Supplementary Material 4

Imaging data preprocessing and processing

DTI image

DTI data were processed in the Camino (http://www.cs.ucl.ac.uk/research/medic/camino/) and FMRIB Software Library (FSL) v5.0 (University of Oxford Center for Functional MRI of the Brain, http://www.fmrib.ox.ac.uk/)[1] software. The probabilistic index of connectivity (PICo) [2,3] algorithm was used in 21 HCs to obtain the nodal brain regions of the "hippocampus-cortex" network based on probabilistic fiber tracking. The procedure was performed as follows[4] : 1) Preprocessing: including eddy currents correction, head movement correction, stripping of nonbrain tissue, and calculation of fractional anisotropy (FA) values, and so on. 2) Determination of seed and target areas: seed and target maps were determined using the automated anatomical labeling (AAL) template[5], including two voxel-based seeds (left and right hippocampus) and two voxel-based target area maps (left and right cortical brain area maps) **(Table S4-1)**. All seed and target areas acquired in the standard atlas were converted to subject-specific native space. We registered FA maps to the corresponding T1-weighted scans in native space using FMRIB's Linear Image Registration Tool (FLIRT) and nonlinearly transformed to register the T1-weighted images to standard MNI space. Subsequently, the transformation parameters estimated above were inversed and then applied to the seed and cortical areas in standard space. 3) Probabilistic tracking: fiber tracing was started 5000 times in diffuse space (threshold: single voxel ≤ 80° or FA of voxel ≥ 0.1) starting with each voxel within the seed point, and PICo was derived from the total number of seed point voxels reaching the target area. 4) Segmentation based on voxel connectivity: To minimize noise, we thresholded the average PICo and selected only voxels with probability connectivity index >1%. 5) Determining the nodal brain regions of the "hippocampus-cortex" network: After averaging the PICo of the seed voxels of all subjects, the target brain regions with seed voxels ≥20 were selected as the cortical nodal brain regions of the "hippocampus-cortex" network. Finally, 37 cortical brain regions were obtained using this method, and together with the bilateral hippocampus, a total of 39 nodal brain regions of the "hippocampus-cortex" network with white matter fiber were identified (**Table S4-1**).

Table S4-1 The seeds and target brain regions by using the automated anatomical labeling (AAL) template

seeds and target (left and right)	**Abbreviation**	**"hippocampus-cortex" network nodes with WM connection**
Precentral gyrus	PreCG	
Superior frontal gyrus, dorsolateral part	SFGdor	LR
Superior frontal gyrus, orbital part	SFGorb	LR
Middle frontal gyrus	MFG	
Middle frontal gyrus, orbital part	MFGorb	R
Inferior frontal gyrus, opercular part	IFGoper	R
Inferior frontal gyrus, triangular part	IFGtri	R
Inferior frontal gyrus, orbital part	IFGorb	LR
Rolandic operculum	ROL	L
Supplementary motor area	SMA	LR
Superior frontal gyrus, medial part	SFGmed	R
Superior frontal gyrus, medial orbital part	SFGmedorb	LR
Hippocampus	HIP	L,R
Cuneus	CUN	
Lingual gyrus	LING	LR
Superior occipital gyrus	SOG	LR
Middle occipital gyrus	MOG	L
Inferior occipital gyrus	IOG	
Postcentral gyrus	PoCG	R
Superior parietal gyrus	SPG	LR
Inferior parietal gyrus	IPL	
Supramarginal gyrus	SMG	

Angular gyrus	ANG	R
Precuneus	PCUN	LR
Paracentral lobule	PCL	
Heschl gyrus	HES	L
Superior temporal gyrus	STG	L,R
Superior temporal gyrus, temporal pole	STGp	L,R
Middle temporal gyrus	MTG	L,R
Middle temporal gyrus, temporal pole	MTGp	L,R
Inferior temporal gyrus	ITG	L,R

Note. WM: white matter; L:left; R:right.

Functional image

Functional image preprocessing and FC calculation were performed using MATLAB 2013b platform (The Mathworks, Inc, Natick, US), Statistical Parametric Mapping 12 (SPM12) (http://www.fil.ion.ucl.ac.uk/spm/), and Data Processing Assistant for Resting-State fMRI[6] (DPARSF, version 5.0) (http://www.rfmri.org/dpabi). The preprocessing steps included: removal of the first 10 time points, slice timing, head motion correction (for excessive translation or rotation, i.e., ≥ 2.5 mm and 2.5°, respectively), spatial normalization (Dartel), regression of nuisance variables (24 head movement parameters, white matter and cerebrospinal fluid), detrend, filter, spatial smoothing (using a 6 mm × 6 mm × 6 mm Gaussian kernel), pre-smoothing for voxel-based FC, region of interest (ROI) based FC were post-smoothed.

FC: FC[7] is obtained by calculating Pearson correlation coefficients between mutually independent brain regions on a time series, which reflects the closeness of the relationship between brain regions. In this study, two methods of FC analysis, voxel-based and ROI-based, were used. We did voxel-based FC analysis with the left and right hippocampus as seed points, respectively, with voxel targets of the AAL whole-brain template. In addition, we did ROI-based FC analysis with the brain regions that were statistically different after group comparison as ROIs for clinical data correlation analysis. The Pearson correlation coefficients obtained by both methods were Fisher-Z transformed.

Construction of individualized stimulation target and 3D precise localization

Designation of optimized target and manufacture of 3D-printed helmets were established in 2 weeks before treatment. The 3D-printed helmets were provided by Zhejiang Futong Huizhi Medical Technology Co., Ltd. We applied spatial transformations to convert the voxel-based seed and cortical areas from subject-specific native space into standard Montreal Neurological Institute (MNI) space. The transformations were performed for each participant after first co-registering the T1-weighted scans with their corresponding FA maps in native space. Next, the co-registered structural images were segmented and transformed into standard MNI space. Finally, the parameters estimated by converting T1-weighted images to a standardized anatomical template were applied to the individual stimulation target. Then, through 3D printing technology, the individual stimulation target is marked on the helmet for precise positioning before TMS stimulation, which aim to ensure that the position of the stimulation target remains unchanged during each intervention of each subject (Figure S4-1). It’s worth noting that, in order to ensure the accuracy of the stimulation target, we utilized the eXimia NBS navigation system (Nextim Limited Company, Helsinki, Finland) to verify each printed 3D point before intervention.

Figure S4-1. Custom-made 3D-printed helmet

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