

# Supplementary Material

Detecting Anosognosia from the Prodromal Stage of Alzheimer’s Disease

**Supplementary Table 1.** Correlations between HABC-M scores and Online awareness during the cognitive task performed by AD patients.

|                      | <b>Online awareness (Discrepancy score) - AD Patients</b> |   |                  |   |
|----------------------|---|---|------------------|---|
|                      | Go/NoGo Session A   | Go/NoGo Session B                       | Stroop Session A | Stroop Session B                        |
| Cognitive HABC-M     | <b>1.2e-07</b><br>(***)<br>[0.80 ± 0.13]                  | <b>3.8e-02</b><br>(* )<br>[0.26 ± 0.11] | N.S.             | N.S.                                    |
| Functional HABC-M    | <b>1.7e-04</b><br>(***)<br>[0.64 ± 0.15]                  | <b>2.7e-02</b><br>(* )<br>[0.34 ± 0.14] | N.S.             | <b>1.5e-02</b><br>(* )<br>[0.40 ± 0.15] |
| Psychological HABC-M | <b>2.8e-02</b><br>(* )<br>[0.54 ± 0.20]                   | N.S.                                    | N.S.             | N.S.                                    |
| Total HABC-M         | <b>1.3e-03</b><br>(**)<br>[0.23 ± 0.06]                   | N.S.                                    | N.S.             | N.S.                                    |
| Caregiver score      | <b>2.6e-02</b><br>(* )<br>[0.79 ± 0.28]                   | N.S.                                    | N.S.             | N.S.                                    |
| HABC-M hybrid scale  | <b>1.3e-04</b><br>(***)<br>[0.51 ± 0.12]                  | N.S.                                    | N.S.             | N.S.                                    |

p-values and [beta ± standard-error] were computed using linear-mixed models, after adjustments for age, education, and gender. Significant differences are indicated by asterisks: \*\*\*p < 0.001, \*\*0.001 ≤ p < 0.01, \*0.01 ≤ p < 0.05.

**Supplementary Table 2A.** Correlations between HABC-M subscales (cognitive, functional, psychological, total, caregiver burden, hybrid scale) for the AD patients' group.

|                      | Cognitive HABC-M | Function HABC-M                              | Psychological HABC-M                         | Total HABC-M                                 | Caregiver burden                                   | HABC-M hybrid scale                                  |
|----------------------|------------------|--|--|--|--|--|
| Cognitive HABC-M     |                  | <b>p = 5.7e-07</b><br>(***)<br>[0.74 ± 0.14] | <b>p = 4.0e-04</b><br>(***)<br>[0.71 ± 0.17] | <b>p = 6.1e-10</b><br>(***)<br>[0.33 ± 0.03] | <b>p = 4.0e-03</b><br>(**)<br>[0.93 ± 0.29]        | <b>p = 5.7e-13</b><br>(***)<br>[0.67 ± 0.05]<br>○○○  |
| Functional HABC-M    |                  |  | <b>p = 9.8e-09</b><br>(***)<br>[1.05 ± 0.12] | <b>p = 1.7e-16</b><br>(***)<br>[0.38 ± 0.02] | <b>p = 3.8e-04</b><br>(***)<br>[1.19 ± 0.29] °     | <b>p = 6.4e-08</b><br>(***)<br>[0.65 ± 0.09]         |
| Psychological HABC-M |                  |  |  | <b>p = 2.5e-10</b><br>(***)<br>[0.29 ± 0.03] | <b>p = 2.0e-02</b><br>(**)<br>[0.89 ± 0.25]        | <b>p = 6.4e-05</b><br>(***)<br>[0.44 ± 0.09]         |
| Total HABC-M         |                  |  |  |  | <b>p = 3.7e-04</b><br>(***)<br>[3.02 ± 0.73]<br>○○ | <b>p = 2.0e-10</b><br>(***)<br>[1.76 ± 0.18]         |
| Caregiver burden     |                  |  |  |  |  | <b>p = 7.0e-07</b><br>(***)<br>[0.33 ± 0.05]<br>○○○○ |
| HABC-M hybrid scale  |                  |  |  |  |  |  |

