Radiology

ORIGINAL RESEARCH · NEURORADIOLOGY

Modulation of Cortical and Hippocampal Functional MRI Connectivity Following Transcranial Alternating Current Stimulation in Mild Alzheimer Disease

Tao Wang, MD[*1,2,3] • *Shaozhen Yan, MD*[*1,2,3] • *Yi Shan, MD*[1,2,3] • *Hanxiao Xue, MS*[1,2,3] • *Yi Xing, MD*[4] • *Sheng Bi, MD*[1,2,3] • *Zhigeng Chen, MD*[1,2,3] • *Hanyu Xi, MD*[1,2,3] • *Zhigang Qi, MD*[1,2,3] • *Yi Tang, MD, PhD*[**4] • *Jie Lu, MD, PhD*[**1,2,3]

* T.W. and S.Y. contributed equally to this work.

** Y.T. and J.L. are co–senior authors.

Author affiliations, funding, and conflicts of interest are listed at the end of this article.

See also the editorial by Shepherd in this issue.

Radiology 2025; 315(3):e241463 • https://doi.org/10.1148/radiol.241463 • Content codes: NR MR

Background: Transcranial alternating current stimulation (tACS) may be effective for improving cognitive function in Alzheimer disease (AD), but its impact on brain functional connectivity (FC) has not been well studied.

Purpose: To evaluate tACS efficacy in improving cognitive performance and modulating FC between brain regions in individuals with AD using functional MRI.

Materials and Methods: In this prospective randomized controlled trial (September 2020 to April 2022), participants with mild AD were assigned to active (40 Hz tACS with 15-mA intensity) or sham (no γ frequency or current) tACS groups for 3 weeks (referred to as week 3), with a 3-month follow-up (referred to as month 3). Functional MRI and cognitive testing were performed at baseline, week 3, and month 3. Primary outcomes were changes in Mini-Mental State Examination and Montreal Cognitive Assessment scores from baseline to week 3. Secondary outcomes included FC changes within multiple cortical networks and between cortex and hippocampus from baseline to week 3 and month 3, assessed using Fisher *z*-transformed correlation coefficient (hereafter, *z* score).

Results: Forty-six participants were randomized into the active group ($n = 23$; median age, 66 years; IQR, 62–69 years; 16 female participants) or the sham group ($n = 23$; mean age, 64 years; IQR, 61–69 years; 14 female participants). The active group had higher Mini-Mental State Examination (median score change, 2 [IQR, 1–5] vs 0 [IQR, −1 to 2]; $P = .001$) and Montreal Cognitive Assessment (median score change, 2 [IQR, 0–4] vs 0 [IQR, −1 to 2]; $P = .03$) scores than the sham group at week 3, respectively. Compared with the sham group, the active group had increased FC between left hippocampus and left middle cingulate gyrus (*z* score difference, 0.29; 95% CI: 0.17, 0.42; false discovery rate [FDR]–adjusted $P < .001$) and between the left hippocampus and the left middle frontal gyrus (*z* score difference, 0.16; 95% CI: 0.03, 0.29; FDR-adjusted $P = .04$) within the posterior default-mode network (*z* score difference, 0.40; 95% CI: 0.07, 0.73; FDR-adjusted $P = .046$) and within the visual network (*z* score difference, 0.45; 95% CI: 0.17, 0.73; FDR-adjusted $P = .007$) from baseline to week 3.

Conclusion: Cognitive performance in mild AD improved following tACS, with increased FC within cortical networks and between the hippocampus and specific cortical regions.

ClinicalTrials.gov Identifier: NCT03920826

Supplemental material is available for this article.

Alzheimer disease (AD), the most common neurodegenerative disease, is increasingly recognized as a costly and debilitating condition (1). Currently, over 50 million people worldwide have AD, and this number is projected to nearly triple to 150 million by 2050 if effective treatments are not developed (2). Trials using anti–amyloid-β immunotherapy in patients with AD demonstrated that removing amyloid-β from the brain can help preserve cognitive function (3). Despite renewed optimism for amyloid-β–modifying therapies such as lecanemab, concerns remain regarding their high cost and risks of infusion-related reactions (incidence of approximately 26.4%) and amyloid-related imaging abnormalities (prevalence of 17.3%) (4). These risks associated with amyloid-β–modifying therapies have led to uncertainties regarding their clinical benefits and potential harms (5).

Noninvasive brain stimulation, such as transcranial electrical stimulation and transcranial magnetic stimulation, effectively modulates neuronal activity and is emerging as a promising nonpharmacologic strategy in AD (6). Transcranial alternating current stimulation (tACS) is more effective at modulating local field potentials of functional networks and the hippocampus (7–9). A previous tACS study of 60 patients with AD reported beneficial effects on memory performance and restoration of cholinergic transmission (10). However, clinical effectiveness evaluations of tACS for AD are limited. In a pilot study of 15 patients with AD, tACS was found to increase cerebral blood flow in the temporal lobe, providing preliminary evidence of the impact of tACS on cortical perfusion in the hippocampus and entorhinal cortex (11). However, to the knowledge of the authors, the potential impact of tACS on MRI-based functional connectivity (FC) in AD has not been investigated, limiting understanding of its clinical utility.

Functional MRI provides evidence of the involvement of specific neuronal networks in cognitive processes (12,13). The

Abbreviations

AD = Alzheimer disease, DMN = default-mode network, FC = functional connectivity, FDR = false discovery rate, FPN = frontoparietal network, MNI = Montreal Neurological Institute, tACS = transcranial alternating current stimulation

Summary

Cognitive performance in individuals with mild Alzheimer disease improved following transcranial alternating current stimulation, with increased functional MRI connectivity within cortical networks and between the hippocampus and specific cortical regions.

Key Results

- In this prospective, randomized, controlled trial including 46 participants with mild Alzheimer disease, participants who underwent active transcranial alternating current stimulation (tACS; 40-Hz tACS with 15-mA current intensity) had higher Mini-Mental State Examination (median change, 2 vs 0; $P = .001$) and Montreal Cognitive Assessment (median change, 2 vs 0; $P = .03$) scores compared with the sham group.
- Compared with the sham group, the active tACS group had increased functional MRI connectivity between the left hippocampus and left middle cingulate gyrus (z score difference, 0.29; false discovery rate [FDR]–adjusted $P < .001$), between the left hippocampus and left middle frontal gyrus (0.16, FDR-adjusted $P = .04$), within the posterior default-mode network (0.40, FDR-adjusted $P = .046$), and within the visual network (0.45, FDR-adjusted $P = .007$) from baseline to week 3.

hippocampus and entorhinal cortex are recognized as the initial vulnerable regions in AD (14,15). Network in AD predominantly involve the default-mode network (DMN) and frontoparietal network (FPN) (16,17). Decreased FC in these regions indicate synaptic dysfunction (18,19). Prior transcranial direct current stimulation studies have demonstrated the capacity to increase FC within the DMN and FPN in patients with mild AD, suggesting a potential for functional network normalization (20–22). Whereas transcranial electrical stimulation studies provided valuable insights, the frequency-specific nature of tACS may offer distinct mechanisms for modulating FC in AD. However, the impact of tACS on FC in the hippocampus, entorhinal cortex, and cortical functional networks remains unexplored. This study aimed to evaluate the efficacy of tACS in improving cognitive performance and modulating FC between brain regions in individuals with AD, as assessed by functional MRI.

Materials and Methods

Study Design and Participants

This prospective, randomized, double-blinded trial (ClinicalTrials.gov identifier: NCT03920826) was conducted at Xuanwu Hospital, Capital Medical University (Beijing, China), from September 2020 to April 2022. The protocol was approved by the Medical Research Ethics Committee at Xuanwu Hospital, Capital Medical University, and reported in accordance with Consolidated Standards of Reporting Trials guidelines. All participants provided written informed consent before undergoing any procedure. The study protocol was previously published (23). The study included a 3-week tACS intervention phase (hereafter, referred to as week 3) and a 3-month follow-up phase without tACS intervention (hereafter, referred to as month 3). The evaluation of cognitive scores and MRI was performed at baseline, week 3, and month 3. The flowchart of the study is shown in Figure 1. The participants recruited in the study were randomly assigned at a 1:1 ratio to undergo the active or the sham tACS according to a computer-generated list of random numbers. All study staff and participants were blinded to the intervention group allocation.

Patients aged 45–75 years with mild AD were recruited according to the following inclusion criteria: right-handed, Chinese, with a minimum of 6 years of education; met the diagnostic criteria of AD according to the National Institute on Aging and the Alzheimer's Association guidelines (24); clinical dementia rating scale score of 1.0 at baseline; amyloid-β–positive findings at PET imaging or cerebrospinal fluid testing; and were administered a fixed dose of a cholinesterase inhibitor, such as rivastigmine or donepezil, consistently for a minimum duration of 6 weeks, with the dose remained unchanged throughout the intervention and follow-up period. The exclusion criteria were as follows: current or history of other neurologic diseases that may affect cognition (eg, epilepsy, stroke, hemorrhage, and mass), other neurodegenerative diseases (eg, Parkinson disease and frontotemporal dementia), severe psychiatric disorders, MRI and tACS contraindications, and patients who were unable to complete cognitive tests.

