**Supplementary Material**

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| **Supplementary Table 1:** Demographic characteristics and hippocampal volumes of the ADNI cohort (n=779).   |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **ε2 carriers**  **(*n*=52)** | **ε3 carriers**  **(*n*=351)** | **ε4 carriers**  **(*n*=376)** |  | |  | ε2/ε3 (n=50)  ε2/ε2 (*n*=2) | ε3 Homozygotes | ε4/ε3 (*n*=290)  ε4/ε4 (n=86) | ***p*-value** | | **Alzheimer’s disease (*n*=177)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 5 (9.6) | 54 (15.4) | 118 (31.4) | -- | | Age (years) | 76.5 ± 9.8 | 77.0 ± 8.4 | 74.5 ± 7.0 | 0.121 | | Male (*n* (%)) **\*\*** | 1 (1.1) | 25 (26.3) | 69 (72.6) | 0.102 | | Education | 14.0 ± 3.2 | 15.1 ± 3.4 | 14.5 ± 3.1 | 0.532 | | MMSE | 21.8 ± 1.6 | 23.5 ± 2.0 | 23.2 ± 2.0 | 0.187 | | ICV (mL) | 1453 ± 127 | 1554 ± 185 | 1550 ± 192 | 0.514 | | Left Hippocampal volume (mL) | 1.60 ± 0.4 | 1.84 ± 0.4C | 1.76 ± 0.3 | **0.028** | | Right Hippocampal volume (mL) | 1.62 ± 0.5B | 1.91 ± 0.5C | 1.79 ± 0.3 | **0.004** | | **Mild cognitive impairment (*n*=383)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 16 (30.8) | 165 (47.0) | 202 (53.7) | -- | | Age (years) | 76.7 ± 7.3 | 75.7 ± 8.1 | 74.0 ± 7.0 | **0.049** | | Male (*n* (%)) **\*\*** | 8 (3.3) | 112 (45.7) | 125 (51.0) | 0.243 | | Education | 15.6 ± 2.7 | 15.7 ± 3.1 | 15.6 ± 3.0 | 0.980 | | MMSE | 27.5 ± 1.5 | 27.1 ±1.8 | 26.8 ± 1.8 | 0.189 | | ICV (mL) | 1511 ± 194 | 1581 ± 172 | 1571 ± 172 | 0.292 | | Left Hippocampal volume (mL) | 2.14 ± 0.3C | 2.03 ± 0.4C | 1.95 ± 0.4B | **0.001** | | Right Hippocampal volume (mL) | 2.19 ± 0.3C | 2.06 ± 0.4C | 1.98 ± 0.4A,B | **0.001** | | **Healthy controls (*n*=219)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 31 (59.6) | 132 (37.6) | 56 (14.9) | -- | | Age (years) | 75.7 ± 5.6 | 76.1 ± 5.0 | 75.7 ± 5.0 | 0.859 | | Male (*n* (%)) **\*\*** | 13 (11.4) | 72 (63.2) | 29 (25.4) | 0.449 | | Education | 15.8 ± 3.5 | 16.2 ± 2.8 | 16.1 ± 2.8 | 0.784 | | MMSE | 28.8 ± 1.2 | 29.2 ± 0.9 | 29.3 ± 0.8 | 0.134 | | ICV (mL) | 1493 ± 173 | 1549 ± 157 | 1534 ± 154 | 0.214 | | Left Hippocampal volume (mL) | 2.43 ± 0.4 | 2.32 ± 0.3 | 2.30 ± 0.3 | 0.187 | | Right Hippocampal volume (mL) | 2.44 ± 0.3 | 2.32 ± 0.3 | 2.30 ± 0.3 | 0.182 | |  |  |  |  |  |   MMSE, Mini-Mental State Examination; ICV, intracranial volume; CANTAB SWM, Cambridge Neuropsychological Test Automated Battery [CANTAB] Spatial Working Memory; IQ, intelligence quotient.  Data are Mean ± SD. Percentages are displayed in parentheses.  **\*\*** percentage calculated as number of males by each ApoE group  A significant compared to ε2 carriers  B significant compared to ε3 carriers  C significant compared to ε4 carriers |