°Co-effect of education (p = 3.5e-2\*); °°Co-effect of education (p = 2.8e-2\*); °°°Co-effect of age (p = 4.9e-2\*), education (p = 4.3e-2\*), and gender (p = 4.8e-2\*); °°°°Co-effect of age (p = 4.9e-2\*), education (p = 4.3e-2\*), and gender (p = 4.8e-2\*)

p-values and [beta ± standard-error] were computed using linear models, after adjustments for age, education, and gender. Significant differences are indicated by asterisks: \*\*\*p < 0.001, \*\*0.001 ≤ p < 0.01, \*0.01 ≤ p < 0.05.

**Supplementary Table 2B.** Correlations between HABC-M subscales (cognitive, functional, psychological, total, caregiver burden, hybrid scale) for the CTRL group.

|                      | Cognitive HABC-M | Function HABC-M                                | Psychological HABC-M                           | Total HABC-M                                   | Caregiver burden                                | HABC-M hybrid scale                             |
|----------------------|------------------|--|--|--|---|---|
| Cognitive HABC-M     |                  | <b>p = 8.6e-05<br/>(***)<br/>[0.96 ± 0.21]</b> | <b>p = 2.9e-05<br/>(***)<br/>[0.45 ± 0.09]</b> | <b>p = 1.7e-09<br/>(***)<br/>[0.30 ± 0.03]</b> | <b>p = 1.6e-01<br/>(N.S.)<br/>[3.09 ± 2.14]</b> | <b>p = 2.0e-18<br/>(***)<br/>[0.97 ± 0.02]</b>  |
| Functional HABC-M    |                  |  | <b>p = 2.1e-05<br/>(***)<br/>[0.33 ± 0.06]</b> | <b>p = 1.7e-08<br/>(***)<br/>[0.20 ± 0.03]</b> | <b>p = 2.2e-02<br/>(N.S.)<br/>[1.49 ± 1.18]</b> | <b>p = 8.6e-05<br/>(***)<br/>[0.47 ± 0.10]</b>  |
| Psychological HABC-M |                  |  |  | <b>p = 1.7e-13<br/>(***)<br/>[0.50 ± 0.04]</b> | <b>p = 7.0e-01<br/>(N.S.)<br/>[1.36 ± 3.5]</b>  | <b>p = 4.6e-05<br/>(***)<br/>[1.07 ± 0.22]</b>  |
| Total HABC-M         |                  |  |  |  | <b>p = 3.5e-01<br/>(N.S.)<br/>[6.16 ± 6.5]</b>  | <b>p = 3.6e-09<br/>(***)<br/>[2.52 ± 0.28]</b>  |
| Caregiver Burden     |                  |  |  |  |   | <b>p = 6.7e-02<br/>(N.S.)<br/>[0.03 ± 0.02]</b> |
| HABC-M hybrid scale  |                  |  |  |  |   |   |

p-values and [beta ± standard-error] were computed using linear models, after adjustments for age, education, and gender. Significant differences are indicated by asterisks: \*\*\*p < 0.001, \*\*0.001 ≤ p < 0.01, \*0.01 ≤ p < 0.05.

**Supplementary Table 3.** Optimal cut point, sensitivity, and specificity of HABC-M *offline* scores to discriminate CTRL versus AD and CTRL versus Prodromal AD.

