence of Non-motor Symptoms in Isolated REM Sleep Behaviour Disorder

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Introduction

Isolated REM sleep behaviour disorder (iRBD) is the most specific prodromal marker of α-synucleinopathies [1]. In addition to its diagnostic relevance, iRBD is frequently associated with non-motor symptoms (NMS) including hyposmia, constipation, depression, and excessive daytime sleepiness—features commonly seen in prodromal and early Parkinson's disease (PD) [2].

The clustering of NMS in iRBD is thought to reflect early, widespread accumulation of α-synuclein pathology in extra-nigral regions during the premotor and prodromal phases [3]. Importantly, NMS burden — particularly cognitive, autonomic, and neuropsychiatric — may vary across phenoconversion trajectories and provide early prognostic insights.

This study aimed to assess and compare the burden of NMS in patients with iRBD, PD with and without RBD, and healthy controls.

Methods

Multicentre cross-sectional study including **iRBD patients and PD patients**, distributed on the basis of RBD diagnosis, and age- and sex-matched **controls.**

Inclusion criteria for each group:

iRBD: Diagnosed according to ICSD-3 criteria and confirmed by video-polysomnography

PD: Hoehn & Yahr stage 1–1.5; Disease duration less than 3 years; Stable dopaminergic treatment for ≥ 4 weeks

Exclusion Criteria:

- Neurological/psychiatric comorbidities
- Neoplastic conditions
- MMSE < 24

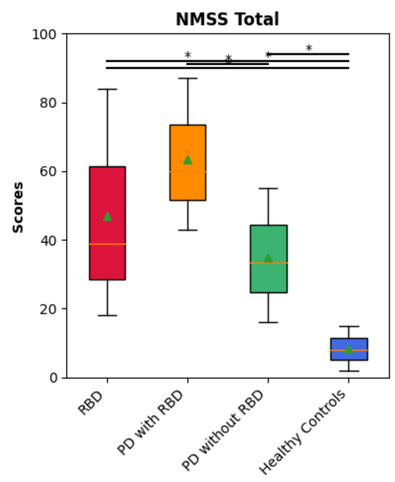
Non-Motor Symptoms Scale (NMSS) assesses 30 non-motor symptoms grouped into **9 domains:**

1. Cardiovascular (e.g., falls);
2. Sleep/Fatigue
3. Mood/Apathy
4. Perceptual Problems
5. Attention/Memory
6. Gastrointestinal
7. Urinary
8. Sexual Function
9. Miscellaneous (pain, smell, weight changes, hyperhidrosis)

Scores (range 0-360) reflect **symptom burden** over the **past month**.

Results

In this multicenter cross-sectional study, **87 iRBD patients** were enrolled (80.5% male; mean age 69.9 ± 6.0) and compared to **37 PD patients with RBD** (PD+RBD, 64.9% male; 66.2 ± 7.4), **36 PD patients without RBD** (PD-RBD, 58.3% male; 66.6 ± 5.5), and **38 controls** (65.8% male; 68.6 ± 10.9). There were no significant differences in sex and age between groups.



One-Way Anova (Welch's test) showed that all patient groups had significantly higher NMSS scores than controls in **cardiovascular** (p < 0.01), **attention/memory** (p<0.01), **mood** (p<0.01), **urinary** (p<0.01), **gastrointestinal** (p<0.01), **miscellaneous** (p<0.01) domains, and **total score.**

Both iRBD and PD+RBD groups reported greater **fatigue** (p<0.01), and higher total **NMSS scores** than controls and PD–RBD. PD+RBD patients exhibited more **fatigue** (p<0.01), **attention/memory** (p<0.01), **urinary** (p<0.01), **cardiovascular** (p<0.01), , **and mood symptoms** (p<0.01) than PD–RBD. **Sexual dysfunction** (p<0.01) was more frequent in iRBD and PD+RBD patients than controls, and PD-RBD patients showed higher scores than PD-RBD.