Intervention

Participants underwent either active or sham stimulation from the tACS stimulator (Nexalin ADI; Nexalin Technologies). Previous clinical studies have confirmed that 40-Hz gamma frequency is crucial for neural communication and network integration (25), and 15-mA procedures can administer electrical currents to the hippocampus (9). Therefore, 40-Hz tACS with 15-mA intensity was chosen in this study. Participants in the active group underwent 30 1-hour tACS sessions across 3 weeks at a fixed time twice daily from Monday to Friday. Participants in the sham group underwent tACS using the same tACS stimulator without any gamma frequency and current intensity, receiving the same sessions and duration with the active group. Additional details of the tACS procedure are available in Appendix S1.

Imaging Acquisition

Imaging data were acquired using a 3.0 T MRI scanner (SIGNA Premier; GE Healthcare). Structural T1-weighted images were obtained using a sagittal three-dimensional magnetization prepared rapid gradient-echo sequence. The functional MRI data were collected using a multiband echo-planar imaging sequence, with an acquisition process lasting 8 minutes. Additional details of imaging acquisition are available in Appendix S1.

Imaging Processing

Data preprocessing and FC analysis were performed by two experienced radiologists (T.W., with 5 years of experience; and S.Y., with 10 years of experience). Details are included in Appendix S1. Functional MRI data were considered eligible if head motion was smaller than 2 mm in translation and 2 degrees in rotation. Poor-quality data were excluded due to excessive artifacts and incomplete acquisition. All coordinates (x-, y-, and z-axes) were reported in Montreal Neurological Institute (MNI) space, where x represented the left-right axis, y represented the anterior-posterior axis, and z represented the superior-inferior axis (hereafter, MNI x-, y-, and z-axes). In short, seed-based FC analysis

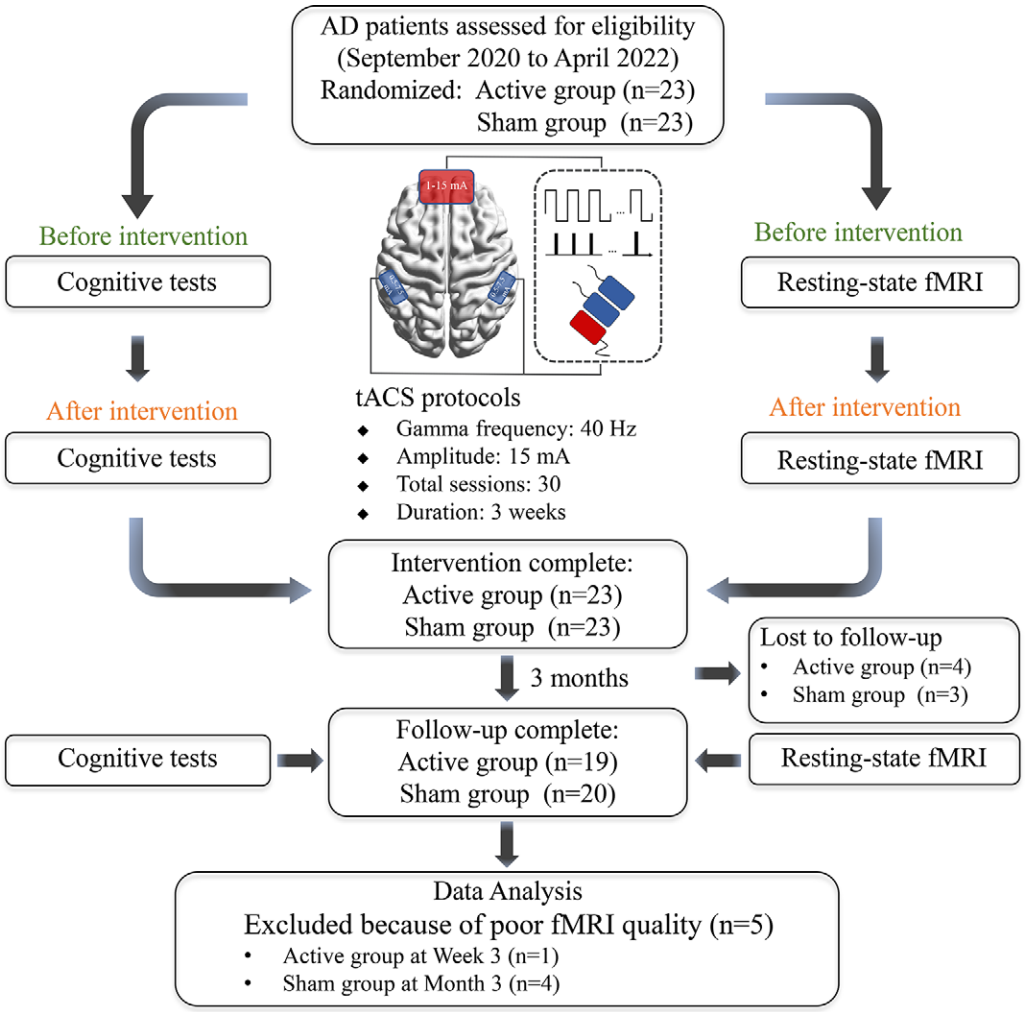

Figure 1: Study flowchart. AD = Alzheimer disease, fMRI = functional MRI, tACS = transcranial alternating current stimulation.

was conducted with left hippocampus, right hippocampus, left entorhinal cortex, and right entorhinal cortex as the regions of interest (Fig S1). The mean time course from each seed was extracted for each participant and correlated with the time course of every voxel in the brain using the Pearson correlation analysis. The map of correlation coefficients was transformed to Fisher *z* transformation score (*z* scores). The group-level independent component analysis was performed to assess FC patterns within the functional networks. The components were selected by visual inspection, including the posterior and anterior DMN, left and right FPN, visual network, auditory network and dorsal attention network (Fig S2).

Cognitive Tests

The following cognitive tests were performed: Mini-Mental State Examination; Montreal Cognitive Assessment; AD Assessment Scale-cognitive subscale; World Health Organization–University of California Los Angeles Auditory Verbal Learning Test, consisting of immediate recall, delay recall, and recognition recall; Trail Making Test, consisting of A and B parts; and Boston Naming Test. Two neurologists (Y.X. and Y.T., each with more than 10 years of experience) performed the cognitive tests and were blinded to the intervention group allocation for each participant.

Statistical Analysis

Details of the sample size calculation are described in Appendix S1. Participant demographics and cognitive scores were analyzed using statistical software (SPSS, version 24.0; IBM). The difference in Mini-Mental State Examination and Montreal Cognitive Assessment scores from baseline to week 3 between the active group and the sham group was used to assess the treatment effect. Differences between the active and sham groups at baseline were assessed using Fisher exact test for categorical variables and Mann-Whitney *U* test for continuous variables. The Wilcoxon signed rank test was conducted to assess the change in cognitive scores from baseline to week 3 and month 3.

SPM, version 12 *(https://www.fil.ion.ucl.ac.uk/spm)* was applied to identify the voxel coordinates with the statistically significant effect from baseline to week 3 or month 3 for functional MRI data analysis based on a generalized linear model (cluster size >10; $P < .001$). The *z* score was extracted for each region of interest from a sphere with a radius of 5 mm. The linear mixed effects model (group × time) was used to assess the *z* score changes of the identified voxel across intervention conditions, exploring tACS treatment effects. The 95% CI was used to provide uncertainty estimates for the mixed-effects model. The model incorporated random intercepts and slopes. The final model was obtained based on the Akaike information criterion and the Bayesian

Table 1: Participant Characteristics

Characteristic	Active Group (n = 23)	Sham Group (n = 23)	Estimated Score Difference*	P Value
Age (y)	66 (62, 69)	64 (61, 69)	−2 (−5, 1)	.22
Sex				.76
Male†	7 (30)	9 (39)	...	...
Female†	16 (70)	14 (61)	...	...
Education (y)	10 (9–12)	9 (7–13)	0 (−3, 2)	.58
MMSE	19 (18–21)	20 (18–23)	1 (−1, 3)	.32
MoCA	14 (12–16)	15 (13–18)	1 (−1, 3)	.27
ADAS-cog	18 (14–22)	17 (11–21)	−1 (−5, 3)	.57
AVLT-IR	15 (11–18)	15 (10–19)	0 (−3, 4)	.95
AVLT-DR	0 (0–2)	0 (0–2)	0 (0, 0)	.99
AVLT-R-R	6 (3–9)	6 (3–7)	0 (−3, 1)	.60
TMT-A	101 (67–150)	74 (46–108)	−19 (−45, 3)	.17
TMT-B	216 (153–300)	160 (102–300)	0 (−84, 11)	.40
BNT	20 (18–22)	22 (18–25)	0 (−2, 3)	.71

Note.—Except where indicated, data are reported as medians, with IQRs in parentheses. For cognitive scores, the unit is the median test score. Categorical data were compared between groups using the Fisher exact test, and continuous data were compared between groups using Mann-Whitney U test. ADAS-cog = Alzheimer Disease Assessment Scale–cognitive subscale, AVLT = Auditory Verbal Learning Test, BNT = Boston Naming Test, DR = delay recall, IR = immediate recall, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, R-R = recognition recall, TMT-A = Trail Making Test part A, TMT-B = Trail Making Test part B.