|                          |                      | Optimal cut-point | Sensitivity      | Specificity      | AUC              |
|--------------------------|----------------------|-------------------|------------------|------------------|------------------|
| CTRL versus AD           | Cognitive HABC-M     | 2.00 [1.00;4.00]  | 0.83 [0.69;0.97] | 0.83 [0.76;1.00] | 0.94 [0.88;0.98] |
|                          | Functional HABC-M    | 2.00 [1.00;2.00]  | 0.73 [0.61;0.88] | 1.00 [0.91;1.00] | 0.90 [0.83;0.96] |
|                          | Psychological HABC-M | 1.00 [1.00;1.00]  | 0.77 [0.64;0.90] | 0.80 [0.67;0.91] | 0.79 [0.68;0.88] |
|                          | Total HABC-M         | 2.00 [-1.00;6.00] | 0.93 [0.81;1.00] | 0.80 [0.68;0.93] | 0.89 [0.82;0.96] |
|                          | Caregiver score      | 1.00 [1.00;2.00]  | 0.77 [0.62;0.88] | 0.97 [0.92;1.00] | 0.88 [0.81;0.94] |
|                          | Hybrid score         | 3.00 [2.00;4.00]  | 0.93 [0.81;1.00] | 0.90 [0.82;1.00] | 0.97 [0.94;0.99] |
| CTRL versus Prodromal AD | Cognitive HABC-M     | 1.00 [-1.00;4.00] | 0.83 [0.62;1.00] | 0.80 [0.61;0.97] | 0.88 [0.78;0.97] |
|                          | Functional HABC-M    | 2.00 [0.00;2.00]  | 0.58 [0.40;1.00] | 1.00 [0.55;1.00] | 0.81 [0.65;0.93] |
|                          | Psychological HABC-M | 1.00 [-1.00;2.00] | 0.50 [0.33;1.00] | 0.80 [0.28;0.94] | 0.65 [0.49;0.80] |
|                          | Total HABC-M         | 3.00 [-1.00;4.00] | 0.83 [0.71;1.00] | 0.80 [0.62;0.93] | 0.81 [0.67;0.93] |
|                          | Caregiver score      | 1.00 [1.00;2.00]  | 0.75 [0.53;0.93] | 0.97 [0.92;1.00] | 0.87 [0.76;0.96] |
|                          | Hybrid score         | 2.00 [2.00;4.00]  | 0.92 [0.71;1.00] | 0.83 [0.76;1.00] | 0.94 [0.86;0.99] |

Data are given as value [95% Bootstrap Confidence Interval]

AD, Alzheimer's disease; AUC, Area Under the ROC Curve; CTRL, controls; HABC-M, Healthy Aging Brain Care Monitor

**Supplementary Table 4A.** Correlations between HABC-M subscales (cognitive, functional, psychological, total, caregiver burden, hybrid scale) and Neuropsychological tests for the AD patients' group.

