**Supplementary materials.**

**Demographic data and autonomic assessment in patients with eliminated confounders**

13 PD, 9 PSP and 16 controls were included in the subgroup analysis of patients with eliminated confounders like age, diseases duration, comorbidities and drugs. In the subgroup analysis patients below 50 years of age and with disease duration >10 years were excluded to eliminate confounding effect of age and disease duration, as well as patients who took drugs, which could potentially affect ANS other than diuretics, selective serotonin reuptake inhibitors (SSRI) and RAS. This subanalysis allowed us to compare PD and PSP patients with relatively short disease duration without confounders.

Suppl. table 1. Demographic and clinical characteristics of the patients in subgroup analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PD, n=13** | **PSP, n=9** | **Control group, n=16** | **p-value** |
| **Age (years)** | 61.5±6.8 | 65.6±4.7 | 60.5±5.4 | 0.109 |
| **Sex (% male)** | 61.5% | 44.4% | 37.5% | 0.427 |
| **Disease duration** | 4.3±3.0 | 2.8±1.8 |  - | 0.203 |
| **HYs** | 2(2-3) | 3(3-3) |  - | 0.037\* |
| **MDS-UPDRS-3 ON** | 14.4±7.5 | 37.7±21.2 |  - | 0.011\* |
| **MDS-UPDRS-3 OFF** | 30.8±16.8 | 41.1±23.1 |  - | 0.274 |
| **LEDD (mg)** | 490 (150-925) | 255 (0-300) |  - | 0.160 |
| **Depression** | 15.4% | 33.3% |  - | 0.609 |
| **Dementia** | 0% | 11.1% |  - | 0.409 |
| **Hypertension** | 7.7% | 44.4% | 25% | 0.135 |
| **RAS** | 0% | 33.3% | 0% | 0.005\* |
| PSP>GK |
| **Diuretics**  | 0% | 33.3% | 0% | 0.005\* |
| PSP>GK |
| **SSRI** | 7.7% | 11.1% | 0% | 0.436 |

Abbreviations: HYs- Hoehn-Yahr scale, MDS-UPDRS-3 - 3-rd part of MDS – Unified Parkinson’s Disease Rating Scale, LEDD - daily levodopa equivalent dose, RAS - renin–angiotensin system antagonists, SSRI -serotonin, n-number of patients

Suppl. table 2. ANS assessment in subgroup with minimalized potentially confounding factors.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PD, n=13** | **PSP, n=9** | **Control group, n=16** | **p-value** |