* Data in parentheses are 95% CIs.

† Data are numbers of patients and data in parentheses are percentages.

information criterion. If both criteria suggest the same model, the one with the lower value would be selected. In cases where the criteria are inconsistent, the model selected by the Bayesian information criterion would be prioritized.

Spearman correlation analysis was used to examine the relationship between the changes in z scores and the corresponding alterations in cognitive scores. False discovery rate (FDR) adjustment was computed to account for multiple comparisons; details are provided in Appendix S1.

Results

Participant Characteristics

A total of 46 participants with mild AD were included and randomized into the active or sham groups, with an equal distribution of 23 participants in the active group (median age, 66 years [IQR, 62–69 years]; seven male participants, 16 female participants) and 23 participants in the sham group (median age, 64 years [IQR, 61–69 years]; nine male, 14 female participants) (Fig 1). There was no evidence of differences in baseline characteristics between the two test groups (P > .05) (Table 1).

Changes in Cognitive Scores

The participants included completed the cognitive assessments at week 3. Seven participants (active group, four participants; sham group, three participants) dropped out at month 3. Participants in the active group had higher Mini-Mental State Examination (week 3: median score change, 3 [95% CI: 1.5, 4; FDR-adjusted P < .001]; month 3: median score change, 2 [95% CI: 0, 3.5l; FDR-adjusted P = .06]) and Montreal Cognitive Assessment (week 3: median score change, 2 [95% CI: 1, 3.5; FDR-adjusted P = .006]; month 3: median score change, 1.5 [95% CI: 0, 3.5; FDR-adjusted P = .06]) scores at week 3 and month 3 compared with baseline. There was no evidence of a difference in Mini-Mental State Examination (week 3: median score change, 0 [95% CI: −1, 1; FDR-adjusted P = .76]; month 3: median score change, 0 [95% CI: −1.5, 1.5; FDR-adjusted P = .87]) and Montreal Cognitive Assessment (week 3: median score change, 0.5 [95% CI: −0.5, 1.5; FDR-adjusted P = .43]; month 3: median score change, 0.5 [95% CI: −0.5, 2; FDR-adjusted P = .98]) in the sham group from baseline to week 3 and month 3. Participants in the active group had higher Mini-Mental State Examination (median score change, 2 [IQR, 1–5] vs 0 [IQR, −1 to 2], respectively; P = .001) and Montreal Cognitive Assessment (median score change, 2 [IQR, 0–4] vs 0 [IQR, −1 to 2], respectively; P = .03) scores than those in the sham group at week 3 after tACS.

From baseline to week 3 and month 3, higher Auditory Verbal Learning Test–Delay Recall (median score change, 1.5; 95% CI: −0, 3.5; FDR-adjusted P = .09) and Boston Naming Test (median score change, 2; 95% CI: 1, 3.5; FDR-adjusted P = .006) scores at week 3 and a lower AD Assessment Scale–cognitive subscale score (median score change, −1.5; 95% CI: −3.5, 0; FDR-adjusted P = .09) score at month 3 were observed in the active group. The sham group showed a change in Trail Making Test B (median score change, −34; 95% CI: −70, −4; FDR-adjusted P = .09) and Boston Naming Test (median score change, 1.5; 95% CI: 0.5, 2; FDR-adjusted P = .009) scores at week 3. A statistically significant increase in the Boston Naming Test score was observed in both the active and sham groups at week 3 (Fig 2; Tables 2, 3).

Changes of FC in the Hippocampus and Entorhinal Cortex

One participant (active group) at week 3 and 11 participants (active group, four participants; sham group, seven participants) at month 3 were excluded due to loss to follow-up or poor-quality

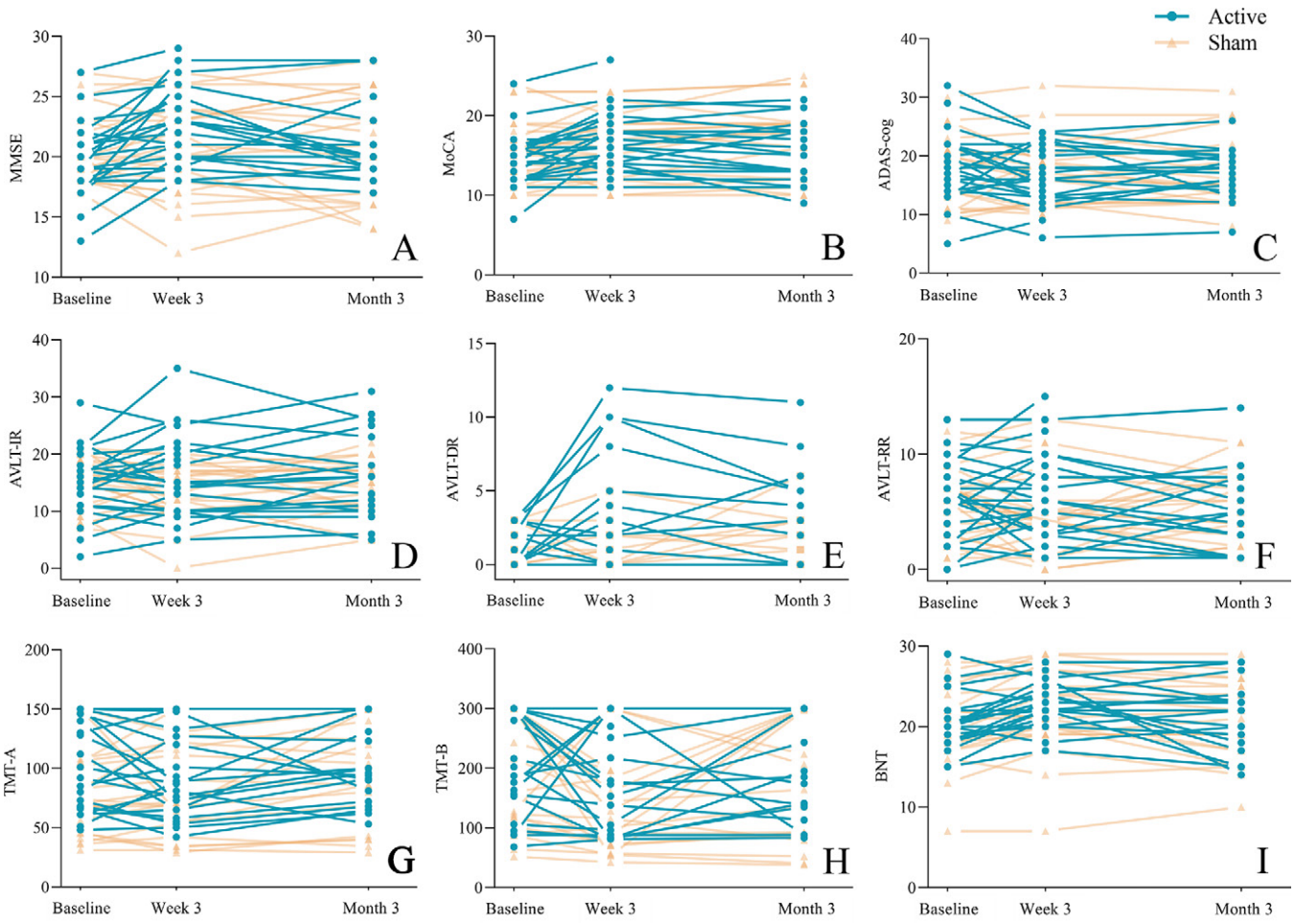

Figure 2: Spaghetti plots show changes in cognitive scores over time. Participants in the active group showed greater improvements in **(A)** Mini-Mental State Examination (MMSE) (false-discovery rate [FDR]–adjusted $P < .001$) and **(B)** Montreal Cognitive Assessment (MoCA) (FDR-adjusted $P = .006$) scores at week 3 compared with baseline. Plots show the **(A)** Mini-Mental State Examination, **(B)** Montreal Cognitive Assessment, **(C)** Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog), **(D)** Auditory Verbal Learning Test immediate recall (AVLT-IR), **(E)** Auditory Verbal Learning Test delay recall (AVLT-DR), **(F)** Auditory Verbal Learning Test recognition recall (AVLT-RR), **(G)** Trail Making Test part A (TMT-A), **(H)** Trail Making Test part B (TMT-B), and **(I)** Boston Naming Test (BNT) scores for participants in the active transcranial alternating current stimulation group ($n = 23$; Active) and the sham group ($n = 23$; Sham) from baseline to week 3 and month 3. Participants in the active group also achieved greater improvement in Mini-Mental State Examination ($P = .001$) and Montreal Cognitive Assessment ($P = .03$) than those in the sham group at week 3. Both the active (FDR-adjusted $P = .006$) and sham (FDR-adjusted $P = .009$) groups had higher Boston Naming Test scores at week 3 compared with baseline.

