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Impact of combined art-based intervention on functional connectivity of multiple brain networks in older adults along the cognitive continuum: result from a parallel randomised controlled trial

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Abstract

Background Combined art-based interventions (CAIs) are considered effective treatment options for older adults along the cognitive continuum; however, the neural mechanisms underlying associated changes in neurocognitive performance remain unclear. Thus, we aimed to investigate the impact of a CAI programme in older adults along the cognitive continuum and to understand its mechanism.

Methods This parallel-arm randomised controlled trial was conducted between April 2021 and January 2023. Participants were randomised in a 1:1 ratio to either intervention group (IG) or waitlist control group (WG). The IG underwent a 16-week CAI programme. Neuropsychological assessments and magnetic resonance imaging were conducted before and after the intervention.

Results After the intervention, the IG showed greater improvement in general cognitive function, language, and memory than the WG. Significant differences were observed in the functional connectivity (FC) values in the temporal and cerebellar anterior lobes, fusiform, inferior occipital, and lingual gyri, and perirhinal and visual cortices between the groups. Further analyses showed that FC values were reduced in these regions in the IG. In addition, changes in FC values were positively correlated with those in neuropsychological test scores in the IG.

Conclusions Our study suggests that the CAI programme can effectively improve general cognitive function, language, and memory in older adults along the cognitive continuum. These improvements may be changed due to

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decreases in FC in key brain regions, deepening the understanding of the neurocentral mechanisms that act as a tool for improving cognitive function.

Trial registration This trial was registered at ChiCTR.org. Identifier: ChiCTR2100044959, 03/04/2021.

Keywords Alzheimer's disease, Art therapy, Brain plasticity, Cognitive function, Central neural mechanisms, Functional network connectivity

Background

Alzheimer's disease (AD) is the most common type of dementia worldwide and presents a growing challenge to global healthcare systems, particularly in ageing populations. AD is characterised by various clinical features, including progressive memory decline, spatial disorientation, and behavioural alterations [1, 2]. Depending on the degree of cognitive impairment, syndromal staging of cognitive continuum can be categorised into three stages: subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia [3]. Individuals with SCD or MCI who also show biomarker evidence of Alzheimer's pathology are considered to be in the prodromal stage of AD [4]. Individuals in these stages require extensive healthcare resources to manage various symptoms, with more severe conditions resulting in greater caregiving and economic burdens [5]. By implementing intervention measures at earlier stages, with a greater focus on appropriateness and adherence to scientific management methods, there is a potential to increased economic benefits [6, 7]. Despite intensive research efforts, effective treatments for cognitive continuum remain elusive, necessitating the exploration of innovative approaches and their mechanisms.

The potential of art-based interventions as a therapeutic strategy for patients along cognitive continuum has received growing attention from the medical and scientific communities [8–10]. This approach harnesses the transformative power of creative activities, such as painting, collage, music, dance, and drama, to improve cognitive function and emotional status, with previous studies demonstrating the efficacy of art-based interventions for older adults with dementia or MCI, resulting in significant improvements in cognitive function, quality of life, and emotional well-being [11–13]. Notably, for some individuals, ongoing therapy involving only a one type of art form may pose challenges. These challenges may occur because of factors associated with a specific art form, the medium used, or an individual's personality characteristics. A meta-analysis has suggested that a combination of therapeutic strategies involving various art activities may offer a more effective approach for mitigating cognitive decline [14]. Considering these factors, the present study involved a carefully designed randomised controlled trial to investigate the effects of a combined art-based intervention (CAI) programme and its underlying neural mechanisms in older adults along the cognitive continuum, which is pivotal for advancing the current understanding and improving cognitive continuum management.

Previous research has confirmed that ageing brains retain plasticity, not only in the sensory and motor cortices but also in higher-level cognitive domains such as language, memory, and executive functions [15–17]. Neuroimaging techniques such as functional magnetic resonance imaging (fMRI) have advanced the current understanding of brain plasticity and the effects of cognitive interventions. fMRI effectively tracks subtle physiological changes over short periods of time and links specific brain regions to cognitive processes. These capabilities are crucial for revealing alterations in brain function and pathological mechanisms, thereby elucidating the central mechanisms that underlie cognitive changes. A study used fMRI to investigate the default mode network of retired older individuals and found that the visual art intervention group (IG) showed greater functional connectivity (FC) between the posterior cingulate cortex (PCC) and frontal and parietal cortices than the control group [18]. Another study reported that the group undergoing a visual art production with creative storytelling therapy showed decreased FC between the PCC and right middle temporal gyrus and increased FC between the ventromedial prefrontal cortex (PFC) and left angular gyrus [12]. These findings suggest that the functional activity levels of the PFC play a pivotal role in AD development. The PFC plays a key role in high-level cognitive activities such as memory, judgement, comprehension, and thinking [19–21]. It serves as a hub for integrating information from diverse brain regions. Therefore, the present trial, focusing on the frontal cortex as the region of interest (ROI), is highly valuable for exploring the impact of the CAI programme on the cognitive and brain network functions in older adults along the cognitive continuum. The current study had three objectives: (1) to investigate the effects of a CAI programme on cognitive function and brain functional connectivity among older adults along the cognitive continuum; (2) to explore the potential differential effects of the intervention across different stages of the disease, including SCD, MCI, and probable AD, and (3) to examine the relationship between cognitive function, and brain functional connectivity among older adults along the cognitive continuum.

