**Supplemental data**

**Clinico-imaging features of subjects at risk of Lewy body disease in NaT-PROBE baseline analysis**

Makoto Hattori, MD, PhD, Keita Hiraga, MD, Yuki Satake, MD, Takashi Tsuboi, MD, PhD, Daigo Tamakoshi, MD, Maki Sato, Katsunori Yokoi, MD, PhD, Keisuke Suzuki, MD, PhD, Yutaka Arahata, MD, PhD, Akihiro Hori, MD, PhD, Motoshi Kawashima, MD, Hideaki Shimizu, MD, PhD, Hiroshi Matsuda, MD, PhD, Katsuhiko Kato, MD, PhD, Yukihiko Washimi, MD, PhD, Masahisa Katsuno, MD, PhD

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**Supplementary Table 1. Difference in clinical indices by the number of prodromal symptoms**

| Number of prodromal symptoms | 3 | 2 | *p*-value[a] |
|---|---|---|---|
| Number (M:F) | 8 (5:3) | 61 (37:24) | |
| Age, years | 65.1±7.2 | 65.0±7.0 | 0.947[b] |
| MDS-UPDRS total | 20.5±10.9 | 13.3±7.1 | 0.014[b] |
| MDS-UPDRS part 1 | 7.7±3.6 | 1.5±1.6 | <0.001[b] |
| MDS-UPDRS part 2 | 3.4±4.0 | 2.0±2.6 | 0.205[b] |
| MDS-UPDRS part 3 | 6.9±5.4 | 3.9±3.3 | 0.028[b] |
| MDS-UPDRS part 4 | 0.0±0.0 | 0.0±0.0 | |
| MoCA-J | 26.4±1.9 | 27.3±1.9 | 0.207[b] |
| Stroop test part 2 – part 1 | 13.0±6.9 | 14.0±8.6 | 0.744[b] |
| Trail making test part B – part A | 48.6±33.6 | 47.6±21.1 | 0.903[b] |
| Line orientation test | 16.9±2.3 | 17.0±2.7 | 0.927[b] |
| Pareidolia test | 0.25±0.46 | 0.10±0.40 | 0.321[b] |
| OSIT-J | 5.9±3.9 | 9.0±2.9 | 0.007[b] |
| CVRR rest, % | 4.05±2.30 | 2.96±1.52 | 0.078[b] |
| CVRR deep breath, % | 5.76±1.99 | 5.06±2.91 | 0.513[b] |
| DaT-SPECT SBR lower | 6.39±1.96 | 6.22±1.48 | 0.779[b] |
| DaT-SPECT Z-score lower | -0.94±1.37 | -1.05±1.04 | 0.782[b] |
| DaT-SPECT SBR higher | 6.64±1.91 | 6.57±1.47 | 0.914[b] |
| DaT-SPECT Z-score higher | -0.76±1.33 | -0.79±1.04 | 0.923[b] |
| DaT-SPECT Asymmetry Index, % | 4.2±2.4 | 5.9±4.8 | 0.345[b] |
| DaT abnormal, % | 2 (25.0) | 15 (24.6) | 1.000[c] |
| MIBG H/M early | 2.67±0.74 | 2.92±0.62 | 0.312[b] |
| MIBG H/M delay | 2.79±1.19 | 3.14±0.88 | 0.319[b] |
| MIBG abnormal, % | 3 (37.5) | 10 (16.4) | 0.167[c] |
| PASE | 124.6±75.5 | 156.6±118.9 | 0.463[d] |
| SCOPA-AUT | 12.4±3.1 | 10.3±5.2 | 0.128[d] |
| SAOQ | 57.1±26.3 | 86.3±23.0 | 0.001[d] |
| RBDSQ | 7.3±1.6 | 3.9±2.8 | 0.001[d] |

| | | | |
|---|---|---|---|
| BDI-II | 14.8±9.1 | 10.6±7.1 | 0.199[d] |
| ESS | 11.9±5.5 | 8.8±5.0 | 0.138[d] |
| PDQ-39 | 13.6±9.6 | 11.5±9.1 | 0.549[d] |
| QUIP | 2.3±2.8 | 0.8±1.2 | 0.102[d] |

MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MoCA-J, the Japanese version of the Montreal Cognitive Assessment; OSIT-J, the odor stick identification test for Japanese; CVRR, coefficient of variation of RR intervals; DaT, dopamine transporter; MIBG, metaiodobenzylguanidine; PASE, Physical Activity Scale for the Elderly; SCOPA-AUT, the Japanese version of the Scale for Outcomes in Parkinson's disease for Autonomic Symptoms; SAOQ, Self-administered Odor Question; RBDSQ, RBD screening scale; BDI-II, Beck Depression Inventory-Second Edition; ESS, Epworth Sleepiness Scale; PDQ-39, Parkinson's Disease Questionnaire-39; QUIP, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease

[a] Comparison between the triple-risk group and the double-risk group.

[b] $p$-values were determined by Student's $t$-test.

[c] $p$-values were determined by Fisher's exact test.

[d] $p$-values were determined by Mann-Whitney U test.

Data represent the mean±standard deviation or value (%).

**Supplementary Table 2. Age-adjusted comparison of clinical indices of the high-risk subjects with DaT and MIBG defects and those without imaging defects**

| | High-risk with abnormal DaT and MIBG | High-risk with normal DaT and MIBG | *p*-value (ANCOVA)[a] |
|---|---|---|---|
| Number, M:F | 7 (4:3) | 46 (25:21) | |
| Age, years | 74.1±2.6 | 63.5±7.4 | |
| MDS-UPDRS total | 21.4±12.4 | 12.8±7.3 | 0.020 |
| MDS-UPDRS part 1 | 8.0±4.3 | 7.7±4.0 | 0.427 |
| MDS-UPDRS part 2 | 3.7±4.0 | 2.0±2.8 | 0.110 |
| MDS-UPDRS part 3 | 9.7±4.8 | 3.2±2.8 | <0.001 |
| MDS-UPDRS part 4 | 0.0±0.0 | 0.0±0.0 | |
| MoCA-J | 26.1±3.0 | 27.4±1.6 | N/A[b] |
| Stroop test part 2 – part 1, sec | 22.0±17.5 | 12.6±6.0 | 0.141 |
| Trail making test part B – part A, sec | 66.5±26.7 | 44.6±20.1 | 0.121 |
| Line orientation test | 14.9±3.1 | 17.4±2.4 | 0.127 |
| Pareidolia test | 0.29±0.76 | 0.09±0.35 | N/A[b] |
| OSIT-J | 4.9±3.6 | 9.7±2.4 | 0.001 |
| CVRR rest, % | 2.92±2.69 | 3.22±1.50 | 0.771 |
| CVRR deep breath, % | 4.48±4.66 | 5.01±2.53 | 0.950 |
| DaT-SPECT SBR lower | 4.02±1.00 | 6.91±1.17 | <0.001 |
| DaT-SPECT Z-score lower | -2.27±0.76 | -0.64±0.95 | <0.001 |
| DaT-SPECT SBR higher | 4.42±1.03 | 7.24±1.18 | <0.001 |
| DaT-SPECT Z-score higher | -1.97±0.79 | -0.39±0.96 | <0.001 |
| DaT-SPECT Asymmetry Index, % | 9.7±7.8 | 4.9±3.5 | 0.012 |
| MIBG H/M early | 1.74±0.32 | 3.09±0.41 | <0.001 |
| MIBG H/M delay | 1.40±0.25 | 3.43±0.53 | <0.001 |
| MIBG washout ratio, % | 62.7±8.0 | 12.9±11.2 | <0.001 |

MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MoCA-J, the Japanese version of the Montreal Cognitive Assessment; OSIT-J, the odor stick identification test for Japanese; CVRR, coefficient of variation of R-R intervals; DaT, dopamine transporter; MIBG, metaiodobenzylguanidine