| **SCOPA-AUT** |
| **Sum** | 10.0±5.2 | 15.4±6.4 | 6.6± 5.3 | 0.002\* |
| PSP>control group |
| **Sum without sexual domain** | 8.9±4.6 | 14.6±6.6 | 5.8±4.6 | 0.001\* |
| PSP>PD, PSP>control group |
| **Gastrointestinal domain** | 3.0 (2-4) | 5 (2-6) | 1 (0-1.5) | 0.009\* |
| PSP>control group |
| **Urinary domain** | 3.0 (2-5) | 6 (5-9) | 2 (1-4.5) | 0.009\* |
| PSP>control group |
| **Cardiovascular domain** | 0 (0-1) | 0 (0-2) | 0 (0-0) | 0.510 |
| **Thermoregulatory domain** | 1.0 (0-3) | 2 (0-2) | 1 (0-2) | 0.881 |
| **Pupillomotor domain** | 0 (0-1) | 1 (0-1) | 0 (0-1) | 0.112 |
| **Sexually active** | 61.2% | 55.6% | 87.5% | 0.155 |
| **Sexual domain** | 2 (0.5-2) | 0 (0-2) | 0 (0-1) | 0.534† |
| **HRV analysis** |
| **Mean NN [ms]** | 905.4 ± 84.1 | 875.0±105.1 | 942.9±106.6 | 0.292 |
| **SDNN [ms]** | 32.8 (18.8-42.8) | 17.9 (14.4-24.0) | 37.7 (30.0-44.4) | 0.008\* |
| PSP<control group |
| **RMSSD [ms]** | 19.8 (14.4 -23.5) | 12.5 (8.6-23.7) | 17.9 (15.1-24.7) | 0.224 |
| **VLF [ms2]** | 530.0 (104.5-608.4) | 171.2 (99.7-311.2) | 649.6 (390.7-957.2) | 0.008\* |
| PSP<control group |
| **LF [ms2]** | 274.7 (32.9-482.1) | 71.3 (42.6-101.2) | 231.6 (132.3-414.3) | 0.012\* |
| PSP<control group |
| **HF [ms2[** | 91.6 (52.5-164.6) | 20.0 (9.3-70.6) | 104.4 (75.8-258.9) | 0.015\* |
| PSP<control group |
| **LF [n.u.]** | 51.1 (44.8-76.2) | 67.7 (56.4-83.1) | 61.6 (51.2-74.1) | 0.665 |
| **HF [n.u.]** | 48.9 (23.8-55.2) | 34.0 (16.9-43.6) | 38.4 (25.9-48.8) | 0.665 |
| **LF/HF rato** | 1.0 (0.8-3.2) | 2.2 (1.3-5.0) | 1.6 (1.0-2.9) | 0.665 |
| **Orthostatic hypotension assessment** |
| **∆SBP [mmHg]** | 11 (5-22) | 7 (4-14) | -0.5 (-3.5-2.5) | 0.016\* |
| PD>control group |
| **∆DBP [mmHg]** | 1.1±8.1 | -2.6±5.2 | -3.8±4.5 | 0.101 |
| **∆HR [bpm]** | 10.1±5.2 | 9.8±4.7 | 10.2±4.2 | 0.978 |
| **SBP drop ≥20 mmHg** | 30.7% | 0% | 0% | 0.014\* |
| **DBP drop ≥ 10 mmHg** | 23.1% | 0% | 0% | 0.044\* |
| **SBP ≥20 mmHg and DBP ≥10 mmHg** | 23.1% | 0% | 0% | 0.044\* |
| **NOH** | 30.7% | 0% | 0% | 0.014\* |