Table 2: Cognitive Scores Differences in the Active Group

	Week 3 vs Baseline		Month 3 vs Baseline		Month 3 vs Week 3	
Active Group	Estimated Score Difference	FDR-adjusted *P* Value	Estimated Score Difference	FDR-adjusted *P* Value	Estimated Score Difference	FDR-adjusted *P* Value
MMSE	3 (1.5, 4)	<.001	2 (0, 3.5)	.06	−1 (−2, 0)	.05
MoCA	2 (1, 3.5)	.006	1.5 (0, 3.5)	.06	−0.75 (−1.5, 0.5)	.21
ADAS-cog	−2 (−4, 0)	.12	−1.5 (−3.5, 0)	.09	0.5 (−1, 2)	.53
AVLT-IR	1.5 (−1, 4)	.57	1 (−1, 3.5)	.39	0.5 (−2, 3)	.72
AVLT-DR	1.5 (0, 3.5)	.09	0.5 (0, 2.5)	.19	−0.5 (−1, 0)	.15
AVLT-R-R	0.5 (−1, 2)	.59	−0.5 (−2.5, 1)	.56	−1 (−2.5, 0.5)	.66
TMT-A	−8 (−20.5, 2)	.48	1.75 (−11, 21.5)	.69	9.5 (−3.5, 20)	.33
TMT-B	−15 (−54.5, 6.5)	.36	−4.75 (−45, 7.5)	.48	6 (−12.5, 45)	.72
BNT	2 (1, 3.5)	.006	0 (−1.5, 1.5)	.79	−1 (−3.5, 0.5)	.21

Note.—Data in parentheses are 95% CIs. Data were compared over time using Friedman and Wilcoxon signed rank tests, with the estimates and 95% CIs. ADAS-cog = Alzheimer Disease Assessment Scale-cognitive subscale, AVLT = Auditory Verbal Learning Test, BNT = Boston Naming Test, DR = delay recall, FDR = false discovery rate, IR = immediate recall, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, R-R = recognition recall, TMT-A = Trail Making Test part A, TMT-B = Trail Making Test part B.

Table 3: Cognitive Scores Differences in the Sham Group

	Week 3 vs Baseline		Month 3 vs Baseline		Month 3 vs Week 3	
Sham Group	Estimated Score Difference	FDR-adjusted *P* Value	Estimated Score Difference	FDR-adjusted *P* Value	Estimated Score Difference	FDR-adjusted *P* Value
MMSE	0 (−1, 1)	.76	0 (−1.5, 1.5)	.87	0.5 (−1, 1.5)	>.99
MoCA	0.5 (−0.5, 1.5)	.43	0.5 (−0.5, 2)	.98	0.5 (−0.5, 1.5)	.60
ADAS-cog	−1 (−3, 0.5)	.94	0 (−1.5, 1.5)	>.99	−0.5 (−2.5, 1)	>.99
AVLT-IR	−1 (−3, 5)	.60	−1 (−3.5, 1.5)	.48	0.5 (−1.5, 2.5)	.52
AVLT-DR	0 (−1, 0.5)	>.99	0 (−1, 0.5)	.66	0 (−0.5, 1)	.85
AVLT-R-R	−0.5 (−2, 1)	.78	0 (−1.5, 1.5)	.92	0.5 (−1, 2.5)	>.99
TMT-A	2 (−5, 8.5)	.62	5.75 (0, 21)	.12	7 (0, 18)	.06
TMT-B	−34 (−70, −4)	.09	−6 (−26, 27)	.73	22.5 (−2, 86)	.14
BNT	1.5 (0.5, 2)	.009	0.5 (0, 1.5)	.13	−1 (−2, 0)	.18

Note.—Data in parentheses are 95% CIs. Data were compared over time using Friedman and Wilcoxon signed rank tests, with the estimates and 95% CIs. ADAS-cog = Alzheimer Disease Assessment Scale-cognitive subscale, AVLT = Auditory Verbal Learning Test, BNT = Boston Naming Test, DR = delay recall, FDR = false discovery rate, IR = immediate recall, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, R-R = recognition recall, TMT-A = Trail Making Test part A, TMT-B = Trail Making Test part B.

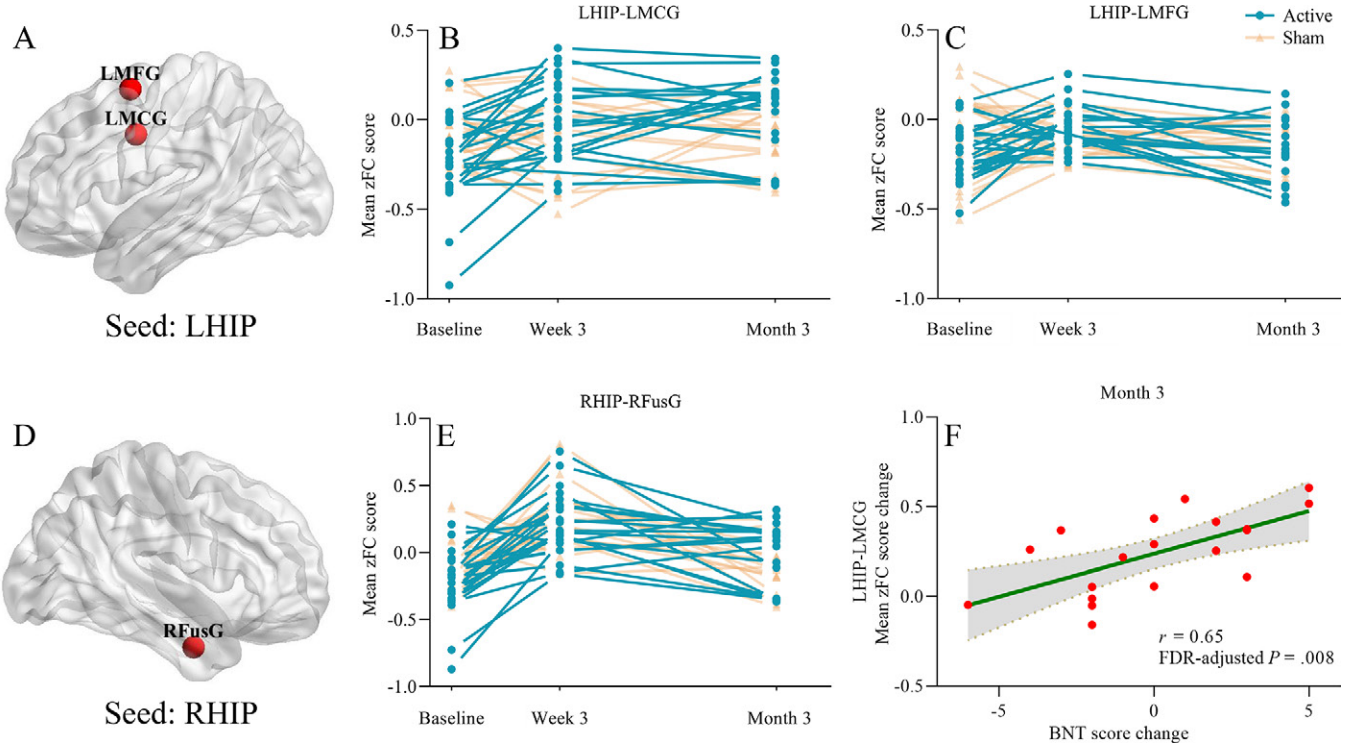

Figure 3: Modulation of functional connectivity (FC) with the seed placed on the left hippocampus (LHIP) and right hippocampus (RHIP). Compared with baseline, the active transcranial alternating current stimulation group (Active) exhibited increased FC between left hippocampus and left middle cingulate gyrus (LMCG), between left hippocampus and left middle frontal gyrus (LMFG) **(A)**, and between right hippocampus and right fusiform gyrus (RFusG) **(D)** at week 3. Spaghetti plots show the **(B)** left hippocampus and left middle cingulate gyrus, **(C)** left hippocampus and left middle frontal gyrus, and **(E)** right hippocampus and right fusiform gyrus mean *z* FC (zFC) score for participants in the active group and the sham group from baseline to week 3 and month 3. **(F)** A significant correlation ($r = 0.65$; false discovery rate [FDR]–adjusted $P = .008$) was observed between Boston Naming Test (BNT) score change and left hippocampus and left middle cingulate gyrus FC changes from baseline to month 3; the dots represent the distribution of the data, the solid line represents the fitted trend of the data, and the gray shaded area represents the 95% CIs.