Methods

Study design

This study was a 16-week, 24-session, prospective, parallel-arm, randomised waitlist-controlled trial, and the methodology has been described in detail following the Consolidated Standards of Reporting Trials reporting guidelines. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Ethics Committee of Fujian Provincial Hospital, Fujian Province, China (reference number: K2020-03-069). Written informed consent was obtained from each participant or a family member. The trial was registered at ChiCTR.org (ChiCTR2100044959, 03/04/2021). Further details on the trial protocol are found in our previous publication [22].

Participants

Participants were recruited from one memory clinic and four community settings. All data were collected between April 2021 and January 2023. The inclusion criteria were as follows: (1) diagnosis of SCD [23], MCI [24], or mild probably AD [25, 26] by a neurologist; (2) age ≥ 60 years; (3) visual and auditory acuity adequate for neuropsychological testing; and (4) provision of informed consent by the participant or a family member. The exclusion criteria were as follows: (1) severe aphasia, physical disabilities, psychiatric disorders, suicidal tendency, or other factors that could preclude cognitive examination or completion of the CAI programme; (2) other neurological or psychiatric conditions that could affect cognition; (3) other systemic diseases likely to impair cognition; (4) alcohol or drug misuse; (5) participation in another clinical study at the same time; and (6) metal implants or other magnetic resonance imaging (MRI) contraindications. The supplementary material presents further details on the diagnostic assessment of SCD, MCI, and probably AD (Supplementary Material: Additional File 1).

Sample size was calculated based on a previous study [13] using PASS version 11.0 (Hintze J, Kaysville, UT, USA). It was determined that a sample size of approximately 22 participants would be required in each group (considering a 15% dropout rate) to achieve 90% statistical power and a two-sided level of statistical significance at 5%; at least 44 participants needed to be included for comparisons of the intervention and control groups at the primary end point. These calculations were based on post-intervention MoCA scores for sample size estimation. The mean MoCA score was 24.9 (standard deviation of 2.5) in the IG and mean MoCA score was 23.7 (standard deviation of 2.7) in the WG.

Randomisation and masking

This study employed a randomised waitlist-controlled trial design involving concealed allocation and blinding of outcome assessors and data analysts. Following the baseline assessment, the participants were stratified according to their degree of cognitive impairment. Subsequently, they were randomly assigned to either IG or waitlist control group (WG) in a 1:1 ratio. The randomisation sequence was generated using Research Randomiser software (http://www.randomizer.org/) by an external staff member who was not associated with this study. Owing to the nature of non-pharmacological interventions, blinding the intervention implementation or participants was impossible. However, group assignments remained undisclosed to the outcome assessors and data analysts throughout the study.

Interventions

The 16-week, 24-session CAI programme was developed by a multidisciplinary team, including art therapists, neurology experts, clinical nursing specialists, and social workers. It was led by nurses who provided 45-h online and offline training sessions with a qualified art therapist. The programme was conducted using neurocognitive function training patterns [27], with both bottom-up and top-down approaches. The art-based intervention sessions were based on the theoretical frameworks of media dimension variables and expressive therapies continuum [28]; they followed the principles of individualisation, changing the difficulty/cognitive level, transitioning from highly structured to semi-structured or freestyle activities, and making timely adjustments to adapt to and gradually improve cognitive function. The intervention aimed to create a warm and inclusive atmosphere, stimulate creative interests, empower participants to adeptly apply various artistic techniques, foster free and creative expression, enhance their creativity and self-expression, and help them discover their intrinsic value. Furthermore, the synergies between different cognitive domains were strengthened through progressively challenging artistic tasks, improving cognitive abilities, and deepening self-awareness.

The intervention comprised three distinct stages: art experience (sessions 1–5), enlightenment (sessions 6–14), and exploration (sessions 15–24); this corresponded to the three phases of cognitive regulation: perception, comprehension, and application. The CAI programme incorporates various forms of art activities, including performing, visual, and literary arts. Each session included an activity introduction, warm-up, artistic creation, and work-sharing, lasting approximately 90 min. The selection of activity themes was deeply rooted in traditional Chinese culture, with a deliberate emphasis on aligning these themes with the historical backgrounds

of the participants. This approach was designed to ignite interest in active participation and exploration, encompassing four major theme types: media exploration, folk culture, self-exploration, and free creation. Participants in the WG engaged in their usual activities before participating in the CAI programme. Further details are presented in Supplementary Table 1: Additional File 2.

Measures

Participant outcome data were obtained at baseline and post-intervention. Regarding the neuropsychological assessments, general cognitive function was measured using the Montreal Cognitive Assessment (MoCA) [29] and Mini-Mental State Examination (MMSE) [30]. The specific domains of cognitive function, including verbal and visual memory, language, executive function, attention, and visuospatial skills, were assessed using the auditory verbal learning test (AVLT) [31], Verbal Fluency Test (VFT) [32], Boston Naming Test (BNT) [33], Shape Trail Test (STT) [34], Digit Span Test (DST) [35], and Rey-Osterrieth Complex Figure Test (ROCFT) [36]. These tests were selected for their demonstrated sensitivity to changes in this Chinese population. In addition, they concisely and effectively captured the key outcomes that the intervention was designed to achieve.

