

Non-motor determinants of cognitive performances in a cohort of PD patient's siblings.

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Introduzione

PD originates from a complex interplay of genetics and environment [1]. Moreover, PD progressively develops over years, during which non-motor symptoms (NMS) such as cognitive impairment can precede the appearance of motor dysfunction [2]. Scarce is the evidence of how cognitive impairment interweaves with other non-motor markers in a cohort at increased "familial" risk of neurodegeneration such as PD siblings. The aim of the study is to evaluate cognitive performances in non-affected siblings (Sibs) of Parkinson's Disease (PD) patients and how the presence other non-motor signs and symptoms could affect them.

Metodi

Within the PROPAG-AGEING Phase 2 project, 100 siblings of PD patients from Bologna underwent a brief evaluation of cognitive impairment by means of Montreal Cognitive Assessment (MoCA) [3]. Clinical and neurological evaluations including demographics, comorbidities and non-motor symptoms such as RBD, hyposmia, and symptoms of dysautonomia were also performed.

Risultati

Siblings (44% males) presented with a mean age of 63.64 ± 9.64 years and were 3.24 ± 6.63 years younger than their relatives with PD; their mean education was 11.12 ± 4.09 years (Table 1).

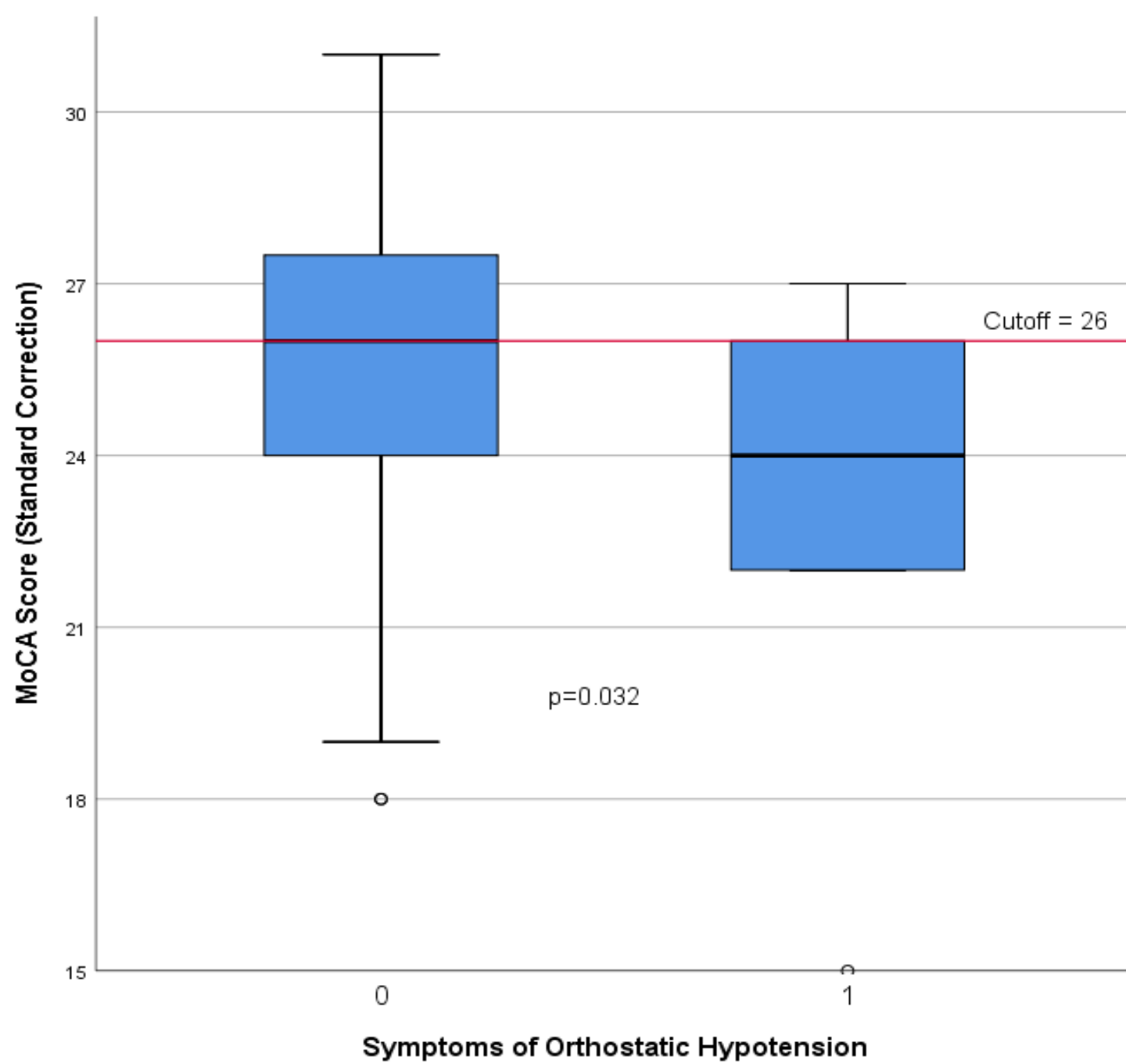
Siblings obtained a mean corrected MoCA score of 25.39 ± 2.98 points, 44 scored below the cutoff value of 26 (Table 2). 10 Sibs reported symptoms of constipation, 7 of thermoregulatory dysfunction and other 7 of depression; 9 Sibs were anosmic (age and sex corrected), 9 scored positive at RBD screening questionnaire. 7 male Sibs referred erectile dysfunction (Figure 1).

