Supplementary text:

**Volumetric analysis**

MPRAGE T1-weighted images were segmented using CAT12, a Computational Anatomy Toolbox based on SPM12. For the current analysis, the default parameters were used for CAT12 segmentation. Briefly, the CAT12 segmentation approach is based on an adaptive maximum a posterior technique that accounts for image intensity inhomogeneities, noise, local variations of intensity, and partial volume within each voxel. Using DARTEL normalization, the integration of the diffeomorphic anatomical was registered to an existing T1-weighted template in MNI space. Grey matter volume was calculated in those subjects.

**MRS data analysis**

Briefly, two MRS files were generated simultaneously by our scanner. One file was the actual (suppressed) MRS data, and the other file was the unsuppressed water signal intensity MRS file. To calculate the absolute concentration, the unsuppressed water signal intensity was used as internal reference. The MRS spectra were processed with jMRUI (4.0) software. Spectrum simulation of various metabolites was completed using the built-in NMR-SCOPE. Signal amplitudes were determined using QUEST (quantification based on quantum estimation). Only metabolite estimates with Cramer Rao lower Bounds (CRLBs) <20% were used for statistical analysis. The unsuppressed water signal was also measured using jMRUI. (Chiu et al., 2018; Chiu et al., 2015; Chiu et al., 2014)

**Sample size calculation for correlation:**

Assuming $\alpha=0.05$, $\beta=0.20$, expected $r=0.4$, total sample size=47;

Assuming $\alpha=0.05$, $\beta=0.20$, expected $r=0.6$, total sample size=19.
Table S1. Demographic, neuropsychological, behavioral, volumetric MRI, ASL MRI and MRS findings of ApoE4 (high risk) and non-ApoE4 (low risk) groups

|                             | Low risk group | High risk group | P value |
|-----------------------------|----------------|-----------------|---------|
| Number                      | 49             | 18              | -       |
| Gender (Female/Male)        | 28/21          | 14/4            | 0.12    |
| age                         | 49.27±16.56    | 49.00±16.18     | 0.95    |
| Educational years           | 14.74±4.43     | 14.89±3.77      | 0.90    |
| MoCA-HK                     | 28.92±1.22     | 29.06±0.94      | 0.67    |
| [Glx]abs_corr. in LH (mM)   | 14.03±3.44     | 13.18±3.29(N=15)| 0.40    |
| [Glx]abs_corr. in RH (mM)   | 13.36±3.29(N=48)| 13.60±3.77(N=16)| 0.81    |
| [ml]abs_corr. in LH         | 9.61±2.38      | 10.39±3.13(N=15)| 0.31    |
| [ml]abs_corr. in RH         | 10.25±1.47(N=48)| 9.54±2.93(N=16)| 0.36    |
| Accuracy of the recognition test | 79.77%±8.59%(N=48)| 81.48%±8.11%(N=48)| 0.47    |
| Response time of recognition test(s) | 2.64±0.78(N=48) | 2.66±1.76 | 0.94    |
| Performance index (PI)      | 3.36±1.07(N=48) | 3.44±2.98 | 0.86    |
| CBF in grey matter (mL/100g of brain tissue/min) | 57.59±9.42(N=46) | 57.78±8.18(N=17) | 0.94    |
| Grey matter volume (cm³)    | 616.94±79.38   | 597.17±82.02    | 0.37    |
| Normalized Grey matter volume(cm³) | 830.06±63.45 | 831.50±62.66 | 0.93    |
| Relative volume of Grey matter | 42.33%±3.14% | 42.08%±3.50% | 0.78    |

Two sample t test was used to calculate the significance between two groups.