MRI was performed at baseline and post-intervention using a 3.0T Prisma scanner (Siemens, Erlangen, Germany) in the same scan mode. Resting-state fMRI was performed using a multiband echo-planar imaging sequence with the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, 33 slices, voxel size = $3.5 \times 3.5 \times 3.5$ mm^3, flip angle = 90°, field of view (FOV) = 224×224 mm^2, measurements = 240, and time = 8 min 6 s. High-resolution T1-weighted images of the whole brain were obtained using a sagittal three-dimensional magnetisation-prepared rapid gradient-echo sequence with the following parameters: TR = 2530 ms, TE = 2.98 ms, time of inversion (TI) = 1100 ms, slice thickness = 1 mm, 192 slices, flip angle = 7°, voxel size = $1.0 \times 1.0 \times 1.0$ mm^3, and FOV = 256×256 mm^2. T2-weighted images were obtained using a blade turbo spin echo (TSE) sequence with the following parameters: TR = 3800 ms, TE = 75 ms, FOV = 220×220 mm^2, 20 slices, flip angle = 150°, voxel size = $0.7 \times 0.7 \times 5.0$ mm^3, and slice thickness/gap = 5 mm/1.5 mm. T2-FLAIR images were obtained using a TSE sequence with the following parameters: TR = 7500 ms, TE = 83 ms, TI = 2298 ms, FOV = 220×220 mm^2, 20 slices, flip angle = 150°, voxel size = $0.7 \times 0.7 \times 5.0$ mm^3, and slice thickness/gap = 5 mm/1.5 mm. Image quality was validated by an imaging specialist. fMRI data were pre-processed using the SPM12 software (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) in MATLAB 2013b (MathWorks, Natick, MA, USA).

The pre-processing steps included removing the first 5 time points, slice-timing correction, head correction (head motion ≤ 3 mm or 3°), spatial normalisation ($3 \times 3 \times 3mm^3$), Gaussian spatial smoothing ($6 \times 6 \times 6$ mm^3), remove linear detrend, and temporal filter (band-pass filtering between 0.01 and 0.08 Hz); the white matter and cerebrospinal fluid signals and their first-order derivatives were included as confounders. The fMRI data were spatially normalized to the Montreal Neurological Institute (MNI) template using the co-registered T1 images (through DARTEL) and then resampled to $3 \times 3 \times 3mm^3$ voxels.

Statistical analyses

Statistical analyses were performed using DPABI (Institute of Psychology, Chinese Academy of Sciences, China), SPM12 (Wellcome Trust Centre for Neuroimaging, University College London, UK), MATLAB R2013b, and IBM SPSS 22.0 (IBM Corporation, Armonk, NY, USA). Participant demographic characteristics were compared between the study groups using independent sample t-tests or the Mann–Whitney U, chi-square, or Fisher's exact tests. Neuropsychological outcomes were analysed using a general linear model. To quantify changes in resting-state connectivity, seed-based FC analysis was performed, with the PFC selected as the seed region, defined based on Brodmann areas 9, 10, and 11. Correlation maps were computed by correlating the regional time courses (averaged over all voxels within the seed region) with every voxel in the brain. The resulting correlation maps were then converted to z-maps using Fisher's transformation. The preprocessing steps, correlation map generation, and Fisher's z-transformation were all carried out using the DPABI toolbox in MATLAB 2013b. The SPM12 software package was used to extract the peak intensity values of the participants' brain regions exhibiting significant differences before and after the intervention. A 2 (group: IG or WG) × 2 (time: pre- or post-intervention) mixed ANOVA was employed to assess the impact of the intervention on the strength of FC in the ROI. Correction analyses for the results of the mixed-factor analysis of variance were performed using the Gaussian random field (GRF) method with voxel- and cluster-level correction thresholds of $P < 0.001$ and $P < 0.05$, respectively. Neuropsychological measurements and FC values were analysed using Pearson's correlation analysis. Statistical significance was set at $P < 0.05$ (two-tailed).

Results

Participant characteristics

A total of 144 participants were assessed for eligibility. Fifty participants were excluded because of MRI contraindications or refusal, and the remaining 94 who underwent baseline neuropsychological tests and MRI were

finally included in this study. All participants completed neuropsychological tests post-intervention, whereas only 70 of the 94 participants completed MRI post-intervention. The flow diagram for participant enrolment is shown in Fig. 1. The participant baseline characteristics were well-balanced between the groups (Table 1). Demographic and neuropsychological performance were similar between participants who were included 70 in and excluded from the analyses, except for living status ($\chi^2 = 6.425$, $P = 0.015$) and family member contact ($\chi^2 = 4.491$, $P = 0.034$) (Supplementary Table 2: Additional File 3).

Neuropsychological performance

After the intervention, the between-group difference in general cognitive function, as measured by MoCA scores (95% confidence interval [CI]: 1.1 to 2.4, $P = 0.081$, η^2=0.389), MMSE scores (95% CI: 0.1 to 1.1, $P = 0.002$, η^2=0.333), language abilities, as measured by VFT scores (95% CI: 0.2 to 2.1, $P = 0.009$, η^2=0.203) and BNT scores (95% CI: 1.4 to 2.7, $P = 0.005$, η^2=0.203), verbal memory performance, as measured by AVLT scores (Immediate term: 95% CI: -0.1 to 2.32, $P = 0.059$, η^2=0.202; Short-term: 95% CI: -0.5 to 0.8, $P = 0.059$, η^2=0.128; Long-term: 95% CI: -0.1 to 1.2, $P = 0.019$, η^2=0.194; Recall-term: 95% CI: 0.1 to 1.8, $P = 0.865$, η^2=0.197), visual memory performance, as measured by RCOFT scores (Immediate term: 95% CI: 4.5 to 7.4, $P = 0.062$, η^2=0.521; Long-term: 95% CI: 4.4 to 7.3, $P = 0.161$, η^2=0.487), visuospatial skill, as measured by RCOFT Copy-term scores (95% CI: -27.7 to 13.5, $P = 0.672$, η^2=0.288), executive function, as measured by STT scores (STT-A: 95% CI: -12.4 to -2.4, $P = 0.315$, η^2=0.173; STT-B: 95% CI: -39.3 to -18.4, $P = 0.079$, η^2=0.295), and attention, as measured by DST scores (DST forward: 95% CI: -0.2 to 0.4, $P = 0.318$, η^2=0.352; DST backward: 95% CI: -0.2 to 0.6, $P = 0.438$, η^2=0.345), are all presented in Table 2.