functional MRI data. Based on voxel analysis, the following five brain regions were identified as functionally connected with the hippocampus or entorhinal cortex, with the significant enhancement effects in *z* score: left middle cingulate gyrus (MNI x-, y-, and z-axes: −9, 0, 36), left middle frontal gyrus (MNI x-, y-, and z-axes: −30, 3, 60), right fusiform gyrus (MNI x-, y-, and z-axes: 36, −3, −30), right middle temporal gyrus (MNI x-, y-, and z-axes: 54, −36, −9), and left fusiform gyrus (MNI x-, y-, and z-axes: −36, 0, −39). A statistically significant group (active group vs sham group) × time (baseline vs week 3) interaction in increased *z* score was observed between the left hippocampus and left middle cingulate gyrus (*z* score difference, 0.29; 95% CI: 0.17, 0.42; FDR-adjusted $P < .001$), and between the left hippocampus and left middle frontal gyrus (*z* score difference, 0.16; 95% CI: 0.03, 0.29; FDR-adjusted $P = .04$). Other associations were not statistically significant, though the exhibited

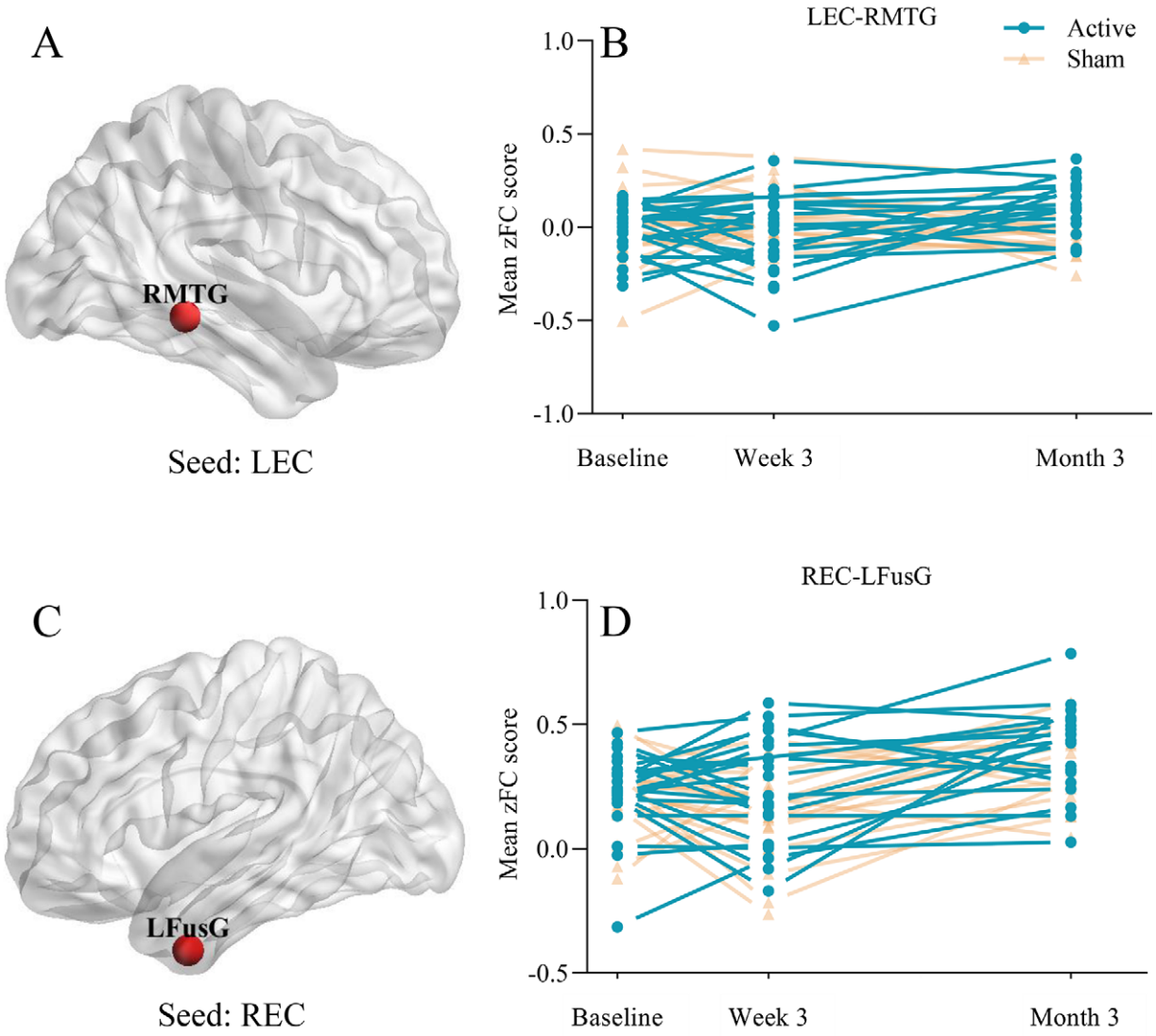

Figure 4: Modulation of functional connectivity (FC) with the seed placed on the left entorhinal cortex (LEC) and right entorhinal cortex (REC). Compared with baseline, the active transcranial alternating current stimulation group (Active) exhibited increased FC between **(A)** left entorhinal cortex and right middle temporal gyrus (RMTG), and **(C)** right entorhinal cortex and left fusiform gyrus (LFusG) at month 3. Spaghetti plots show the **(B)** left entorhinal cortex and right middle temporal gyrus and **(D)** right entorhinal cortex and left fusiform gyrus mean *z* FC (zFC) score for participants in the active group and the sham group from baseline to week 3 and month 3.

increased effect sizes (range of *z* score differences, 0.16 [95% CI: 0.03, 0.29] to 0.17 [95% CI: −0.01, 0.34]; FDR-adjusted *P* value range, .07–.11). No statistically significant interactions were found for the entorhinal cortex (range of *z* score differences, 0.06 [95% CI: −0.08, 0.19] to 0.14 [95% CI: 0.00, 0.27]; FDR-adjusted *P* value range, .10–.41) (Figs 3, 4; Table S1).

Correlation analyses between hippocampal FC changes and cognitive score alterations demonstrated that the change in FC between the left hippocampus and left middle cingulate gyrus from baseline to month 3 was significantly correlated with change in the Boston Naming Test score (r = 0.65; 95% CI: 0.27, 0.85; FDR-adjusted P = .008). No statistically significant correlation was observed between the changes in other FC pairs and cognitive scores (*P* value range, .06–.99) (Table 4).

Changes in FC within Functional Networks

Participants in the active group exhibited increased FC in some regions within the posterior DMN, anterior DMN, and visual network from baseline to week 3, and within the left FPN, right FPN, auditory network, and dorsal attention network from baseline to month 3. Seven regions were identified: the left precuneus (MNI x-, y-, and z-axes: −10, −50, 36), right superior frontal gyrus (MNI x-, y-, and z-axes: 24, 33, 48), left middle frontal gyrus (MNI x-, y-, and z-axes: −48, 15, 48), right inferior parietal lobe (MNI x-, y-, and z-axes: 51, −42, 54), left middle occipital gyrus (MNI x-, y-, and z-axes: −31, −78, 13), right temporal pole middle temporal gyrus (MNI x-, y-, and z-axes: 42, 15, −39) and right cuneus (MNI x-, y-, and z-axes: 12, −84, 39). A significant group (active vs sham) × time interaction of increased FC was observed within functional networks. This included the posterior DMN (*z* score difference, 0.40; 95% CI: 0.07, 0.73; FDR-adjusted *P* = .046), anterior DMN (*z* score difference, 0.31; 95% CI: 0.01, 0.60; FDR-adjusted *P* = .046), visual network (*z* score difference, 0.45; 95% CI: 0.17, 0.73; FDR-adjusted *P* = .007) at week 3, and the left FPN (*z* score difference, 0.54; 95% CI: 0.11, 0.97; FDR-adjusted *P* = .046), right FPN (*z* score difference, 1.65; 95% CI:

Table 4: Correlation Between Changes of Hippocampus Functional Connectivity and Alterations in Cognitive Scores