**Supplementary Table 3. Clinical indices of the high-risk subjects with normal imaging findings**

| | High-risk with normal DaT and MIBG | Low-risk group | $p$-value[a] |
|---|---|---|---|
| Number (M:F) | 46 (25:21) | 32 (22:10) | |
| Age, years | 63.5±7.4 | 63.1±5.0 | 0.798[b] |
| MDS-UPDRS total | 12.8±7.3 | 3.4±2.7 | <0.001[b] |
| MDS-UPDRS part 1 | 7.7±4.0 | 1.5±1.6 | <0.001[b] |
| MDS-UPDRS part 2 | 2.0±2.8 | 0.3±1.2 | 0.002[b] |
| MDS-UPDRS part 3 | 3.2±2.8 | 1.6±1.5 | 0.004[b] |
| MDS-UPDRS part 4 | 0.0±0.0 | 0.0±0.0 | |
| MoCA-J | 27.4±1.6 | 27.6±2.3 | 0.608[b] |
| Stroop test part 2 – part 1, sec | 12.6±6.0 | 9.5±4.7 | 0.018[b] |
| Trail making test part B – part A, sec | 44.6±20.1 | 43.2±26.7 | 0.804[b] |
| Line orientation test | 17.4±2.4 | 18.5±2.2 | 0.049[b] |
| Pareidolia test | 0.09±0.35 | 0.03±0.18 | 0.415[b] |
| OSIT-J | 9.7±2.4 | 10.5±1.5 | 0.091[b] |
| CVRR rest, % | 3.22±1.50 | 3.08±1.65 | 0.675[b] |
| CVRR deep breath, % | 5.01±2.53 | 5.02±2.46 | 0.980[b] |
| DaT-SPECT SBR lower | 6.91±1.17 | 7.79±1.37 | 0.003[b] |
| DaT-SPECT Z-score lower | -0.64±0.95 | 0.08±1.03 | 0.002[b] |
| DaT-SPECT SBR higher | 7.24±1.18 | 8.06±1.29 | 0.005[b] |
| DaT-SPECT Z-score higher | -0.39±0.96 | 0.29±0.98 | 0.003[b] |
| DaT-SPECT SBR average | 7.07±1.17 | 7.93±1.32 | 0.004[b] |
| DaT-SPECT Asymmetry Index, % | 4.9±3.5 | 3.9±6.0 | 0.389[b] |
| MIBG H/M early | 3.09±0.41 | 2.97±0.45 | 0.243[b] |
| MIBG H/M delay | 3.43±0.53 | 3.28±0.65 | 0.273[b] |
| MIBG washout ratio, % | 12.9±11.2 | 16.3±14.3 | 0.192[b] |
| PASE | 160.0±130.5 | 106.0±62.9 | 0.034[c] |
| SCOPA-AUT | 10.3±5.1 | 2.1±1.7 | <0.001[c] |
| SAOQ, % | 90.7±13.2 | 99.8±1.1 | <0.001[c] |

| | | | |
|---|---|---|---|
| RBDSQ | 4.2±2.7 | 0.7±0.8 | <0.001[c] |
| BDI-II | 11.6±8.2 | 2.0±2.1 | <0.001[c] |
| ESS | 9.5±5.3 | 4.7±2.8 | <0.001[c] |
| PDQ-39 | 13.0±10.3 | 1.2±1.5 | <0.001[c] |
| QUIP | 1.1±1.3 | 0.1±0.4 | <0.001[c] |

MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MoCA-J, the Japanese version of the Montreal Cognitive Assessment; OSIT-J, the odor stick identification test for Japanese; CVRR, coefficient of variation of RR intervals; MIBG, metaiodobenzylguanidine; PASE, Physical Activity Scale for the Elderly; SCOPA-AUT, the Japanese version of the Scale for Outcomes in Parkinson's disease for Autonomic Symptoms; SAOQ, Self-administered Odor Question; RBDSQ, RBD screening scale; BDI-II, Beck Depression Inventory-Second Edition; ESS, Epworth Sleepiness Scale; PDQ-39, Parkinson's Disease Questionnaire-39; QUIP, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease

[a] Comparison between the high-risk group with normal DaT-SPECT and MIBG findings and the low-risk group.

[b] p-values were determined by Student's t-test.

[c] p-values were determined by Mann-Whitney U test.

Data represent the mean±standard deviation.