In the subgroup analysis, statistically significant improvements were observed in language abilities (VFT scores, $P = 0.015$, η^2=0.285), and verbal memory performance (AVLT short-term scores, $P = 0.044$, η^2=0.206; Long-term scores, $P = 0.041$, η^2=0.212) among the SCD group after the intervention. In MCI subgroup analysis, statistically significant improvements were observed in general cognitive function (MoCA scores, $P = 0.005$, η^2=0.252; MMSE scores, $P = 0.008$, η^2=0.227) after the

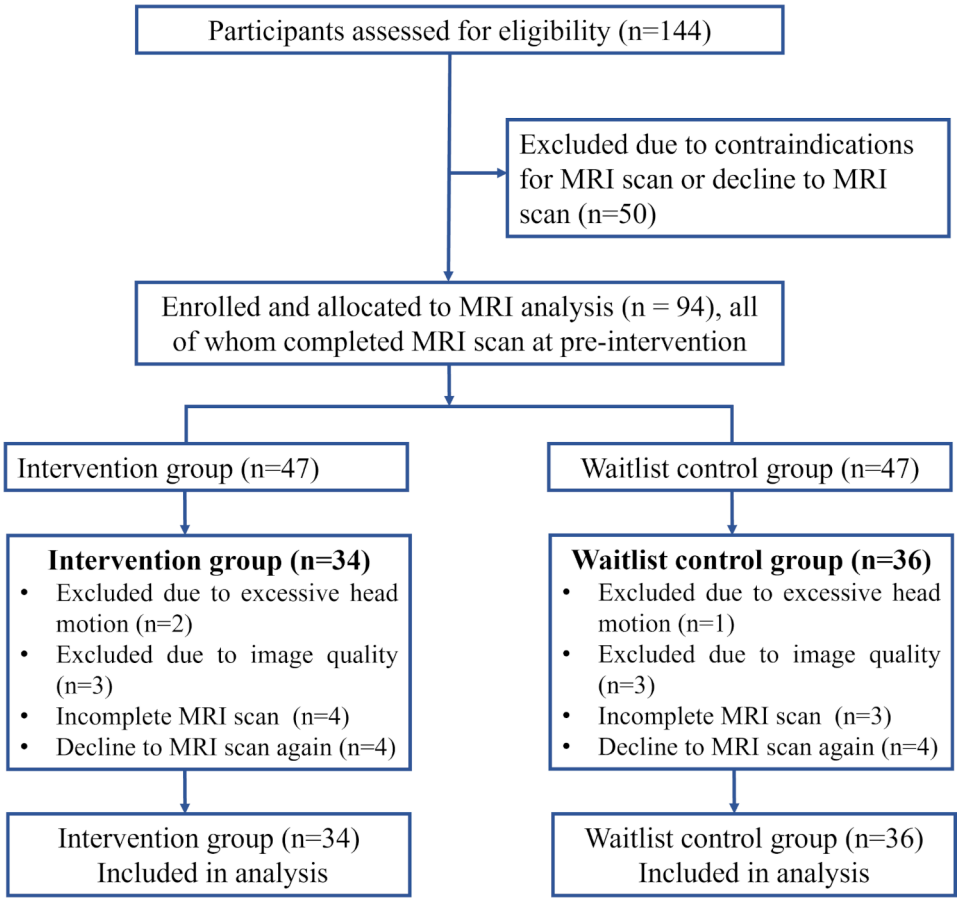

Fig. 1 CONSORT diagram

Table 1 Participants' baseline characteristics

		IG (*n* = 34)	WG (*n* = 36)	X^2/t/Z	*P*
Demographic characteristics					
Disease phase, n (%)	SCD	10 (14.3)	11 (15.7)	0.503	0.777
	MCI	14 (20.0)	17 (24.3)		
	Probable AD	10 (14.3)	8 (11.4)		
Sex, n (%)	Male	9 (12.9)	16 (22.9)	2.460	0.117
	Female	25 (35.7)	20 (28.6)		
Age, years, mean (s.d.)		70.8 (6.2)	70.2 (5.4)	-0.453	0.652
Education level, n (%)	Primary school	2 (2.9)	1 (1.4)	2.986	0.449
	Junior school	5 (7.1)	9 (12.9)		
	Senior high school	18 (25.7)	13 (18.6)		
	College or above	9 (12.9)	13 (18.6)		
Marital status, n (%)	Married	28 (40.0)	34 (48.6)		0.145
	Unmarried, widowed or divorced	6 (8.6)	2 (2.9)		
Living status, n (%)	Living alone	2 (2.9)	1 (1.4)		0.609
	Living with others	32 (45.7)	35 (50.0)		
BMI (kg/m^2), mean (s.d.)		23.3 (3.2)	22.7 (3.0)	-0.707	0.482
Diabetes, n (%)	Yes	12 (17.1)	12 (17.1)	0.030	0.863
	No	22 (31.4)	24 (34.3)		
Hypertension, n (%)	Yes	17 (24.3)	21 (30.0)	0.489	0.484
	No	17 (24.3)	15 (21.4)		
Family history of AD, n (%)	Yes	4 (5.7)	11 (15.7)	3.667	0.055
	No	30 (42.9)	25 (35.7)		
Smoking, n (%)	Never	31 (44.3)	29 (41.4)	2.149	0.483
	Former	3 (4.3)	5 (7.1)		
	Current	0 (0.0)	2 (2.9)		
Alcohol consumption, n (%)	Never	30 (42.9)	25 (35.7)	3.517	0.204
	Former	1 (1.4)	3 (4.3)		
	Current	3 (4.3)	8 (11.4)		
Physical activity, n (%)	Never	0 (0.0)	2 (2.9)	1.765	0.717
	Seldom	7 (10.0)	7 (10.0)		
	Often	6 (8.6)	5 (7.1)		
	Usually	21 (30.0)	22 (31.4)		
Cognitive leisure activity, n (%)	Never	14 (20.0)	15 (21.4)	2.204	0.531
	Seldom	7 (10.0)	12 (17.1)		
	Often	6 (8.6)	5 (7.1)		
	Usually	7 (10)	4 (5.7)		
Family member contact, n (%)	Seldom	4 (5.7)	5 (7.1)		1.000
	Often	30 (42.9)	31 (44.3)		
Friend contact, n (%)	Seldom	6 (8.6)	5 (7.1)	0.186	0.666
	Often	28 (40.0)	31 (44.3)		
Outcome measures					
MoCA, mean (s.d.)		22.7 (3.1)	22.8 (3.1)	0.210	0.834
MMSE, mean (s.d.)		26.2 (2.2)	26.3 (2.0)	-0.357	0.721
VFT, mean (s.d.)		13.9 (3.8)	14.0 (3.6)	0.099	0.922
BNT, mean (s.d.)		20.6 (3.2)	21.3 (3.4)	-1.093	0.275
