SUPPLEMENTARY MATERIAL

APOE genotyping

DNA was isolated from blood using the QIAmp Blood DNA Maxi Kit protocol (Qiagen, Valencia, CA, USA). Genotypes for two APOE SNPs, rs429358 (E*4) and rs7412 (E*2) were determined using TaqMan SNP genotyping assays (Applied Biosystems, Foster City, California).

Structural and functional MRI data acquisition

Imaging data were collected by the Department of Radiology of Yeouido Saint Mary's Hospital at the Catholic University of Korea using a 3-T Siemens Skyra MRI machine and a 32-channel Siemens head coil (Siemens Medical Solutions, Erlangen, Germany). The parameters used for the T1-weighted volumetric magnetization-prepared rapid gradient echo scan sequences were TE=2.6 ms, TR=1,940 ms, inversion time=979 ms, FOV=230 mm, matrix =256×256, and voxel size=1.0×1.0×1.0 mm^3. Resting-state fMR images were collected using a T2* weighting gradient echo sequence with TR=2,000 ms, TE=30 ms, matrix=128×128×29, and voxel size=1×1× 2 mm^3. We acquired 150 volumes in 5 minutes, with the instruction, "keep your eyes closed and think of nothing in particular."

The preprocessing included slice timing, realignment for motion corrections, spatial registration, normalization, and smoothing.

Functional MRI data preprocessing

We used the Data Processing Assistant for Resting-State fMRI (DPARSF; GNU GENERAL PUBLIC LICENSE, Beijing, China), which is based on Statistical Parametric Mapping (SPM 12; http://www.fil.ion.ucl.ac.uk/spm, Wellcome Centre for Human Neuroimaging, London, England), to preprocess the fMRI images. Slice timing and realignment for motion corrections were performed on the images. Subjects with excessive head motion (cumulative translation or rotation >2 mm or 2°) were excluded. To prevent group-related differences caused by microscopic head motion, framewise displacement (FD) was compared between the groups. Mean FD scores did not differ between *APOE* ε4 carrier and non-carrier (p>0.05, 2-sample t-test). For spatial registration, T1-weighted images were co-registered to the mean rsfMRI image based on rigid-body transformation. For spatial normalization, the International Consortium for Brain Mapping template was applied (resampling voxel size=3×3×3 mm) and fitted to the "East Asian brain." After this, the functional images were spatially smoothed with a 6 mm full width at half maximum Gaussian kernel. For local FC (regional homogeneity), spatial smoothing was performed after a map for local FC was obtained, not to increase the regional similarity.[1] We further processed our functional data to fit them to local and remote FC analysis with DPARSF. Linear trends were removed from the functional images, and data were filtered with a temporal band-pass of 0.01−0.08 Hz, to reduce low-frequency drift as well as physiological high-frequency respiratory and cardiac noise. Several nuisance covariates were regressed out, including six head motion parameters and signals from the white matter and CSF.

Calculation of intra- and inter-network functional connectivity

Intra-network functional connectivity[2]

$$Z_X = \frac{1}{\frac{n_X(n_X-1)}{2}} \sum_{ij=1:n_X} |z_{i,j}|,$$

where n_X is the number of ROIs within a specific network X

Inter-network functional connectivity[2]

$$Z_{X,Y} = \frac{1}{n_X n_Y} \sum_{i \in X, j \in Y} |z_{i,j}|,$$

where X and Y denotes the network of the three resting state networks.

PET scanners

Each scanner was commissioned by scanning a NEMA phantom and adjusting the reconstruction parameters to obtain a spatial resolution of approximately 6.5 mm. This optimization was performed in advance of the scanning of patients and the images received by GE were not subject to any further post-processing in regards of spatial resolution.

REFERENCES

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