After correcting for education and age, the 5 Sibs referring symptoms of orthostatic hypotension scored 2.71 points less than the others (CI: -5.19 - -0.23; $p=0.032$), this was largely due to the effect on memory tasks [-1.93 (CI -3.28 - -0.58) points, $p=0.006$]. The result was replicated adopting the Italian validated available corrections ($p=0.041$ and $p=0.047$ respectively) (Figure 2).

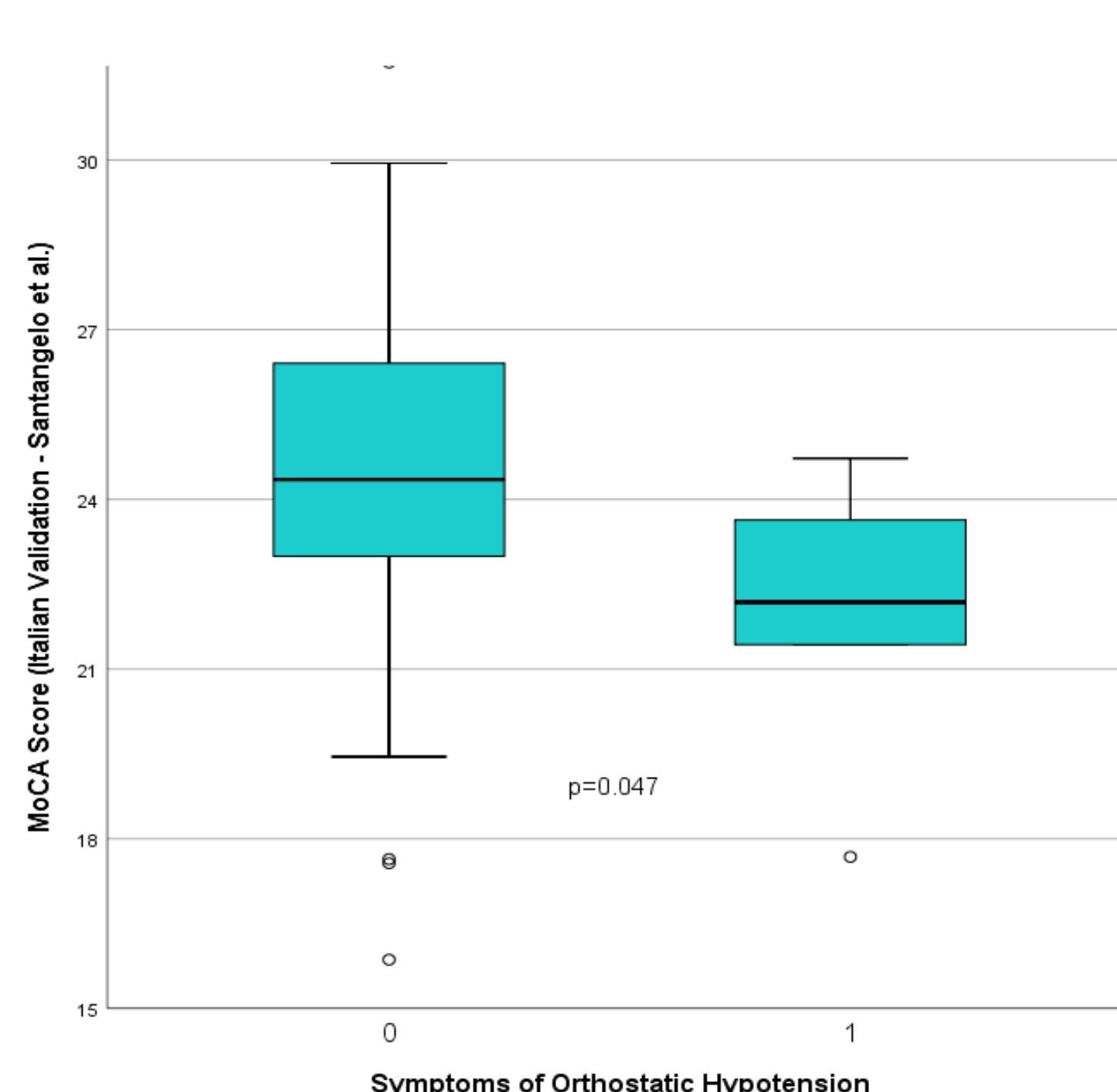
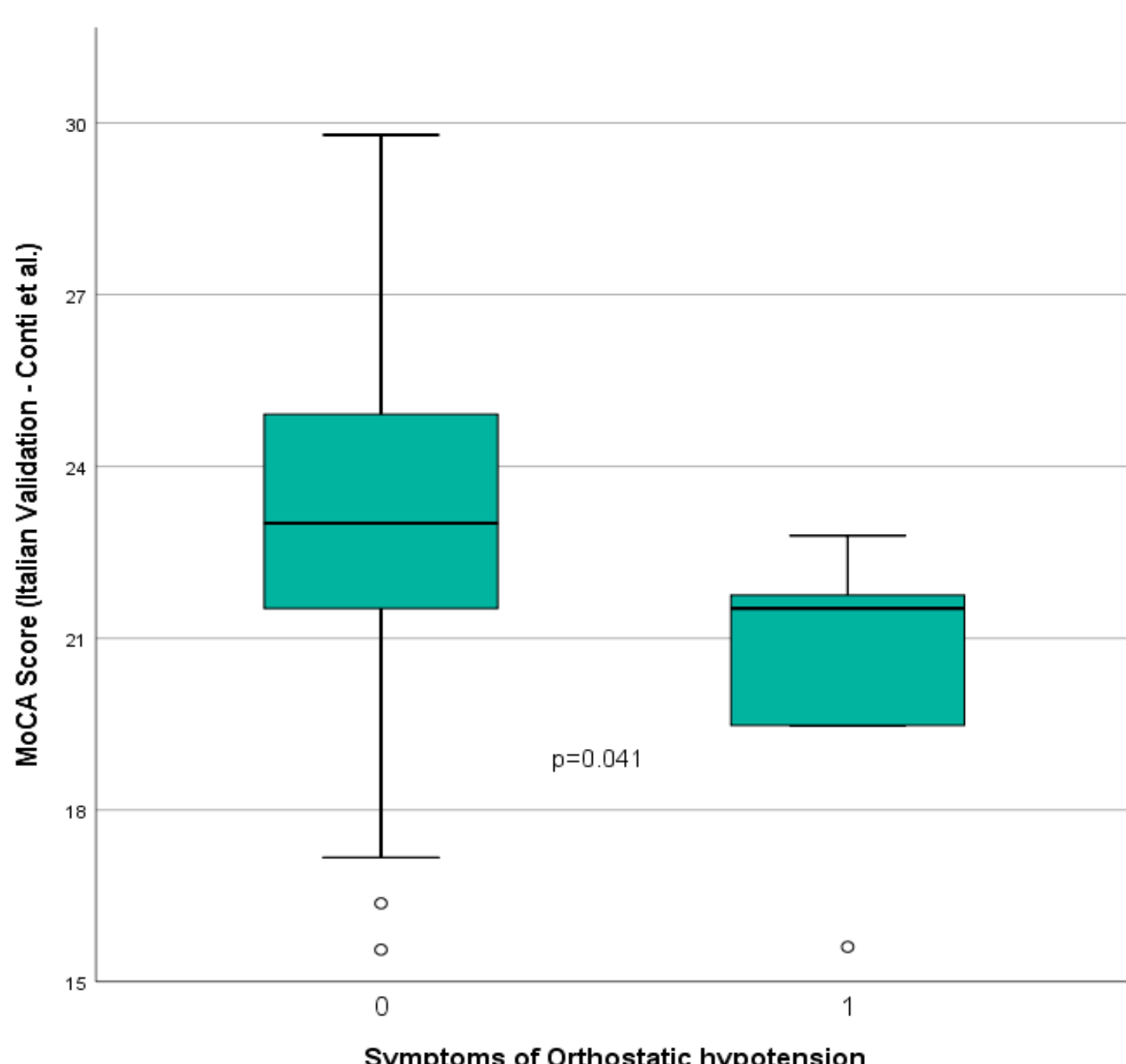
Neither the presence of other non-motor symptoms nor their association, affected Sibs cognitive performances or increased the risk of being below the norm.