AVLT Immediate-term, mean (s.d.)		15.1 (3.9)	15.5 (3.8)	0.448	0.656
AVLT Short-term, mean (s.d.)		4.6 (2.4)	4.7 (2.1)	0.139	0.890
AVLT Long-term, mean (s.d.)		4.1 (2.0)	4.1 (2.0)	-0.074	0.941
AVLT Recall-term, mean (s.d.)		19.1 (4.8)	20.7 (2.1)	-0.917	0.359
ROCFT Immediate-term, mean (s.d.)		13.9 (7.3)	12.0 (6.5)	-1.173	0.245
ROCFT Long-term, mean (s.d.)		13.0 (6.7)	12.6 (6.8)	-0.232	0.817
ROCFT Copy-term, mean (s.d.)		172.9 (68.9)	206.3 (110.0)	1.513	0.135
STT-A, mean (s.d.)		65.3 (15.0)	67.4 (22.5)	-0.159	0.874

Table 1 (continued)

	IG ($n=34$)	WG ($n=36$)	X^2/t/Z	*P*
STT-B, mean (s.d.)	163.3 (43.9)	163.5 (43.4)	-0.106	0.916
DST forward, mean (s.d.)	8.2 (1.5)	8.1 (1.2)	-0.042	0.966
DST backward, mean (s.d.)	4.3 (1.5)	4.1 (1.8)	-0.601	0.550

Abbreviations: AD, Alzheimer's disease; AVLT, auditory verbal learning test; BMI, body mass index; BNT, Boston naming test; DST, digit span test; MCI, mild cognitive impairment; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; ROCFT, Rey-Osterrieth Complex Figure Test; SCD, subjective cognitive decline; s.d., standard deviation; STT, shape trail test; VFT, verbal fluency test

Table 2 Neuropsychological outcomes after the intervention

	IG ($n=34$)	WG ($n=36$)	Between-group difference	F	*P*	η^2
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)			
MoCA	25.1 (24.2 to 26.0)	24.0 (23.1 to 24.8)	1.7 (1.1 to 2.4)	3.141	0.081	0.389
MMSE	27.6 (27.0 to 28.2)	26.2 (25.6 to 26.8)	0.6 (0.1 to 1.1)	10.647	0.002	0.333
VFT	16.1 (15.1 to 17.2)	14.2 (13.2 to 15.2)	1.2 (0.2 to 2.1)	7.223	0.009	0.203
BNT	23.7 (23.0 to 24.4)	22.3 (21.6 to 23.0)	2.0 (1.4 to 2.7)	8.295	0.005	0.437
AVLT Immediate-term	17.6 (16.0 to 19.1)	15.4 (13.9 to 17.0)	1.1 (-0.1 to 2.32)	3.702	0.059	0.202
AVLT Short-term	5.4 (4.6 to 6.2)	4.3 (3.5 to 5.1)	0.2 (-0.5 to 0.8)	3.688	0.059	0.128
AVLT Long-term	5.4 (4.6 to 6.2)	4.0 (3.2 to 4.8)	0.5 (-0.1 to 1.2)	5.801	0.019	0.194
AVLT Recall-term	20.9 (20.1 to 21.7)	20.8 (20.1 to 21.6)	1.0 (0.1 to 1.8)	0.029	0.865	0.197
ROCFT Immediate-term	20.3 (18.2 to 22.3)	17.6 (15.6 to 19.5)	6.0 (4.5 to 7.4)	3.613	0.062	0.521
ROCFT Long-term	19.7 (17.6 to 21.8)	17.6 (15.6 to 19.7)	5.9 (4.4 to 7.3)	2.008	0.161	0.487
ROCFT Copy-term	186.8 (161.6 to 212.0)	179.3 (154.8 to 203.8)	-7.1 (-27.7 to 13.5)	0.181	0.672	0.288
STT-A	56.8 (50.7 to 62.8)	61.0 (55.2 to 66.9)	-7.4 (-12.4 to -2.4)	1.023	0.315	0.173
STT-B	126.1 (112.9 to 139.3)	142.5 (129.7 to 155.4)	-28.9 (-39.3 to -18.4)	3.177	0.079	0.295
DST forward	8.4 (8.0 to 8.8)	8.1 (7.7 to 8.5)	0.1 (-0.2 to 0.4)	1.011	0.318	0.352
DST backward	4.5 (4.1 to 5.0)	4.3 (3.9 to 4.7)	0.2 (-0.2 to 0.6)	0.609	0.438	0.345