*indicates p<0.05

**means p<0.01
Table S2. One sample t test of low-risk group during contrast: encoding-fixation.

| Regions of low-risk | x(mm) | y(mm) | z(mm) | Cluster size(voxels) | Peak T value |
|---------------------|-------|-------|-------|---------------------|--------------|
| **Encoding-Fixation** |       |       |       |                     |              |
| Fusiform_L          | -42   | -51   | -21   | 3338                | 16.81        |
| Fusiform_R          | 42    | -57   | -21   | 322                 | 16.30        |
| Lingual_L           | -30   | -81   | -12   | 134                 | 15.07        |
| Lingual_R           | 24    | -87   | -3    | 183                 | 12.48        |
| Precentral          | -48   | 6     | 30    | 1019                | 13.66        |
| Postcentral         | -45   | -9    | 42    | 435                 | 8.19         |
| Anterior cingulate  | -9    | 21    | 30    | 61                  | 6.50         |
| Middle cingulate    | 6     | 15    | 45    | 158                 | 9.40         |
| Precuneus           | -18   | -66   | 36    | 71                  | 7.87         |
| Insula_L            | -30   | 21    | 0     | 173                 | 10.37        |
| Insula_R            | 33    | 24    | 0     | 97                  | 7.12         |
| Thalamus_L          | -15   | -6    | 0     | 74                  | 6.87         |
| Thalamus_R          | 21    | -27   | 9     | 164                 | 6.07         |
| Superior frontal    | 15    | 6     | 60    | 359                 | 7.21         |
| Middle frontal_L    | -33   | 0     | 51    | 440                 | 11.74        |
| Middle frontal_R    | 42    | 6     | 54    | 420                 | 11.32        |
| Inferior frontal_L  | -48   | 9     | 27    | 1245                | 14.86        |
| Inferior frontal_R  | 51    | 12    | 27    | 937                 | 11.91        |
| Middle temporal_L   | -45   | -63   | -3    | 196                 | 7.27         |
| Middle temporal_R   | 42    | -72   | 0     | 219                 | 9.63         |
| Inferior temporal_L | -45   | -51   | -24   | 224                 | 14.83        |
| Inferior temporal_R | 45    | -57   | -21   | 262                 | 15.31        |
| Superior parietal_L | -27   | -63   | 45    | 264                 | 14.42        |
| Superior parietal_R | 27    | -66   | 51    | 212                 | 11.51        |
| Inferior parietal_L | -27   | -66   | 45    | 542                 | 14.37        |
| Inferior parietal_R | 36    | -54   | 45    | 219                 | 10.70        |
| Angular_L           | -36   | -60   | 42    | 61                  | 9.02         |
| Angular_R           | 27    | -63   | 48    | 122                 | 11.00        |
| Hippocampus_L       | -21   | -3    | -21   | 140                 | 8.08         |
| Hippocampus_R       | 24    | -3    | -21   | 123                 | 7.34         |
| Parahippocampus_L   | -18   | -3    | -24   | 88                  | 8.32         |
| Parahippocampus_R   | 18    | -3    | -21   | 92                  | 6.41         |
| Supramarginal_L     | -45   | -42   | 36    | 85                  | 7.86         |
| Supramarginal_R     | 48    | -39   | 45    | 88                  | 6.51         |
| Amygdala_L          | -21   | 0     | -24   | 49                  | 8.15         |
| Amygdala_R          | 24    | 0     | -21   | 54                  | 7.53         |
| Supplementary motor cortex | 6 | 9 | 54 | 542 | 12.48 |
| Occipital gyrus     | -42   | -69   | -12   | 1554                | 15.00        |

FDR correction, p<0.01, cluster size>810 mm^3
Table S3. One sample t test of high-risk group during contrast: encoding-fixation.

| Regions of High-risk | x(mm) | y(mm) | z(mm) | Cluster size(voxels) | Peak T value |
|----------------------|-------|-------|-------|----------------------|--------------|
| **Encoding-Fixation** |       |       |       |                      |              |
| Fusiform_L           | -39   | -51   | -21   | 271                  | 14.98        |
| Fusiform_R           | 42    | -54   | -21   | 279                  | 13.42        |
| Lingual_L            | -18   | -93   | -12   | 108                  | 12.05        |
| Lingual_R            | 21    | -84   | -6    | 149                  | 16.95        |
| Precentral           | -48   | 3     | 24    | 433                  | 8.71         |
| Insula_L             | -33   | 27    | 9     | 83                   | 6.90         |
| Insula_R             | 33    | -24   | 6     | 76                   | 5.22         |
| Superior frontal     | 27    | 3     | 48    | 67                   | 5.40         |
| Middle frontal_L     | -42   | 3     | 54    | 78                   | 7.84         |
| Middle frontal_R     | 39    | 6     | 54    | 184                  | 7.03         |
| Inferior frontal_L   | -48   | 6     | 27    | 484                  | 9.52         |
| Inferior frontal_R   | 45    | 12    | 24    | 358                  | 15.06        |
| Inferior temporal_L  | -48   | -57   | -15   | 124                  | 10.92        |
| Inferior temporal_R  | 45    | -51   | -24   | 208                  | 12.82        |
| Superior parietal_L  | -24   | -63   | 42    | 177                  | 10.62        |
| Superior parietal_R  | 30    | -60   | 51    | 79                   | 8.14         |
| Inferior parietal_L  | -27   | -57   | 42    | 189                  | 9.79         |
| Inferior parietal_R  | 30    | -54   | 48    | 83                   | 7.55         |
| Angular_R            | 27    | -57   | 45    | 76                   | 9.77         |
| Hippocampus_R        | 21    | -3    | -18   | 37                   | 7.12         |
| Supplementary motor cortex | -6 | 9     | 48    | 227                  | 8.40         |
| Occipital gyrus      | 36    | -78   | -9    | 1431                 | 19.73        |