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| **Supplementary Table 2:** Demographic characteristics and hippocampal volumes of the AIBL cohort (n=228).   |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | **ε2 carriers**  **(*n*=24)** | **ε3 carriers**  **(*n*=91)** | **ε4 carriers**  **(*n*=113)** |  | |  | ε2/ε3 (n=24)  ε2/ε2 (*n*=0) | ε3 Homozygotes | ε4/ε3 (*n*=93)  ε4/ε4 (n=20) | ***p*-value** | | **Alzheimer’s disease (*n*=46)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 5 (20.8) | 15 (16.5) | 26 (23.0) | -- | | Age (years) | 78.6 ± 6.0 | 76.7 ± 6.7 | 76.8 ± 7.7 | 0.864 | | Male (*n* (%)) **\*\*** | 2 (4.3) | 8 (17.4) | 13 (28.3) | 0.875 | | Education | -- | -- | -- | -- | | MMSE | 18.6 ± 8.2 | 22.3 ± 2.9 | 19.6 ± 4.9 | 0.155 | | ICV (mL) | 1411 ± 158 | 1555 ± 115 | 1593 ± 195 | 0.101 | | Left Hippocampal volume (mL) | 2.36 ± 0.4 | 2.36 ± 0.3 | 2.14 ± 0.4 | 0.096 | | Right Hippocampal volume (mL) | 2.44 ± 0.3C | 2.39 ± 0.3C | 2.13 ± 0.4A,B | **0.034** | | **Mild cognitive impairment (*n*=42)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 4 (16.6) | 16 (17.6) | 22 (19.5) | -- | | Age (years) | 79.5 ± 6.6 | 74.3 ± 7.6 | 75.6 ± 9.4 | 0.556 | | Male (*n* (%)) **\*\*** | 2 (4.8) | 5 (11.9) | 11 (26.2) | 0.491 | | Education | -- | -- | -- | -- | | MMSE | 28.5 ± 1.7 | 26.6 ±2.7 | 27.1 ± 2.2 | 0.380 | | ICV (mL) | 1467 ± 104 | 1491 ± 176 | 1533 ± 116 | 0.542 | | Left Hippocampal volume (mL) | 2.45 ± 0.2 | 2.47 ± 0.5 | 2.14 ± 0.4 | 0.068 | | Right Hippocampal volume (mL) | 2.46 ± 0.2 | 2.50 ± 0.5 | 2.22 ± 0.4 | 0.175 | | **Healthy controls (*n*=140)** |  |  |  |  | | Number of subjects (*n* (%)) **†** | 15 (62.5) | 132 (65.9) | 65 (57.5) | -- | | Age (years) | 78.3 ± 7.4 | 77.5 ± 7.9 | 76.4 ± 6.6 | 0.561 | | Male (*n* (%)) **\*\*** | 8 (5.7) | 28 (20.0) | 33 (23.6) | 0.852 | | Education | -- | -- | -- | -- | | MMSE | 28.7 ± 1.0 | 28.7 ± 1.1 | 28.9 ± 1.2 | 0.509 | | ICV (mL) | 1588 ± 189 | 1516 ± 169 | 1524 ± 150 | 0.298 | | Left Hippocampal volume (mL) | 2.33 ± 0.2 | 2.41 ± 0.4C | 2.23 ± 0.4 | **0.008** | | Right Hippocampal volume (mL) | 2.42 ± 0.3 | 2.49 ± 0.4C | 2.28 ± 0.4 | **0.003** | |  |  |  |  |  |   MMSE, Mini-Mental State Examination; ICV, intracranial volume; CANTAB SWM, Cambridge Neuropsychological Test Automated Battery [CANTAB] Spatial Working Memory; IQ, intelligence quotient.  Data are Mean ± SD. Percentages are displayed in parentheses.  **\*\*** percentage calculated as number of males by each ApoE group  A significant compared to ε2 carriers  B significant compared to ε3 carriers  C significant compared to ε4 carriers |