\* - significant differences, † - sexual domain of SCOPA-AUT was not analyzed in PSP due to too small number of sexually active patients. Abbreviations: PD -Parkinson’s disease, MSA – multiple system atrophy, PSP -progressive supranuclear palsy, , HRV – heart rate variability, SDNN - standard deviation of all normal RR intervals, RMSSD -root mean square of the successive differences between adjacent normal RR intervals, VLF - power of very low frequency band, LF - power of low frequency band, HF - power of high frequency band, SBP -systolic blood pressure, DBP -diastolic blood pressure, NOH – neurogenic orthostatic hypotension, n-number of patients

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**Demographic data and autonomic assessment with indication of PSP-P and PSP-RS phenotypes.**

Suppl. table 3. Demographics of patients with indicated PSP-P and PSP-RS phenotypes.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PD** | **MSA** | **PSP-RS** | **PSP-P** | **Control group** | **p-value** | **Post hoc comparisons** |
| **Clinical characteristics of the patients** |  |
| **Age (years)** | 61.7±9.1 | 68.2±6.3 | 67.9±5.6 | 68.1±4.7 | 62.5±6.6 | 0.002\* |  - |
| **Sex (% male)** | 61.8% | 16.7% | 25.0% | 55.6% | 40% | 0.019\* | PD>MSA |
| **Disease duration** | 7 (3-10) | 2.5 (2-3.5) | 2 (2-3) | 6 (4-8) |  - | 0.002\* | PD>MSA, PSP-RS |
| **HYs** | 2 (2-3) | 4 (3-4) | 3 (3-3.5) | 3 (3-4) |  - | <0.001\* | MSA>PD |
| **MDS-UPDRS-3 ON** | 18 (9-25.5) | 38.5 (28.5-61) | 44.0 (35.5-47.5) | 47.0 (32.0-63.0) |  - | <0.001\* | MSA, PSP-RS, PSP-P>PD |
| **MDS-UPDRS-3 OFF** | 40.1±19.4 | 48.2±21.9 | 44.3±11.3 | 50.7±19.5 |  - | 0.265 |  - |
| **LEDD (mg)** | 810 (420-1500) | 590 (100-980) | 277.5 (0-760) | 460 (300-780) |  - | 0.002\* |  - |
| **Depression** | 31.6% | 58.3% | 50.0% | 22.2% |  - | 0.012\* |  - |
| **Dementia** | 14.5% | 0% | 8.3% | 11.1% |  - | 0.262 |  - |
| **Diabetes mellites** | 3.9% | 0% | 16.7% | 0% | 5% | 0.294 |  - |
| **Hypertension** | 32.9% | 66.7% | 75.0% | 55.6% | 35% | 0.046\* |  - |
| **Heart disease** | 8.6% | 33.3% | 8.3% | 11.1% | 10% | 0.133 |  - |
| **Cancer** | 5.3% | 0 | 0% | 0% | 15% | 0.242 |  - |
| **Medications:** |  |
| **α-adrenergic antagonists** | 9.2% | 8.3% | 16.7% | 11.1% | 0% | 0.557 |  - |
| **β-blockers** | 13.2% | 50.0% | 41.7% | 11.1% | 20% | 0.011\* |  - |
| **Anticholinergics** | 9.2% | 8.3% | 8.3% | 0% | 0% | 0.587 |  - |
| **Amantadine** | 17.1% | 8.3% | 0% | 22.2% | 0% | 0.132 |  - |
| **Selegiline/Rasagiline** | 22.4% | 8.3% | 8.3% | 0% | 0% | 0.054 |  - |
| **Cholinesterase inhibitors** | 6.6% | 0% | 16.7% | 33.3% | 0% | 0.015\* |  - |
| **RAS** | 18.4% | 25.0% | 50.0% | 22.2% | 5% | 0.043\* |  - |
| **Diuretics**  | 10.5% | 16.7% | 0% | 22.2% | 0% | 0.254 |  - |
| **SSRI** | 15.8 | 50.0% | 16.7% | 33.3% | 0% | 0.005\* | MSA>Control group |
| **Other anti-depressive** | 5.3% | 0% | 8.3% | 0% | 0% | 0.611 |  - |
| **Atypical antypsychotics** | 14.5% | 0% | 0% | 0% | 0% | 0.078 |  - |
| **Calcium-blocker\*** | 7.9% | 16.7% | 0% | 22.2% | 10.0% | 0.410 |  - |

\* Significant differences. Abbreviations: HYs- Hoehn-Yahr scale, MDS-UPDRS-3 - 3-rd part of MDS – Unified Parkinson’s Disease Rating Scale, LEDD - daily levodopa equivalent dose, RAS - renin–angiotensin system antagonists, SSRI -serotonin