Abbreviations: AVLT, auditory verbal learning test; BNT, Boston naming test; CI, confidence interval; DST, digit span test; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; ROCFT, Rey-Osterrieth Complex Figure Test; STT, shape trail test; VFT, verbal fluency test

intervention. In the probable AD group did not show any statistically significant improvements in these assessments. The details of subgroup analysis results are presented in Supplementary Tables 3–5: Additional Files 4–6.

Resting-state FC

There were no significant differences in the baseline FC values between the groups. The results of mixed-model analyses of interaction differences (group × time interaction) revealed significant differences in FC values in various brain regions within clusters 1 and 2, including the temporal and cerebellar anterior lobes; fusiform, inferior occipital, and lingual gyri; and perirhinal and visual cortices between the groups from baseline to post-intervention (Fig. 2) (GRF-corrected, voxel $P<0.001$, cluster $P<0.05$). Detailed information on the brain regions that exhibited significant differences between the two groups before and after the intervention is presented in Table 3. Further post hoc analyses revealed that the IG exhibited reduced FC values in these brain regions, whereas the WG showed increased FC values, as shown in Fig. 2. In addition, the results of the group and condition main effects are provided in Supplementary Table 6: Additional File 7, Supplementary Fig. 1: Additional File 8; Supplementary Table 7: Additional File 9, and Supplementary Fig. 2: Additional File 10. Furthermore, the changes in FC values in cluster 1 were positively correlated with those in ROCFT Copy-term and DST backward scores, whereas changes in FC values in cluster 2 were positively correlated with those in AVLT Recall-term scores in the IG (Fig. 3). The changes in neuropsychological test scores before and after the intervention in the IG are presented in Supplementary Table 8: Additional File 11. No correlations were found between alterations in FC values and changes in neuropsychological test scores in the WG.

Discussion

To the best of our knowledge, this study is the first to use fMRI to investigate the neuroplasticity mechanism of the CAI programme in older adults along the cognitive continuum. The study demonstrated the efficacy of the CAI programme in improving general cognitive function, language, and memory, and these improvements may be affected by decreased FC in key brain regions. Compared with the WG, the IG exhibited reduced FC in various brain regions, including the temporal and cerebellar anterior lobes; fusiform, inferior occipital, and lingual gyri; and perirhinal and visual cortices. Moreover,

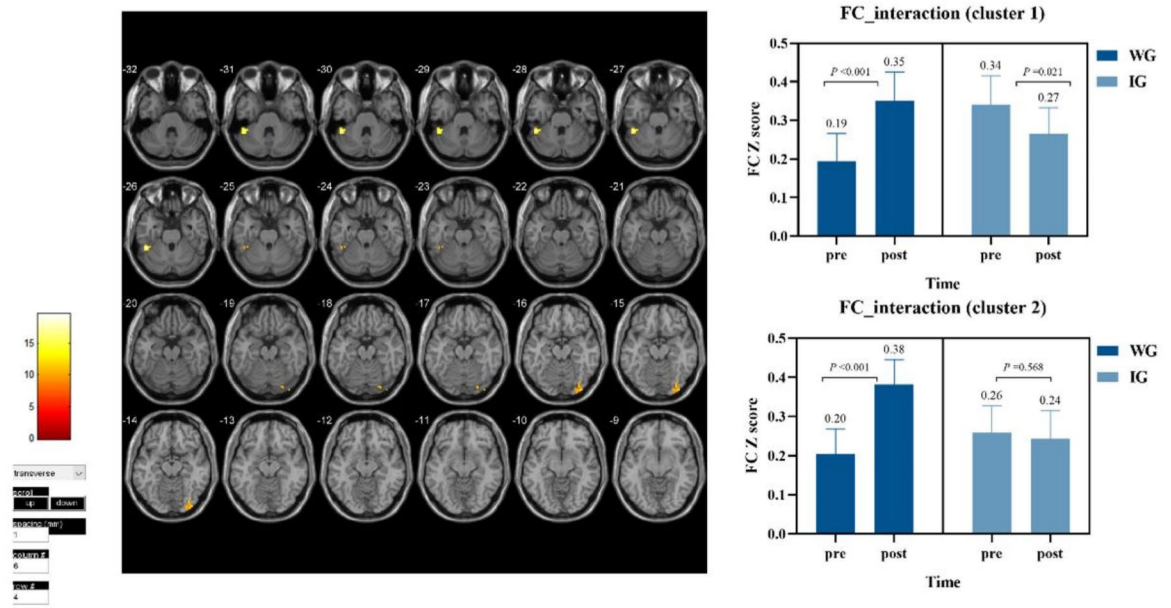

Fig. 2 Brain regions with significant interaction and post hoc test results

Table 3 Functional connectivity changes in the brain regions altered by the CAI programme

Cluster	Anatomical region	Voxel	Peak MNI coordinates			F
			X	Y	Z	
Cluster 1		27	-45	-45	-27	24.717
	Temporal_Inf_L (AAL)					
	Cerebelum_Crus1_L (AAL)					
	Cerebelum_6_L (AAL)					
	Fusiform_L (AAL)					
	BA 36					
	BA 37					
Cluster 2		22	39	-90	-15	14.724
	Occipital_Inf_R (AAL)					
	Lingual_R (AAL)					
	Fusiform_R (AAL)					
	BA 17, 18, 19					

Abbreviations: AAL, Automated anatomical labelling; BA, Brodmann area; CAI, combined art-based intervention

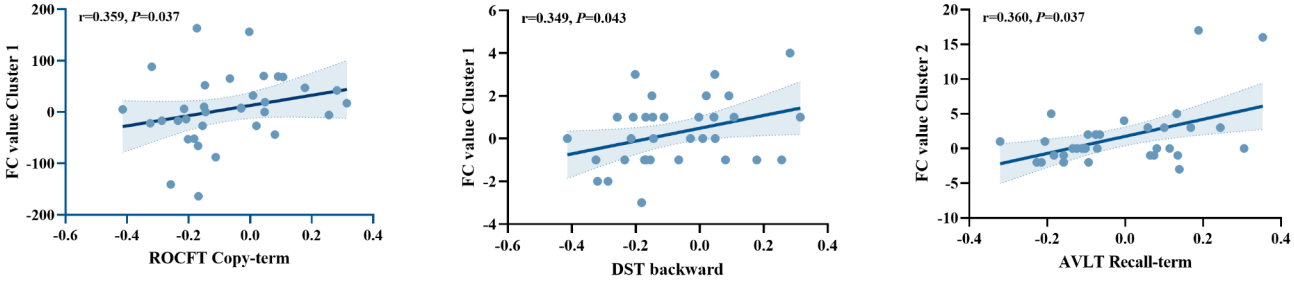

Fig. 3 Correlations between altered neuroimaging indexes and neuropsychological performance in the IG

the changes in FC values were positively correlated with those in neuropsychological test scores in the IG. Additionally, the subgroup analysis further suggested that the intervention may be more effective in the earlier stages of cognitive decline.

Consistent with other studies on art-based interventions in older adults with cognitive impairments [12, 13, 37–38], the present study first evaluated the group differences in multiple cognitive domains after the intervention. Three existing randomised controlled trials reported consistent findings of significant differences in general cognitive function, language, memory, attention, and executive function after visual art programmes for older adults with MCI [11, 12, 38]. A randomised 10-week art intervention study reported an improvement in processing speed and visuo-spatial cognition in participants with SCD [39]. A mixed-method study using thematic analysis revealed well-being benefits from art viewing and making, alongside self-reported enhancements in cognitive capacities among people with mild-to-moderate dementia [40]. This might be related to brain plasticity that can be improved in individuals with dementia. By establishing neural scaffolding, cognitive function can be regulated through brain plasticity. This enhancement is positively influenced by engaging in an environment requiring sustained cognitive effort. When engaging in artistic creation, participants need to enhance their information processing, encompassing vision, hearing, thinking, planning, and memory, requiring them to connect their stored knowledge with new information to produce creative work. Additionally, according to the literature, a change of -1 to -2 points on the MMSE is considered clinically meaningful in patients with MCI, while a change of -1.4 to -3 points is considered meaningful for patients with mild AD [41]. In our study, the intervention group showed an improvement in MMSE from 26.2 to 27.6, reflecting a change of + 1.4 points, thus the change aligns with the literature on clinically significant thresholds for MMSE.

Moreover, in further subgroup analyses, we found significant improvements in specific cognitive domains such as language ability and verbal memory performance in the SCD group, and general cognitive function in MCI group, respectively, with no significant differences observed in the probable AD group. These findings are consistent with existing studies, which underscore the importance of intervention timing and disease phase on intervention effectiveness [42]. The subgroup analysis results may reflect a ceiling effect due to the higher baseline cognitive function in the SCD group. As a result, assessments of specific cognitive domains might have been more sensitive to changes, future studies targeting SCD may benefit from focusing on specific cognitive domains to better capture intervention effects. However, due to the small sample size, these results should be interpreted with caution.

Recent research on various art forms, including visual art, music, and art evaluation, has predominantly focused on psychological and physiological effects in older adults along the cognitive continuum. It is advisable to investigate how art-based interventions work instead of comparing separate approaches for understanding their mechanisms. A study that synthesised data from 32 functional neuroimaging studies and applied activation likelihood estimation meta-analysis revealed a domain-general pattern across three artistic forms (music improvisation, drawing, and literary creativity) [43]. Each artistic form relied on domain-specific neural circuits to some degree; however, the overlap between essential brain regions in the same participants across different artistic modalities remains unknown, particularly in the context of AD. The present findings provide valuable evidence for this research field. We found that participants in the IG, who underwent the CAI programme, incorporating visual, performing, and literature arts, showed reduced FC in the temporal and cerebellar anterior lobes; fusiform, inferior occipital, and lingual gyri; and perirhinal and visual cortices. These changes in the FC brain regions were associated with cognitive correlates.