|                      | Neuropsychological tests - AD Patients |                                    |                                    |                                     |                                    |                                    |                                    |                                    |
|----------------------|--|------------------------------------|------------------------------------|-------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
|                      | MMSE                                   | FCRST Free Recall                  | FCRST Total Recall                 | TMT B - A                           | FAB                                | Lexical fluency                    | AV Span                            | VS Span                            |
| Cognitive HABC-M     | 3.3e-4<br>(***)<br>[-0.92 ± 0.22]      | 3.8e-3<br>(**)<br>[-0.33 ± 0.10]   | 5.8e-2<br>(N.S.)<br>[-0.14 ± 0.07] | 7.2e-1<br>(N.S.)<br>[-0.005 ± 0.01] | 2.2e-2<br>(*)<br>[-0.91 ± 0.37]    | 4.1e-1<br>(N.S.)<br>[-0.16 ± 0.19] | 8.1e-1<br>(N.S.)<br>[-0.11 ± 0.48] | 1.6e-1<br>(N.S.)<br>[-0.65 ± 0.45] |
| Functional HABC-M    | 2.2e-3<br>(**)<br>[-0.87 ± 0.26]       | 4.7e-2<br>(*)<br>[-0.27 ± 0.13]    | 1.1e-1<br>(N.S.)<br>[-0.14 ± 0.08] | 3.3e-1<br>(N.S.)<br>[-0.01 ± 0.01]  | 1.2e-1<br>(N.S.)<br>[-0.69 ± 0.43] | 5.2e-1<br>(N.S.)<br>[-0.14 ± 0.21] | 8.5e-1<br>(N.S.)<br>[0.10 ± 0.54]  | 1.9e-2<br>(*)<br>[-1.18 ± 0.47]    |
| Psychological HABC-M | 6.2e-3<br>(**)<br>[-0.65 ± 0.22]       | 5.6e-2<br>(N.S.)<br>[-0.21 ± 0.10] | 1.5e-1<br>(N.S.)<br>[-0.10 ± 0.07] | 7.5e-1<br>(N.S.)<br>[0.004 ± 0.01]  | 5.9e-1<br>(N.S.)<br>[-0.20 ± 0.36] | 9.4e-1<br>(N.S.)<br>[0.01 ± 0.17]  | 2.6e-1<br>(N.S.)<br>[0.50 ± 0.43]  | 1.5e-1<br>(N.S.)<br>[-0.61 ± 0.41] |
| Total HABC-M         | 5.0e-4<br>(***)<br>[-2.44 ± 0.61]      | 1.4e-1<br>(*)<br>[-0.80 ± 0.30]    | 7.2e-2<br>(N.S.)<br>[-0.37 ± 0.20] | 7.2e-1<br>(N.S.)<br>[0.01 ± 0.04]   | 1.1e-1<br>(N.S.)<br>[-1.79 ± 1.07] | 5.9e-1<br>(N.S.)<br>[-0.28 ± 0.52] | 7.2e-1<br>(N.S.)<br>[0.49 ± 1.35]  | 5.2e-2<br>(N.S.)<br>[-2.44 ± 1.21] |
| Caregiver score      | 1.0e-1<br>(N.S.)<br>[-0.27 ± 0.16]     | 4.6e-2<br>(*)<br>[-0.14 ± 0.07]    | 4.2e-2<br>(*)<br>[-0.09 ± 0.04]    | 4.5e-1<br>(N.S.)<br>[0.01 ± 0.01]   | 7.7e-1<br>(N.S.)<br>[-0.07 ± 0.24] | 4.7e-1<br>(N.S.)<br>[-0.08 ± 0.10] | 4.3e-1<br>(N.S.)<br>[0.22 ± 0.27]  | 2.2e-1<br>(N.S.)<br>[-0.33 ± 0.26] |
| Hybrid scale         | 1.2e-3<br>(**)<br>[-1.18 ± 0.32]       | 3.4e-3<br>(**)<br>[-0.47 ± 0.14]   | 2.6e-2<br>(*)<br>[-0.23 ± 0.10]    | 9.6e-1<br>(N.S.)<br>[0.01 ± 0.02]   | 8.0e-2<br>(N.S.)<br>[-0.98 ± 0.54] | 3.7e-1<br>(N.S.)<br>[-0.23 ± 0.26] | 8.8e-1<br>(N.S.)<br>[0.10 ± 0.65]  | 1.2e-1<br>(N.S.)<br>[-0.97 ± 0.60] |

p-values and [beta ± standard-error] were computed using linear models, after adjustments for age, education, and gender. Significant differences are indicated by asterisks: \*\*\*p < 0.001, \*\*0.001 ≤ p < 0.01, \*0.01 ≤ p < 0.05.

**Supplementary Table 4B.** Correlations between HABC-M subscales (cognitive, functional, psychological, total, caregiver burden, hybrid scale) and Neuropsychological tests for the CTRL group.