Suppl. table 4. ANS assessment of patients with indicated PSP-P and PSP-RS phenotypes.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **PD** | **MSA** | **PSP-RS** | **PSP-P** | **Control group** | **p-value** |
| **SCOPA-AUT** |
| **Sum** | 13 (7-18.5) | 20 (12-31) | 16 (12-24) | 18 (11-25) | 5 (3-11) | 0.003 |
| PD, MSA, PSP-P, PSP-RS> Control group |
| **Sum without sexual domain** | 12 (6-17.5) | 20 (11-28) | 16 (12-24) | 18 (11-22) | 5 (3-9.5) | <0.001 |
| PD, MSA, PSP-P, PSP-RS> Control group |
| **Gastrointestinal domain** | 3 (1-6) | 5,5 (1-6.5) | 3 (2-5) | 7 (6-10) | 1 (0-1) | 0.002 |
| PD, MSA, PSP-P> Control group |
| **Urinary domain** | 5 (2-7) | 8 (5.5-13.5) | 6 (1-9) | 7 (6-8) | 2.5 (1-4.5) | 0.004 |
| MSA, PSP-P> Control group |
| **Cardiovascular domain** | 1 (0-2) | 2 (0.5-6) | 2 (0-3) | 0 (0-1) | 0 (0-0) | 0.007 |
| PD, MSA, PSP-RS> Control group |
| **Thermoregulatory domain** | 2 (0-4) | 3.5 (0.5-5) | 3 (1-5) | 2 (1-3) | 1 (0-2) | 0.159 |
| **Pupillomotor domain** | 0 (0-1) | 0 (0-0) | 1 (0-2) | 0 (0-1) | 0 (0-1) | 0.096 |
| **Sexually active** | 60.5% | 33.3% | 16.7% | 55.6% | 75% | 0.007 |
|  | Control group, PD>PSP-RS |
| **HRV analysis** |
| **Mean NN [ms]** | 873.9±131.1 | 808.8±137.0 | 919.2±121.2 | 927.7±72.3 | 951.9±103.0 | 0.021 |
| MSA<GK |
| **SDNN [ms]** | 22.0 (15.9-33.2) | 15.6 (12.2-21.9) | 15.8 (9,8-25.2) | 34.5 (17.9-41.5) | 36.6 (29.1-44.4) | 0.001 |
| PD, MSA, PSP-RS< Control group |
| **RMSSD [ms]** | 14.3 (9.4-20.3) | 10.1 (6.8-12.0) | 11.9 (8.6-14.9) | 21.2 (13.9-31.2) | 17.8 (15.1-22.1) | 0.003 |
| MSA< Control group |
| **VLF [ms2]** | 194.9 (92.7-377.1) | 130.3 (59.3-189.1) | 109.2 (34,2-228.0) | 209.6 (169.2-272.9) | 609.3 (450.7-957.2) | <0.001 |
| PD, MSA, PSP-RS< Control group |
| **LF [ms2]** | 92.7 (36.0-197.2) | 51.2 (25.7-96.4) | 33.2 (19.1-70.8) | 120.3 (71.7-401.0) | 231.6 (132.3-365.5) | <0.001 |
| PD, MSA, PSP-RS< Control group |
| **HF [ms2[** | 60.2 (25.6-140.1) | 22.8 (15.6-36.7) | 23.2 (9.4-72.6) | 138.0 (51.0-303.3) | 104.4 (73.5-193.0)  | 0.002 |
| PSP-RS, MSA<GK |
| **LF [n.u.]** | 61.9 (46.6-77.0) | 68.8 (50.9-83.3) | 63.7 (60.5-67.1) | 63.3 (30.6-71.7) | 62.9 (54.0-77.7) | 0.898 |
| **HF [n.u.]** | 38.0 (23.0-53.4) | 31.2 (16.8-49.1) | 36.3 (32.9-39.5) | 36.7 (28.3-69.4) | 37.1 (22.3-46.0) | 0.898 |
| **LF/HF ratio** | 1.6 (0.9-3.3) | 2.3 (1.0-5.0) | 1.69 (0.37-1.94) | 1,7 (0.4-2.5) | 1.6 (1.2-3.5) | 0.765 |
| **Orthostatic hypotension assessment** |
| **∆SBP [mmHg]** | 11.4±14.4 | 22.2±20.7 | 0.3±11.3 | 2.7±7.0 | -0.7±9.7 | <0.001 |
| MSA>PSP-RS, PSP-P, Control group |
| **∆DBP [mmHg]** | 1.7±8.2 | 5.1±10.4 | -3.5 (-6 – (-1.5)) | -5 (-5 -0) | -3.4±6.1 | 0.014 |
| **∆HR [bpm]** | 9.7±6.3 | 5.4±6.0 | 7.3±3.3 | 8.0±5.4 | 10.1±4.4 | 0.105 |
| **SBP drop ≥20 mmHg** | 20 (26.3%) | 7 (58.3%) | 0% | 0% | 0 (0%) | <0.001 |
| MSA>PSP-RS |
| **DBP drop ≥ 10 mmHg** | 17 (22.4%) | 5 (41.7%) | 0% | 0% | 1 (5.0%) | 0.036 |
| **SBP ≥20 mmHg and DBP ≥10 mmHg** | 14 (18.4%) | 5 (41.7%) | 0% | 0% | 0 (0%) | 0.005 |

\* - significant differences, † - sexual domain of SCOPA-AUT was not analyzed in MSA due to too small number of sexually active MSA patients. Abbreviations: PD -Parkinson’s disease, MSA – multiple system atrophy, PSP -progressive supranuclear palsy, CG – control group, HRV – heart rate variability, SDNN - standard deviation of all normal RR intervals, RMSSD -root mean square of the successive differences between adjacent normal RR intervals, VLF - power of very low frequency band, LF - power of low frequency band, HF - power of high frequency band, SBP -systolic blood pressure, DBP -diastolic blood pressure, NOH – neurogenic orthostatic hypotension.