**Supplementary Table 4. Anthropometric and serological indices in high-risk and low-risk subjects**

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | High-risk group | Low-risk group | $p$-value | High-risk group | Low-risk group | $p$-value |
| Number | 42 | 22 | | 27 | 10 | |
| Age, years | 65.8±6.5 | 63.0±4.9 | 0.109 | 64.0±8.0 | 62.1±6.7 | 0.527 |
| Height, cm | 167.3±5.8 | 169.4±4.5 | 0.190 | 156.0±5.1 | 156.9±4.6 | 0.662 |
| Weight, kg | 65.7±11.8 | 67.1±8.6 | 0.667 | 53.8±7.9 | 54.3±5.7 | 0.860 |
| BMI, kg/m$^2$ | 23.5±4.0 | 23.3±2.3 | 0.892 | 22.1±3.1 | 22.1±2.7 | 0.984 |
| WBC, /μL | 5721±1356 | 6200±1270 | 0.220 | 5043±1171 | 4867±899 | 0.681 |
| Hemoglobin, g/dL | 15.1±1.1 | 15.1±1.0 | 0.981 | 13.7±0.8 | 14.0±1.0 | 0.398 |
| RBC, $10^4$/μL | 480.1±42.1 | 488.2±29.4 | 0.478 | 443.1±28.8 | 461.6±35.4 | 0.124 |
| Hematocrit, % | 44.0±2.6 | 45.4±2.4 | 0.061 | 40.9±2.2 | 43.0±2.7 | 0.025 |
| Platelet, $10^4$/μL | 21.6±4.3 | 23.8±4.0 | 0.073 | 22.2±5.0 | 23.5±4.7 | 0.491 |
| Total protein, g/dL | 7.34±0.41 | 7.22±0.24 | 0.281 | 7.25±0.32 | 7.31±0.34 | 0.616 |
| Uric acid, mg/dL | 5.80±1.10 | 5.69±1.28 | 0.750 | 4.77±1.16 | 4.99±1.02 | 0.623 |
| Creatinine, mg/dL | 0.88±0.14 | 0.88±0.10 | 0.879 | 0.67±0.15 | 0.71±0.04 | 0.505 |
| Glucose, mg/dL | 102.3±28.0 | 99.1±7.5 | 0.648 | 95.5±12.8 | 95.6±6.2 | 0.984 |
| HbA1c, % | 5.89±0.61 | 5.80±0.25 | 0.584 | 5.86±0.34 | 5.76±0.25 | 0.396 |
| Triglyceride, mg/dL | 125.9±81.4 | 106.5±44.4 | 0.360 | 98.8±59.8 | 147.7±78.8 | 0.057 |
| T-Cho, mg/dL | 200.0±31.6 | 208.4±28.6 | 0.357 | 224.7±34.2 | 243.7±42.8 | 0.182 |
| HDL-Cho, mg/dL | 61.8±16.4 | 59.1±16.3 | 0.569 | 71.9±11.7 | 65.7±15.5 | 0.214 |
| LDL-Cho, mg/dL | 117.7±28.0 | 121.9±26.1 | 0.615 | 130.7±29.8 | 144.6±34.1 | 0.251 |
| AST, U/L | 25.6±11.0 | 21.8±5.4 | 0.180 | 23.0±6.2 | 21.8±4.9 | 0.582 |
| ALT, U/L | 25.2±17.8 | 20.0±11.5 | 0.270 | 21.0±7.5 | 19.1±8.0 | 0.531 |
| γ-GTP, U/L | 42.7±40.3 | 35.1±20.0 | 0.460 | 22.2±12.1 | 20.7±8.0 | 0.730 |
| ALP, U/L | 213.1±58.5 | 203.0±31.0 | 0.504 | 209.1±45.4 | 211.2±58.4 | 0.912 |
| T-bil, mg/dL | 0.92±0.43 | 0.98±0.32 | 0.624 | 0.80±0.29 | 0.92±0.16 | 0.235 |

BMI, body mass index; WBC, white blood cells; RBC, red blood cells; HbA1c, hemoglobin A1c; T-Cho, total cholesterol; HDL-Cho, high-density lipoprotein cholesterol; LDL-Cho, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; T-bil, total bilirubin.

$p$-values were determined by Student's t-test.

Data represent the mean±standard deviation.