	LHIP-LMCG*		LHIP-LMFG*		LHIP-LMCG†		RHIP-RFusG†		LEC-RMTG†		REC-LFusG†	
Parameter	*r* Coefficient	*P* Value	*r* Coefficient	*P* Value	*r* Coefficient	*P* Value	*r* Coefficient	*P* Value	*r* Coefficient	*P* Value	*r* Coefficient	*P* Value
MMSE	−0.24	.28	0.16	.47	0.03	.89	−0.21	.40	0.01	.97	0.25	.31
MoCA	0.28	.21	0.001	.99	0.001	.99	0.04	.88	0.16	.50	−0.09	.73
ADAS-cog	0.14	.54	−0.17	.46	0.09	.72	−0.07	.77	0.20	.41	−0.45	.06
AVLT-IR	0.05	.83	−0.44	.05	−0.10	.70	−0.11	.65	0.23	.34	0.30	.21
AVLT-DR	0.01	.99	−0.31	.16	−0.44	.06	−0.09	.72	−0.20	.41	0.39	.10
AVLT-R-R	−0.18	.43	0.20	.37	0.09	.73	0.12	.62	0.27	.27	0.17	.49
TMT-A	0.05	.81	−0.19	.41	0.25	.30	0.12	.62	0.11	.65	−0.40	.09
TMT-B	0.18	.42	−0.10	.66	0.06	.81	−0.39	.10	−0.16	.52	0.04	.88
BNT	0.01	.98	0.03	.90	0.65	.002‡	0.29	.23	−0.03	.89	−0.15	.54

Note.—Data were calculated with Spearman correlation analysis. ADAS-cog = Alzheimer Disease Assessment Scale–cognitive subscale, AVLT = Auditory Verbal Learning Test, BNT = Boston Naming Test, DR = delay recall, IR = immediate recall, LEC = left entorhinal cortex, LFusG = left fusiform gyrus, LHIP = left hippocampus, LMCG = left middle cingulate gyrus, LMFG = left middle frontal gyrus, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, REC = right entorhinal cortex, RFusG = right fusiform gyrus, RHIP = right hippocampus, RMTG = right middle temporal gyrus, R-R = recognition recall, TMT-A = Trail Making Test part A, TMT-B = Trail Making Test part B.

* Change from baseline to week 3.

† Change from baseline to Month 3.

‡ False discovery rate–adjusted $P < .05$.

0.88, 2.41; FDR-adjusted $P < .001$), and auditory network (*z* score difference, 0.62; 95% CI: 0.08, 1.16; FDR-adjusted $P = .046$) at month 3 (Figs 5, 6; Table S2). No statistically significant correlation was observed between FC changes and cognitive score alterations (*P* value range, .08–.99) (Table S3).

Discussion

Prior studies (20–22) used functional connectivity (FC) to evaluate transcranial direct current stimulation effects in Alzheimer disease (AD). To our knowledge, our study is the first to investigate the impact of 40-Hz transcranial alternating current stimulation on FC in participants with AD. We found that the active group showed improved global cognitive performance (Mini-Mental State Examination median score change, 3 [95% CI: 1.5, 4; false-discovery rate {FDR}-adjusted $P < .001$]; Montreal Cognitive Assessment median score change, 2 [95% CI: 1, 3.5; FDR-adjusted $P = .006$]), as well as increased FC of the left middle cingulate gyrus (*z* score difference, 0.29; 95% CI: 0.17, 0.42; FDR-adjusted $P < .001$) and left middle frontal gyrus (*z* score difference, 0.16; 95% CI: 0.03, 0.29; FDR-adjusted $P = .04$) to the hippocampus and within the posterior default-mode network (DMN) (*z* score difference, 0.40; 95% CI: 0.07, 0.73; FDR-adjusted $P = .046$) and anterior DMN (*z* score difference, 0.31; 95% CI: 0.01, 0.60; FDR-adjusted $P = .046$) at week 3 compared with the baseline and sham groups. Increased FC was also found in the left frontoparietal network (FPN) (*z* score difference, 0.54; 95% CI: 0.11, 0.97; FDR-adjusted $P = .046$) and right FPN (*z* score difference, 1.65; 95% CI: 0.88, 2.41; FDR-adjusted $P < .001$) at month 3 compared with baseline.

Our study showed that tACS can enhance cognition in patients with AD, consistent with previous studies (26,27). The changes observed in executive function (Trail Making Test B score) and language function (Boston Naming Test score) in the sham group may suggest the existence of a practice effect or placebo effect, supporting further exploration.

Patients with AD often experience hippocampal functional disconnections (28,29). Our findings highlight a central role of altered hippocampal FC underlying the tACS effects. Specifically, we demonstrated that tACS enhances FC between the hippocampus and cortical regions, such as the left middle cingulate gyrus and left middle frontal gyrus, suggesting that tACS rebalances neuronal activity. This builds on prior studies (11,30,31) that reported tACS-induced improvements in hippocampal perfusion and neuronal activity but lacked evidence of FC modulation. It also provides potential targets for MRI-guided, individualized tACS treatment of AD.

The DMN typically exhibits disrupted FC in patients with AD (32–34). Modulating the DMN is a promising strategy for AD (35,36). A pilot study (20) of 18 patients with mild cognitive impairment found that a single session of transcranial electrical stimulation in the left inferior frontal gyrus partially normalized cortical networks, without specific focus on DMN modulation. Another study (21) of 20 patients with AD suggested that 10 sessions of transcranial electrical stimulation in the right inferior parietal lobule enhanced DMN FC to improve memory but lacked a sham group as a control and long-term follow-up. However, our randomized, sham-controlled trial of 46 participants with mild AD showed that tACS enhanced DMN FC, differentially modulating anterior and posterior regions, which aligned with prior studies but uniquely showed frequency-specific efficacy. Our results suggest that tACS-induced DMN modulation may underlie cognitive improvements.

The FPN mediates cognitive control through network coordination (37). Patients with AD exhibit a 14%–64% reduction in FPN FC (38). A previous study involved a 3-week, nine-session transcranial electrical stimulation trial in 46 patients with AD prodromal stage. While no memory improvement was observed, enhanced FC in the right superior parietal lobule suggested FPN modulation (22). Our study showed that 30-session tACS increased bilateral FPN FC at month 3, suggesting

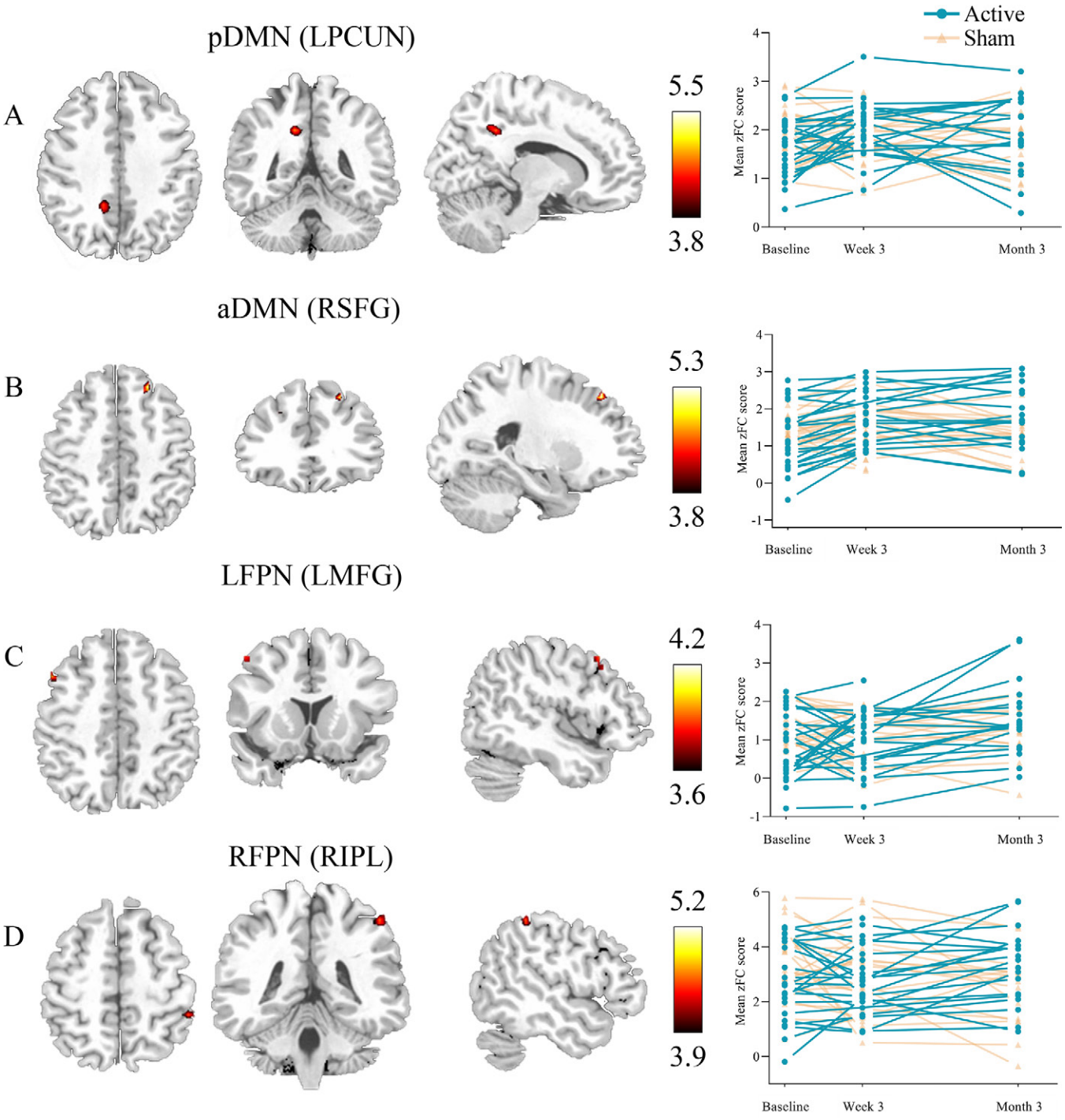

Figure 5: Modulation of functional connectivity (FC) within the default-mode network (DMN) and frontoparietal network. Compared with baseline, the active transcranial alternating current stimulation group (Active) exhibited increased FC within the **(A)** posterior DMN (pDMN) and **(B)** anterior DMN (aDMN) at week 3, and within the **(C)** left frontoparietal network (LFPN) and **(D)** right frontoparietal network (RFPN) at month 3. Spaghetti plots show the mean *z* FC (zFC) score for participants in the active group and the sham group from baseline to week 3 and month 3. The color scale bar shows *t* values, warm colors represent increases in *z* FC score. LMFG = left middle frontal gyrus, LPCUN = left precuneus, RIPL = right inferior parietal lobe, RSFG = right superior frontal gyrus.