Conclusioni

PD siblings show in general normal cognitive performances at MoCA, non-motor symptoms alone do not affect general cognition. The outlined effect of orthostatic hypotension in our results could underline either a susceptibility towards an underlying neurodegenerative process or a direct effect of chronic reduced cerebral blood flow during daytime on cognitive tasks.



← ↓ **Figure 2.** General cognitive performances in Sibs with and without symptoms of orthostatic hypotension, corrected by means of the different available validations.



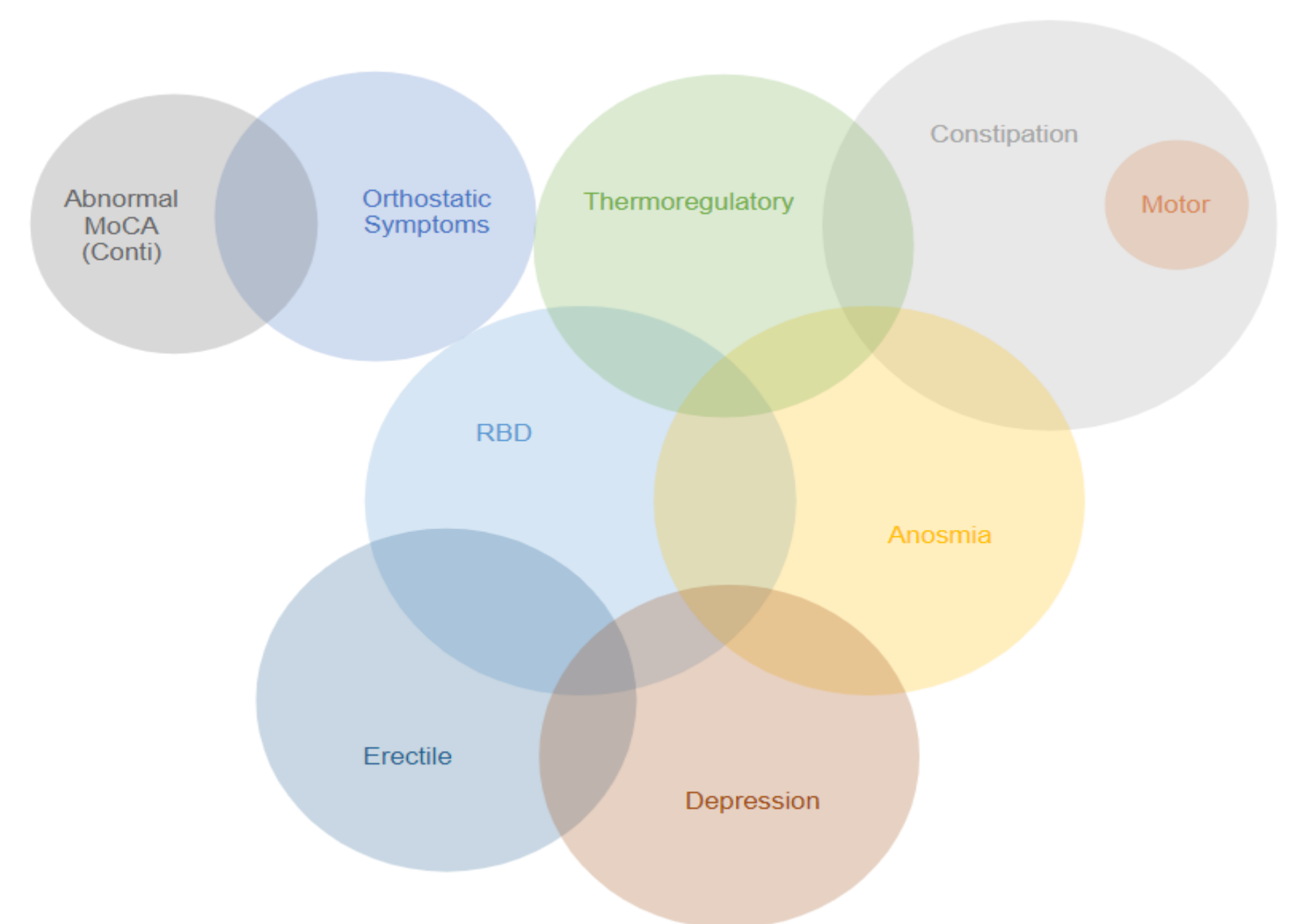
↓ **Table 1.** General and Prodromal features of PD Siblings.