FDR correction, p<0.01, cluster size>810 mm³
### Table S4. One sample t test of low-risk group during contrast: recall-fixation.

| Regions of low-risk | x(mm) | y(mm) | z(mm) | Cluster size(voxels) | Peak T value |
|---------------------|-------|-------|-------|----------------------|--------------|
| **Recall-Fixation** |       |       |       |                      |              |
| Fusiform_L          | -42   | -51   | -21   | 318                  | 19.16        |
| Fusiform_R          | 39    | -54   | -21   | 316                  | 19.87        |
| Lingual_L           | -30   | -81   | -12   | 157                  | 15.13        |
| Lingual_R           | 9     | -87   | -9    | 210                  | 15.13        |
| Precentral          | -33   | -3    | 48    | 1052                 | 17.12        |
| Postcentral         | -60   | -18   | 21    | 614                  | 9.61         |
| Anterior cingulate  | 9     | 33    | 27    | 352                  | 9.30         |
| Middle cingulate    | 9     | 18    | 45    | 325                  | 13.22        |
| Precuneus           | -18   | -66   | 36    | 353                  | 10.03        |
| Insula_L            | -30   | 24    | -3    | 263                  | 14.24        |
| Insula_R            | 33    | 24    | -3    | 183                  | 10.33        |
| Thalamus_L          | -18   | -9    | 0     | 235                  | 9.67         |
| Thalamus_R          | 12    | -18   | 6     | 232                  | 8.04         |
| Superior frontal    | -12   | 9     | 54    | 1339                 | 11.56        |
| Middle frontal_L    | -33   | 0     | 51    | 862                  | 16.61        |
| Middle frontal_R    | 42    | 6     | 54    | 880                  | 12.02        |
| Inferior frontal_L  | -42   | 9     | 30    | 1275                 | 15.91        |
| Inferior frontal_R  | 45    | 12    | 24    | 1040                 | 14.50        |
| Middle temporal_L   | -42   | -63   | -3    | 432                  | 8.05         |
| Middle temporal_R   | 45    | -72   | 0     | 333                  | 8.86         |
| Inferior temporal_L | -45   | -51   | -24   | 235                  | 15.70        |
| Inferior temporal_R | 45    | -57   | -21   | 264                  | 15.92        |
| Superior parietal_L | -24   | -66   | 42    | 290                  | 15.46        |
| Superior parietal_R | 27    | -66   | 51    | 229                  | 12.50        |
| Inferior parietal_L | -33   | -51   | 45    | 615                  | 15.15        |
| Inferior parietal_R | 36    | -54   | 42    | 291                  | 11.47        |
| Angular_L           | -33   | -51   | 36    | 136                  | 11.87        |
| Angular_R           | 30    | -66   | 48    | 217                  | 12.66        |
| Hippocampus_L       | -21   | -3    | -24   | 119                  | 7.51         |
| Hippocampus_R       | 21    | -3    | -21   | 92                   | 7.64         |
| Parahippocampus_L   | -18   | 0     | -24   | 62                   | 7.91         |
| Parahippocampus_R   | 18    | -3    | -21   | 93                   | 7.32         |
| Supramarginal_L     | -51   | -24   | 36    | 266                  | 9.41         |
| Supramarginal_R     | 45    | -42   | 45    | 193                  | 8.66         |
| Amygdala_L          | -21   | 0     | -24   | 57                   | 8.51         |
| Amygdala_R          | 24    | 0     | -18   | 50                   | 8.18         |
| Supplementary motor cortex | -9 | 12 | 51 | 619 | 14.18 |
| Occipital gyrus     | -27   | -66   | 39    | 1525                 | 15.87        |

FDR correction, p<0.01, cluster size>810 mm³
Table S5. One sample t test of high-risk group during contrast: recall-fixation.