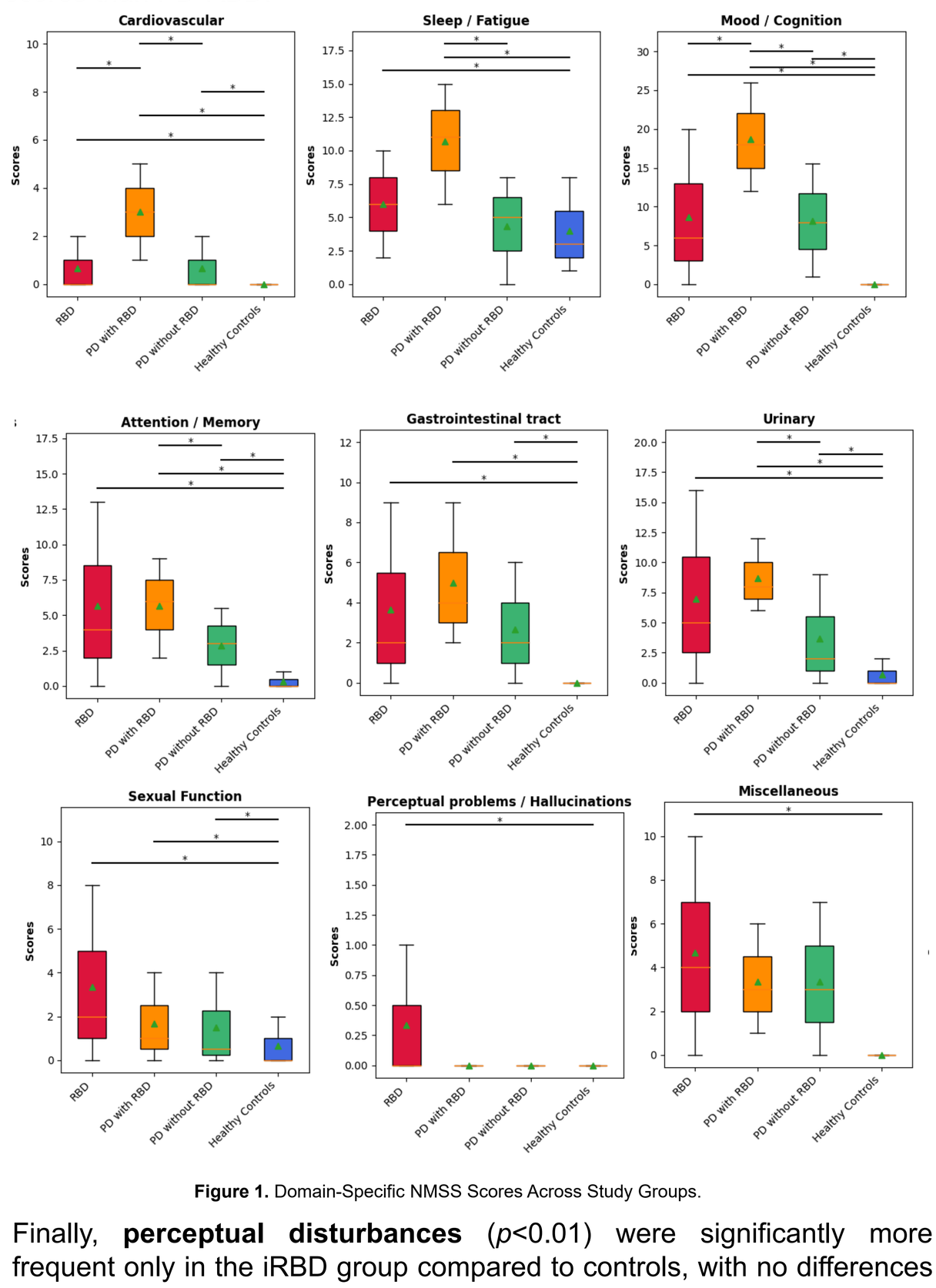


Figure 1. Domain-Specific NMSS Scores Across Study Groups.

Finally, **perceptual disturbances** (p<0.01) were significantly more frequent only in the iRBD group compared to controls, with no differences observed between PD groups or between iRBD and PD patients.

Conclusions

These findings indicate that iRBD and PD with RBD are associated with a greater burden of NMS, possibly reflecting more widespread neurodegeneration, supporting the notion that RBD indicates a more diffuse disease phenotype and may signal higher risk for faster progression and complex symptomatology.

24-28 Ottobre 2025
Padova Congress
55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA