**Supplementary Material**

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| **Supplementary Table 1:** Demographic characteristics and hippocampal volumes of the ADNI cohort (n=779).

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| --- | --- | --- | --- | --- |
|  | **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 groupA significant compared to ε2 carriersB significant compared to ε3 carriersC 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 groupA significant compared to ε2 carriersB significant compared to ε3 carriersC significant compared to ε4 carriers |