|                      | Neuropsychological tests - CTRL    |                                   |                                    |                                     |                                    |                                     |                                    |                                    |
|----------------------|------------------------------------|-----------------------------------|------------------------------------|-------------------------------------|------------------------------------|-------------------------------------|------------------------------------|------------------------------------|
|                      | MMSE                               | FCRST Free Recall                 | FCRST Total Recall                 | TMT B - A                           | FAB                                | Lexical fluency                     | AV Span                            | VS Span                            |
| Cognitive HABC-M     | 5.5e-2<br>(N.S.)<br>[0.95 ± 0.47]  | 8.7e-2<br>(N.S.)<br>[0.21 ± 0.12] | 8.3e-1<br>(N.S.)<br>[-0.09 ± 0.40] | 9.7e-1<br>(N.S.)<br>[-0.001 ± 0.03] | 7.9e-1<br>(N.S.)<br>[0.11 ± 0.39]  | 8.2e-1<br>(N.S.)<br>[-0.01 ± 0.05]  | 6.0e-1<br>(N.S.)<br>[0.09 ± 0.16]  | 6.8e-1<br>(N.S.)<br>[0.10 ± 0.24]  |
| Functional HABC-M    | 4.7e-1<br>(N.S.)<br>[0.26 ± 0.36]  | 6.5e-2<br>(N.S.)<br>[0.16 ± 0.08] | 7.9e-1<br>(N.S.)<br>[0.08 ± 0.29]  | 1.4e-1<br>(N.S.)<br>[0.03 ± 0.02]   | 3.6e-1<br>(N.S.)<br>[0.25 ± 0.28]  | 4.3e-1<br>(N.S.)<br>[-0.03 ± 0.04]  | 8.2e-1<br>(N.S.)<br>[0.03 ± 0.12]  | 8.1e-1<br>(N.S.)<br>[0.04 ± 0.17]  |
| Psychological HABC-M | 7.3e-1<br>(N.S.)<br>[0.28 ± 0.80]  | 5.3e-1<br>(N.S.)<br>[0.12 ± 0.19] | 4.6e-1<br>(N.S.)<br>[-0.48 ± 0.63] | 9.7e-2<br>(N.S.)<br>[0.08 ± 0.05]   | 7.6e-1<br>(N.S.)<br>[-0.19 ± 0.62] | 3.1e-2<br>(* )<br>[-0.18 ± 0.08]    | 1.5e-1<br>(N.S.)<br>[-0.37 ± 0.25] | 2.4e-1<br>(N.S.)<br>[-0.45 ± 0.37] |
| Total HABC-M         | 3.3e-1<br>(N.S.)<br>[1.49 ± 1.48]  | 1.8e-1<br>(N.S.)<br>[0.49 ± 0.35] | 6.9e-1<br>(N.S.)<br>[-0.49 ± 1.19] | 2.3e-1<br>(N.S.)<br>[0.11 ± 0.09]   | 8.8e-1<br>(N.S.)<br>[0.17 ± 1.17]  | 1.7e-1<br>(N.S.)<br>[-0.22 ± 0.15]  | 6.0e-1<br>(N.S.)<br>[-0.26 ± 0.48] | 6.7e-1<br>(N.S.)<br>[-0.30 ± 0.72] |
| Caregiver score      | 7.9e-1<br>(N.S.)<br>[-0.01 ± 0.05] | 5.4e-1<br>(N.S.)<br>[0.01 ± 0.01] | 8.0e-1<br>(N.S.)<br>[-0.01 ± 0.04] | 5.4e-2<br>(N.S.)<br>[0.01 ± 0.003]  | 5.7e-1<br>(N.S.)<br>[0.02 ± 0.04]  | 5.0e-1<br>(N.S.)<br>[0.003 ± 0.005] | 5.5e-1<br>(N.S.)<br>[-0.01 ± 0.01] | 7.2e-1<br>(N.S.)<br>[-0.01 ± 0.02] |
| Hybrid scale         | 6.6e-2<br>(N.S.)<br>[0.94 ± 0.49]  | 8.6e-2<br>(N.S.)<br>[0.21 ± 0.12] | 8.1e-1<br>(N.S.)<br>[-0.10 ± 0.41] | 9.0e-1<br>(N.S.)<br>[0.004 ± 0.03]  | 7.5e-1<br>(N.S.)<br>[0.13 ± 0.40]  | 8.7e-1<br>(N.S.)<br>[-0.01 ± 0.06]  | 6.5e-1<br>(N.S.)<br>[0.08 ± 0.17]  | 7.1e-1<br>(N.S.)<br>[0.09 ± 0.25]  |

p-values and [beta ± standard-error] were computed using linear models, after adjustments for age, education, and gender. Significant differences are indicated by asterisks: \*\*\*p < 0.001, \*\*0.001 ≤ p < 0.01, \*0.01 ≤ p < 0.05.