long-term neuroplastic changes across broader regions. Other studies about transcranial electrical stimulation and transcranial magnetic stimulation also reported FPN modulation (39–41). To our knowledge, our study is the first to report tACS-induced FPN connectivity enhancements in patients with AD. Furthermore, tACS modulated visual and auditory network, supporting its cross-system integration potential.

Our findings provide evidence that tACS modulates FC in cognition-related regions, such as the hippocampus, DMN, and FPN. Enhanced FC indicates tACS promotes neuronal synchronization and network rebalancing. Our work uniquely integrates cognitive assessments with FC analyses to elucidate neuronal mechanisms, advancing the understanding of tACS in AD.

Our study had limitations. First, tACS efficacy across different AD stages remains unknown. Second, cognitive improvements were immediate but not sustained at month 3, possibly due to a small sample size, severe cognitive impairment, and a brief duration. Third, the global effect size appeared modest,

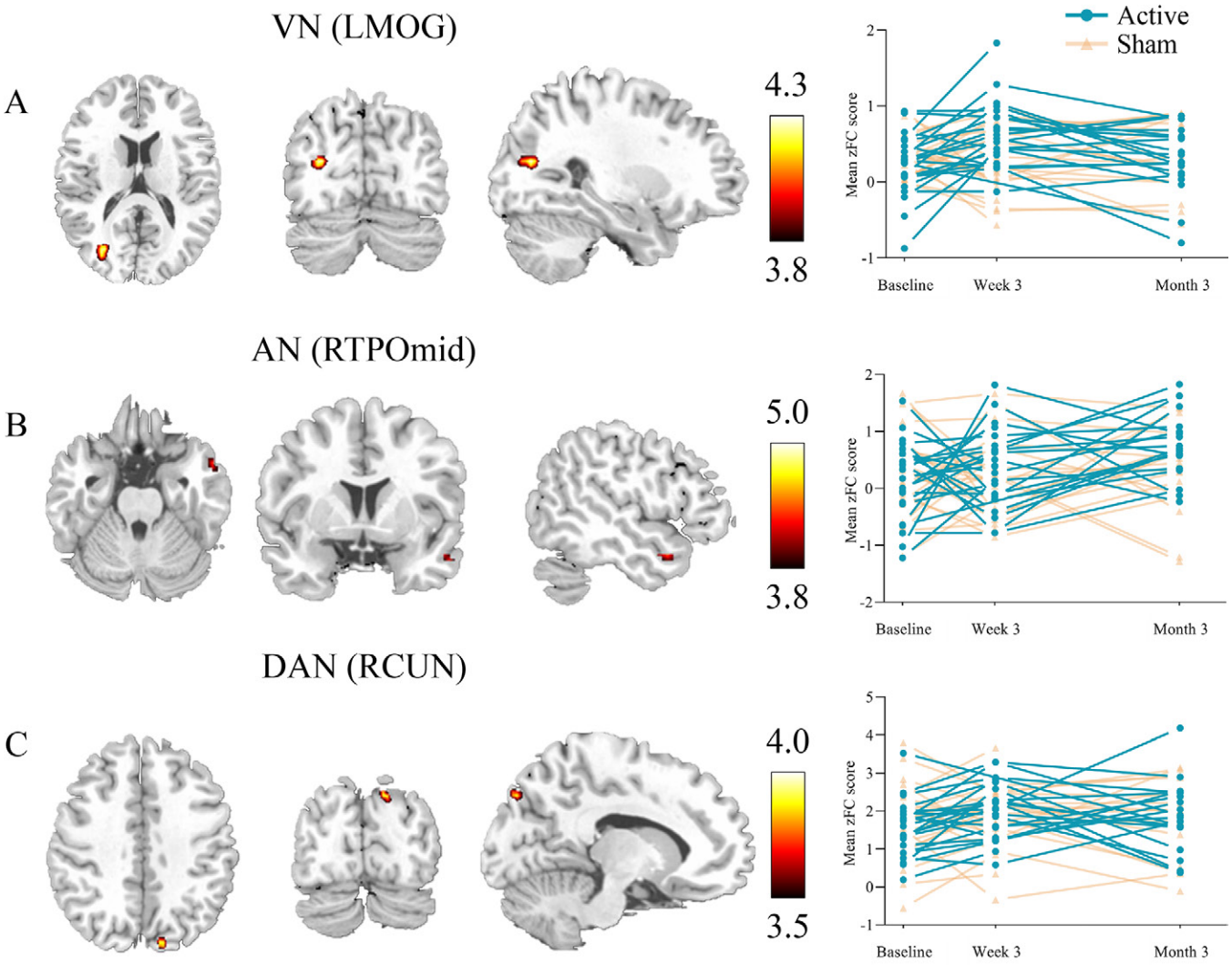

Figure 6: Modulation of functional connectivity (FC) within the visual network (VN), auditory network (AN), and dorsal attention network (DAN). Compared with baseline, the active transcranial alternating current stimulation group exhibited increased FC within the visual network **(A)** at week 3, and within the **(B)** auditory network and **(C)** dorsal attention network at month 3. Spaghetti plots show the mean *z* FC (zFC) score for participants in the active group (Active) and the sham group (Sham) from baseline to week 3 and month 3. The color scale bar shows *t* values, where warm colors represent increases in *z* FC scores. LMOG = left middle occipital gyrus, RCUN = right cuneus, RTPOmid = right temporal pole: middle temporal gyrus.

which may be attributed to the irreversible progression and refractory nature of AD, limiting the potential for improvement. The 2-hour daily tACS was slightly longer. Future work should aim to reduce daily time while enhancing effect size. More trials are needed to optimize effects, expediting tACS practicality on a widespread scale. However, an optimal protocol remains unknown. We considered these results to be exploratory and preliminary, supporting further refinement.

In conclusion, our study demonstrates that 40-Hz transcranial alternating current stimulation (tACS) with 15-mA current intensity may improve cognitive function in individuals with Alzheimer disease. The improvement in cognitive performance after tACS was accompanied by the functional connectivity (FC) regulation of the hippocampus and cortical networks. However, there was insufficient evidence to conclude that tACS also modulated FC in the entorhinal cortex. Future research should concentrate on the development of individualized therapeutic strategies with larger sample sizes, shorter daily time, more sessions, and varied stimulation frequencies.

Deputy Editor: Sven Haller
Scientific Editor: Jenna Saleh

Author affiliations:

[1] Department of Radiology and Nuclear Medicine, Xuanwu Hospital, Capital Medical University, Beijing, China

[2] Beijing Key Laboratory of Magnetic Resonance Imaging and Brain Informatics, Beijing, China

[3] Key Laboratory of Neurodegenerative Diseases, Ministry of Education, Beijing, China

[4] Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, China

Received May 21, 2024; revision requested July 15; revision received April 20, 2025; accepted May 13.

Address correspondence to: J.L. (email: imaginglu@hotmail.com).

Funding: Supported by the National Key Research and Development Program of China (grant numbers 2022YFC2406900, 2022YFC2406904) and the National Natural Science Foundation of China (grant numbers 62333002, 82220108009).

Acknowledgments: The authors are sincerely grateful to the patients who voluntarily contributed to this research.