The results of connectivity analysis with the PFC as the seed ROI indicated that the specific brain regions exhibited significant differences in FC. These brain regions are closely associated with functions, such as visual memory, logical analysis, motion perception, abstract concepts, and language-related processes. Following a 5-week cognitive intervention in older participants, Brehmer et al. [44] observed a decrease in cerebral cortex activity in the IG, suggesting a potential mechanism involving increased neural efficiency in the relevant brain regions, which is consistent with the findings of the present study. Consequently, the IG experienced a decrease in FC in these brain regions, possibly because of the intervention's effect on decreasing excessive FC in these areas. This may occur without the need for increased FC to engage in information transmission, integration, and functioning, ultimately enhancing the efficiency of brain network operations.

This study has some limitations. First, this was a single-center study with a relatively small sample size, short intervention period, and limited to resource constraints, we were unable to include a control group with a similar social interaction component, which could have provided a better comparison. Further multi-center studies with larger sample sizes, longer intervention periods, and more rigorous controls are necessary to validate and generalize these findings. Second, it is important to acknowledge the presence of selection bias in this study. This bias is not solely related to differences in educational levels

but also extends to general health and lifestyle factors. The study participants exhibited characteristics such as regular physical exercising and non-smoking/alcohol consumption habits. While these factors may have contributed to adherence to the CAI programme, they could introduce bias and limit the generalisability of our findings to populations with different health and lifestyle profiles. Third, the absence of biomarkers such as CSF/PET tau, beta-amyloid, NfL, and GFAP data limits our ability to more precisely define the underlying pathology of MCI type and better understand the mechanisms of intervention effects. Finally, we assessed neuropsychological measurements and conducted MRI before and after the intervention. However, a significant limitation is the lack of long-term follow-up data. The enduring central neurological effects of CAI in older adults along the cognitive continuum remain unknown, and further research is required to investigate the sustained impact of this intervention over extended periods.

Conclusion

This study has practical and clinical implications for the treatment in older adults along the cognitive continuum. This study successfully demonstrated the innovative concept of the CAI approach. The IG demonstrated significant improvements in general cognitive function and specific cognitive domains including language and memory, suggesting a range of potential benefits associated with the intervention and thereby making it a viable long-term management strategy for delaying the progression of AD and onset of dementia. Furthermore, this study explored the underlying neurocentral mechanisms of CAIs, indicating that a 16-week, 24-session intervention can modulate the strength of FC, which may facilitate cognitive performance in the IG. Subgroup analysis further suggested that the intervention may be more effective in the earlier stages of cognitive decline. Future research should focus on conducting multi-center studies with larger sample size, longer intervention period, and active control, incorporating biomarkers and long-term follow-up to better understand the underlying pathology and sustained effects of the CAI intervention on cognitive function in older adults across the cognitive continuum.

Abbreviations

AD	Alzheimer's disease
AVLT	Auditory verbal learning test
BMI	Body mass index
BNT	Boston Naming Test
CAI	Combined art-based intervention
CI	Confidence interval
DST	Digit Span Test
FC	Functional connectivity
GRF	Gaussian random field
IG	Intervention group
MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
MRI	Magnetic resonance imaging
PCC	Posterior cingulate cortex
PFC	Prefrontal cortex
ROCFT	Rey-Osterrieth Complex Figure Test
ROI	Region of interest
SCD	Subjective cognitive decline
STT	Shape Trail Test
TSE	Turbo spin echo
VFT	Verbal Fluency Test
WG	Waitlist control group

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-06741-3.

Supplementary Material 1: Supplementary methods: Additional file 1 Diagnostic assessment. Supplementary table 1: Additional file 2 Description of the CAI programme. Supplementary table 2: Additional file 3 Baseline characteristics of participants included and excluded in FC analysis of CAI programme. Supplementary table 3: Additional file 4 Analysis of neuropsychological outcomes after the intervention between the SCD subgroup. Supplementary table 4: Additional file 5 Analysis of neuropsychological outcomes after the intervention between the MCI subgroup. Supplementary table 5: Additional file 6 Analysis of neuropsychological outcomes after the intervention between the probable AD subgroup. Supplementary table 6: Additional file 7 Group main effect of CAI programme on functional connectivity changes of the brain region. Supplementary fig. 1: Additional file 8 Brain regions with significant group main effect. Supplementary table 7: Additional file 9 Condition main effect of CAI programme on functional connectivity changes of the brain region. Supplementary fig. 2: Additional file 10 Brain regions with significant condition main effect. Supplementary table 8: Additional file 11 Changes of neuropsychological test scores in the IG.

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Author contributions

Y.J.Y. contributed to conceptualisation, methodology, investigation, project administration, data curation, formal analysis, writing– original draft, and funding acquisition. R.L. contributed to conceptualisation, methodology, project administration, and writing– original draft. Y.T.L. contributed to methodology, investigation, project administration, and data curation.C.S.H. contributed to methodology, investigation, project administration, data curation, and writing– original draft. W.C.C. contributed to investigation, project administration, and data curation. J.W.S. contributed to investigation, project administration, and data curation. S.M.L. contributed to investigation, project administration, and data curation. M.J.L. contributed to conceptualisation, project administration, writing– review & editing, and supervision. H.L. contributed to conceptualisation, project administration, writing– review & editing, supervision, and funding acquisition. All authors read and approved the final manuscript.

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Data availability

Deidentified participant data can be accessed for research purposes, such as meta-analysis or systematic reviews, following approval and executing a data agreement signed by the corresponding author.

Declarations

Ethics approval and consent to participate

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Ethics Committee of Fujian Provincial Hospital, Fujian Province, China (reference number: K2020-03-069).

Consent for publication

Written informed consent was obtained from each participant or a family member.

Competing interests

The authors declare no competing interests.

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