| Regions of High-risk       | x(mm)  | y(mm)  | z(mm)  | Cluster size(voxels) | Peak T value |
|----------------------------|--------|--------|--------|----------------------|--------------|
| **Recall-Fixation**        |        |        |        |                      |              |
| Fusiform_L                 | -42    | -51    | -18    | 267                  | 12.18        |
| Fusiform_R                 | 27     | -81    | 0      | 272                  | 10.93        |
| Lingual_L                  | -30    | -81    | -15    | 135                  | 10.35        |
| Lingual_R                  | 21     | -84    | -6     | 163                  | 11.99        |
| Precentral                 | -39    | 0      | 51     | 571                  | 12.13        |
| Middle cingulum            | 9      | 18     | 42     | 124                  | 9.89         |
| Precuneus                  | 18     | -69    | 48     | 105                  | 8.16         |
| Thalamus_L                 | -21    | -12    | 3      | 41                   | 6.27         |
| Thalamus_R                 | 15     | -9     | 12     | 66                   | 7.38         |
| Superior frontal           | -12    | 18     | 45     | 231                  | 8.30         |
| Middle frontal_L           | -39    | 3      | 51     | 161                  | 9.02         |
| Middle frontal_R           | 36     | 6      | 45     | 323                  | 9.69         |
| Inferior frontal_L         | -33    | 30     | -6     | 642                  | 10.73        |
| Inferior frontal_R         | 45     | 12     | 24     | 510                  | 12.18        |
| Inferior temporal_L        | -48    | -48    | -21    | 117                  | 9.89         |
| Inferior temporal_R        | 39     | -63    | -9     | 171                  | 9.18         |
| Superior parietal_L        | -33    | -60    | 51     | 179                  | 9.98         |
| Superior parietal_R        | 30     | -63    | 51     | 82                   | 7.61         |
| Inferior parietal_L        | -30    | -51    | 45     | 337                  | 11.24        |
| Inferior parietal_R        | 39     | -54    | 42     | 140                  | 8.14         |
| Angular_L                  | -30    | -51    | 36     | 41                   | 6.67         |
| Angular_R                  | 30     | -60    | 45     | 105                  | 9.75         |
| Supramarginal_L            | -63    | -21    | 27     | 51                   | 8.12         |
| Supplementary motor cortex | -9     | 18     | 45     | 472                  | 11.53        |
| Occipital gyrus            | 36     | -78    | -9     | 1281                 | 12.59        |

FDR correction, p<0.01, cluster size>810 mm³
Table S6. The two sample t test results between high-risk and age-matched low-risk (High-Low):

| Regions of High-Low          | x(mm) | y(mm) | z(mm) | Cluster size(voxels) | Peak T value |
|------------------------------|-------|-------|-------|----------------------|--------------|
| **Encoding-Fixation**        |       |       |       |                      |              |
| Fusiform_R                   | 33    | -66   | -9    | 115                  | 4.33         |
| Lingual_L                    | -12   | -42   | -9    | 67                   | 3.06         |
| Lingual_R                    | 24    | -45   | -9    | 21                   | 2.82         |
| Precuneus                    | 15    | -75   | 48    | 14                   | 2.65         |
| Middle temporal_L            | -54   | -69   | 24    | 14                   | 2.52         |
| Inferior temporal_L          | -48   | -66   | -6    | 28                   | 3.06         |
| Superior parietal_L          | -24   | -69   | 54    | 77                   | 3.40         |
| Superior parietal_R          | 24    | -78   | 48    | 20                   | 3.13         |
| Angular_L                    | -48   | -72   | 27    | 13                   | 2.37         |
| Parahippocampus_R            | 24    | -3    | -30   | 4                    | 2.81         |
| Occipital gyrus              | -30   | -90   | 12    | 430                  | 4.41         |
| **Recall-Fixation**          |       |       |       |                      |              |
| Fusiform_R                   | 33    | -66   | -12   | 130                  | 4.35         |
| Lingual_L                    | -12   | -45   | -9    | 68                   | 2.77         |
| Lingual_R                    | 24    | -48   | -6    | 24                   | 2.76         |
| Middle temporal_R            | 45    | -72   | 15    | 17                   | 2.72         |
| Superior parietal_R          | 24    | -78   | 48    | 17                   | 2.53         |
| Hippocampus_L                | -18   | -36   | 0     | 11                   | 2.46         |
| Parahippocampus_L            | -18   | -36   | -3    | 5                    | 2.34         |
| Parahippocampus_R            | 24    | -42   | -6    | 4                    | 2.39         |
| Occipital gyrus              | 39    | -78   | 18    | 201                  | 3.33         |

Alphasim correction method, p<0.05, cluster size>4158 mm³
Figure S1. Position of voxel placed in the left and right hippocampi, voxels were of size 2.5×1.5×1 cm³.
**Figure S2.** Block design of face-name memory task