| | PD Siblings |
|---------------------------------------|---------------|
| | <i>n</i> =100 |
| Age (mean ± SD) | 63.64 ± 9.64 |
| Males (%) | 44 (44%) |
| Education (mean ± SD) | 11.12 ± 4.09 |
| Comorbidities | |
| Hypertension (%) | 29 (29.0%) |
| Diabetes (%) | 4 (4.0%) |
| Dyslipidemia (%) | 22 (22.0%) |
| Hyperuricemia (%) | 4 (4.0%) |
| Depression (%) | 7 (7.0%) |
| Sleep | |
| RBDSQ - Score (mean ± SD) | 1.94 ± 1.82 |
| - Positive (%) | 9 (9.0%) |
| Olfaction | |
| SSS Score (mean ± SD) | 9.06 ± 2.35 |
| Anosmic (%) | 9 (9.0%) |
| Autonomic Functions | |
| Orthostatic symptoms (%) | 5 (5%) |
| Constipation symptoms (%) | 10 (10%) |
| Erectile symptoms (<i>n</i> =44 - %) | 7 (14.3%) |
| Thermoregulatory symptoms (%) | 7 (7.0%) |
| MDS-UPDRS | |
| Part I (IQR) | 1 (0 - 2) |
| Part III (IQR) | 1 (0 - 2) |
| Total (IQR) | 2,5 (1 - 4) |
| Mild motor PD signs (%) | 1 (1%) |

↓ **Table 2.** Cognitive performances of PD Siblings.

| | PD Siblings |
|--|---------------|
| | <i>n</i> =100 |
| General Cognition | |
| Raw MoCA Score (mean ± SD) | 24,00 ± 2,37 |
| MoCAc Score - Standard (mean ± SD) | 25.39 ± 2.38 |
| Abnormal MoCA - Standard (%) | 44 (44.0%) |
| MoCAc Score - Conti et al. (mean ± SD) | 22.82 ± 2.91 |
| Abnormal MoCA - Conti et al. (%) | 4 (4.0%) |
| MoCAc Score - Santangelo et al. (mean ± SD) | 24.47 ± 2.93 |
| Abnormal MoCA - Santangelo et al. (%) | 1 (1.0%) |
| Cognitive Areas | |
| - Visuospatial-executive (mean ± SD) | 4.34 ± 0.97 |
| - Language (mean ± SD) | 4.93 ± 1.08 |
| - Attention, Concentration, Working Memory (mean ± SD) | 5.59 ± 0.67 |
| - Abstraction (mean ± SD) | 1.48 ± 0.64 |
| - Short-term Memory (mean ± SD) | 2.23 ± 1.53 |
| - Orientation (mean ± SD) | 5.88 ± 0.33 |

↓ **Figure 1.** Distribution of Prodromal PD markers in the cohort.



Bibliografia

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