Author contributions: Guarantors of integrity of entire study, **T.W., Y.X., Z.C., H. Xi, J.L.**; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, **S.Y., H. Xue, Y.X., S.B., Z.C., H. Xi, Z.Q., Y.T.**; clinical studies, **T.W., Y.S., Y.X., S.B., Z.C., H. Xi, Z.Q., Y.T., J.L.**; experimental studies, **S.Y., H. Xue, Z.C., H. Xi, Z.Q., Y.T.**; statistical analysis, **T.W., S.Y., H. Xue, Z.C., H. Xi, Z.Q.**; and manuscript editing, **T.W., S.Y., Y.X., S.B., Z.C., H. Xi, Z.Q., Y.T., J.L.**

Disclosures of conflicts of interest: **T.W.** No relevant relationships. **S.Y.** No relevant relationships. **Y.S.** No relevant relationships. **H. Xue** No relevant relationships. **Y.X.** No relevant relationships. **S.B.** No relevant relationships. **Z.C.** No relevant relationships. **H. Xi** No relevant relationships. **Z.Q.** No relevant relationships. **Y.T.** No relevant relationships. **J.L.** No relevant relationships.

References

1. Scheltens P, De Strooper B, Kivipelto M, et al. Alzheimer's disease. Lancet 2021;397(10284):1577–1590.
2. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet 2020;396 (10248):413–446.
3. Rafii MS, Aisen PS. Detection and treatment of Alzheimer's disease in its preclinical stage. Nat Aging 2023;3(5):520–531.
4. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in Early Alzheimer's Disease. N Engl J Med 2023;388(1):9–21.
5. Ramanan VK, Armstrong MJ, Choudhury P, et al; AAN Quality Committee. Antiamyloid Monoclonal Antibody Therapy for Alzheimer Disease: Emerging Issues in Neurology. Neurology 2023;101(19):842–852.
6. Grover S, Fayzullina R, Bullard BM, et al. A meta-analysis suggests that tACS improves cognition in healthy, aging, and psychiatric populations. Sci Transl Med 2023;15(697):eabo2044.
7. Liu A, Vöröslakos M, Kronberg G, et al. Immediate neurophysiological effects of transcranial electrical stimulation. Nat Commun 2018;9(1):5092.
8. Grover S, Wen W, Viswanathan V, et al. Long-lasting, dissociable improvements in working memory and long-term memory in older adults with repetitive neuromodulation. Nat Neurosci 2022;25(9):1237–1246.
9. Shan Y, Wang H, Yang Y, et al. Evidence of a large current of transcranial alternating current stimulation directly to deep brain regions. Mol Psychiatry 2023;28(12):5402–5410.
10. Benussi A, Cantoni V, Grassi M, et al. Increasing Brain Gamma Activity Improves Episodic Memory and Restores Cholinergic Dysfunction in Alzheimer's Disease. Ann Neurol 2022;92(2):322–334.
11. Sprugnoli G, Munsch F, Cappon D, et al. Impact of multisession 40Hz tACS on hippocampal perfusion in patients with Alzheimer's disease. Alzheimers Res Ther 2021;13(1):203.
12. Ekhtiari H, Ghobadi-Azbari P, Thielscher A, et al. A checklist for assessing the methodological quality of concurrent tES-fMRI studies (ContES checklist): a consensus study and statement. Nat Protoc 2022;17(3):596–617.
13. Barkhof F, Haller S, Rombouts SARB. Resting-state functional MR imaging: a new window to the brain. Radiology 2014;272(1):29–49.
14. Zarei M, Beckmann CF, Binnewijzend MAA, et al. Functional segmentation of the hippocampus in the healthy human brain and in Alzheimer's disease. Neuroimage 2013;66:28–35.
15. Adams JN, Kim S, Rizvi B, et al. Entorhinal-Hippocampal Circuit Integrity Is Related to Mnemonic Discrimination and Amyloid-β Pathology in Older Adults. J Neurosci 2022;42(46):8742–8753.
16. Jagust W. Imaging the evolution and pathophysiology of Alzheimer disease. Nat Rev Neurosci 2018;19(11):687–700.
17. Buckley RF, Schultz AP, Hedden T, et al. Functional network integrity presages cognitive decline in preclinical Alzheimer disease. Neurology 2017;89(1):29–37.
18. Palop JJ, Mucke L. Amyloid-beta-induced neuronal dysfunction in Alzheimer's disease: from synapses toward neural networks. Nat Neurosci 2010;13(7):812–818.
19. Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7(3):280–292.
20. Meinzer M, Lindenberg R, Phan MT, et al. Transcranial direct current stimulation in mild cognitive impairment: behavioral effects and neural mechanisms. Alzheimers Dement 2015;11(9):1032–1040.
21. Pini L, Pizzini FB, Boscolo-Galazzo I, et al. Brain network modulation in Alzheimer's and frontotemporal dementia with transcranial electrical stimulation. Neurobiol Aging 2022;111:24–34.
22. Antonenko D, Fromm AE, Thams F, et al. Cognitive training and brain stimulation in patients with cognitive impairment: a randomized controlled trial. Alzheimers Res Ther 2024;16(1):6.
23. Xing Y, Wei P, Wang C, et al. TRanscranial AlterNating current Stimulation FOR patients with Mild Alzheimer's Disease (TRANSFORM-AD study): protocol for a randomized controlled clinical trial. Alzheimers Dement (N Y) 2020;6(1):e12005.
24. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7(3):263–269.
25. Fries P. Rhythms for Cognition: Communication through Coherence. Neuron 2015;88(1):220–235.
26. Benussi A, Cantoni V, Cotelli MS, et al. Exposure to gamma tACS in Alzheimer's disease: a randomized, double-blind, sham-controlled, crossover, pilot study. Brain Stimul 2021;14(3):531–540.
27. Zhou D, Li A, Li X, et al. Effects of 40 Hz transcranial alternating current stimulation (tACS) on cognitive functions of patients with Alzheimer's disease: a randomised, double-blind, sham-controlled clinical trial. J Neurol Neurosurg Psychiatry 2022;93(5):568–570.
28. Devanand DP, Pradhaban G, Liu X, et al. Hippocampal and entorhinal atrophy in mild cognitive impairment: prediction of Alzheimer disease. Neurology 2007;68(11):828–836.
29. Yan S, Zheng C, Cui B, et al. Multiparametric imaging hippocampal neurodegeneration and functional connectivity with simultaneous PET/MRI in Alzheimer's disease. Eur J Nucl Med Mol Imaging 2020;47(10):2440–2452.
30. Tang Y, Xing Y, Sun L, et al. TRanscranial AlterNating current stimulation FOR patients with mild Alzheimer's Disease (TRANSFORM-AD): a randomized controlled clinical trial. Alzheimers Res Ther 2024;16(1):203.
31. Jones KT, Gallen CL, Ostrand AE, et al. Gamma neuromodulation improves episodic memory and its associated network in amnestic mild cognitive impairment: a pilot study. Neurobiol Aging 2023;129:72–88.
32. Pievani M, Filippini N, van den Heuvel MP, et al. Brain connectivity in neurodegenerative diseases–from phenotype to proteinopathy. Nat Rev Neurol 2014; 10(11):620–633.
33. Buckner RL, Andrews-Hanna JR, Schacter DL. The brain's default network: anatomy, function, and relevance to disease. Ann N Y Acad Sci 2008;1124:1–38.
34. Greicius MD, Srivastava G, Reiss AL, et al. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. Proc Natl Acad Sci U S A 2004;101(13):4637–4642.
35. Pievani M, Mega A, Quattrini G, et al. Targeting Default Mode Network Dysfunction in Persons at Risk of Alzheimer's Disease with Transcranial Magnetic Stimulation (NEST4AD): rationale and Study Design. J Alzheimers Dis 2021;83(4):1877–1889.
36. Wei L, Zhang Y, Wang J, et al. Parietal-hippocampal rTMS improves cognitive function in Alzheimer's disease and increases dynamic functional connectivity of default mode network. Psychiatry Res 2022;315:114721.
37. Murphy AC, Bertolero MA, Papadopoulos L, et al. Multimodal network dynamics underpinning working memory. Nat Commun 2020;11(1):3035.
38. Mohammadian F, Zare Sadeghi A, Noroozian M, et al. Quantitative Assessment of Resting-State Functional Connectivity MRI to Differentiate Amnestic Mild Cognitive Impairment, Late-Onset Alzheimer's Disease From Normal Subjects. J Magn Reson Imaging 2023;57(6):1702–1712.
39. Zhang Y, Li C, Chen D, et al. Repeated High-Definition Transcranial Direct Current Stimulation Modulated Temporal Variability of Brain Regions in Core Neurocognitive Networks Over the Left Dorsolateral Prefrontal Cortex in Mild Cognitive Impairment Patients. J Alzheimers Dis 2022;90(2):655–666.
40. Esposito S, Trojsi F, Cirillo G, et al. Repetitive Transcranial Magnetic Stimulation (rTMS) of Dorsolateral Prefrontal Cortex May Influence Semantic Fluency and Functional Connectivity in Fronto-Parietal Network in Mild Cognitive Impairment (MCI). Biomedicines 2022;10(5):994.
41. Keeser D, Meindl T, Bor J, et al. Prefrontal transcranial direct current stimulation changes connectivity of resting-state networks during fMRI. J Neurosci 2011;31(43):15284–15293.