Original Article

White matter integrity of default mode network after a 3-month aerobic dance program in patients with amnestic mild cognitive impairment: a secondary analysis of a randomized clinical trial

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Background: Exercise is an effective non-pharmacological strategy to enhance cognitive function in individuals with mild cognitive impairment (MCI). Our previous studies confirmed that aerobic dance can increase the amplitude of low-frequency fluctuations (LFF) in bilateral fronto-temporal, entorhinal, anterior cingulate, and para-hippocampal cortices. However, its effects on structural connections remain unclear. The present study comprised a secondary analysis of a randomized clinical trial and aimed to examine the impact of a 3-month aerobic dance program on white matter integrity of default mode network (DMN) in older adults with amnestic MCI, as assessed by magnetic resonance imaging (MRI).

Methods: A total of 112 patients with memory decline were recruited, 38 of whom completed cognitive assessments and magnetic resonance scans and were randomized to the exercise group (n=19) or the control group (n=19). The exercise group received 3 months of aerobic dance and health education, whereas the control group only received health education. All participants underwent cognitive assessments and MRI scans at baseline and after the 3-month intervention. A series of neuropsychological assessments, including Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Wechsler Memory Scale-Revised Logical Memory (WMS-RLM), Trail Making Test Part A&B (TMT-A&B), Symbol Digit Modalities Test (SDMT), and Forward and Backward Digit Span Task (DST) Chinese version, were used to assess the participants' global cognitive function, memory function, and executive function. Structural connections of the hippocampus-hub temporal network were analyzed using the network-based statistic.

Results: Finally, 16 participants in each group were included in the statistics and analysis. There was no statistical difference in cognitive functions at 3 months in the control group compared with those at baseline. However, the cognitive functions of the exercise group improved significantly after 3 months of aerobic dance, including MMSE (P=0.006), MoCA (P=0.009), WMS-RLM (P=0.005), TMT-A (P=0.007), and DST (P=0.025). Moreover, the exercise group had significantly improved WMS-RLM (P=0.003) compared to the control group after 3 months of intervention. In addition, they showed significant increases in structural connections within the DMN, including the structural connection between hippocampus and para-hippocampus, hippocampus and fusiform gyrus, hippocampus and middle temporal gyrus, and precuneus and middle temporal gyrus. The structural connection between DMN and supplementary motor area was also significantly increased in the exercise group, correlating positively with MMSE (R=0.31, P=0.04) and negatively with TMT-A (R=−0.40, P=0.011), respectively.

Conclusions: A 3-month aerobic dance program may enhance the structural connections in the hippocampus-hub temporal network and improve episodic memory and global cognition in older adults with amnestic MCI.

Keywords: Mild cognitive impairment (MCI); aerobic dance; default mode network; structural connection (DMN); cognitive performance

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Introduction

Alzheimer's disease (AD) is one of the greatest challenges for public health worldwide (1). However, disease-modifying treatment strategies for AD are still under investigation. Therefore, the intervention in the early stage of AD deserves extensive attention of researchers. Amnestic mild cognitive impairment (aMCI) is mainly characterized by memory decline. It is an intermediate stage between normal cognitive decline and dementia, and has a very high conversion rate to AD (2,3). The 5-year conversion rate of mild cognitive impairment (MCI) to probable dementia could be as high as 241.3 (189.6, 307.0)/1,000 person-years without any intervention (4).

Neuroimaging can decode the neuropathological basis and intervention mechanism of AD and MCI from the macroscopic neurological connections. In the last 2 decades, the altered of the default mode network (DMN) in structural connections (SC) have been recognized as important markers of AD (5-9). The DMN predominately comprises the ventromedial prefrontal cortex, dorsomedial prefrontal cortex, posterior hub, posterior cingulate cortex, adjacent precuneus, and angular gyrus (10). The hippocampus, para-hippocampus, and middle temporal gyrus (MTG) are also important brain regions in the DMN, which plays a vital role in memory function, especially episodic memory (11,12). The precuneus is mainly involved in self-reflection processes and episodic memory retrieval (13). The DMN also involves complex cognitive functions, such as attentional focus, daydreaming, social evaluation, and cognitive control (14-16). Significant gray matter volumetric reductions in the fronto-temporo-parietal structures in the DMN among aMCI have been reported (17). In addition, disrupted SC have been found among DMN components both in aMCI and AD patients, which was significantly correlated with their cognitive functions decline. Interestingly, cognitive training could increase SC in the left parietal DMN regions of MCI (18). However, most of the current cognitive training needs to rely on the corresponding equipment or software, which is difficult to be widely carried out in the elderly population. Exercise such as dancing, cycling, and walking is an effective treatment and may be well applied in the elderly population.

Compared with traditional exercise, dancing is cognitively demanding. Therefore, dancing may promote greater cognitive gains (19). One meta-analysis showed that the cognitive functions of MCI patients were significantly improved after dance intervention, including global cognition, attention, immediate and delayed recall, and visuospatial ability (20). Our previous meta-analyses also showed that aerobic dance significantly improved global cognitive function and memory in older adults with MCI (21). In addition, our randomized controlled trial (RCT) also found the increased hippocampus volume (22) and amplitude of low frequency fluctuation (ALFF) of the brain regions involved in DMN in older adults with MCI after a 3-month aerobic dance program and amplitude of ALFF of the brain regions involved in the DMN in older adults with MCI after 3 months of aerobic dance (23). However, the effect of aerobic dance on structural connection has not been reported.

The present study comprised a secondary analysis of the RCT mentioned above (registration No. ChiCTR-INR-15007420). We aimed to explore the change in the structural connections of white matter fiber in older adults with aMCI after a 3-month aerobic dance program based on this randomized controlled single blind trial. We speculated that improvement of the internal structure connectivity within the DMN and supplementary motor area (SMA) may be an important way to improve the cognitive function of MCI, and may become an important indicator to observe the effect of treatment in MCI.

Methods

Study design

This study comprised a secondary analysis of a single-blind RCT, and the purpose of the research was to explore the effect of aerobic dance on the structural connectivity of the default network in elderly people with aMCI. This primary study was registered on the Chinese Clinical Trial Registry (Registration No. ChiCTR-INR-15007420). The primary study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (No. 2012-SR-098). All participants signed the informed consent form.

Patients

We performed a secondary analysis of the dataset previously reported by Zhu *et al.* (22). Briefly, a cohort of 112 participants was recruited from the memory clinic of the First Affiliated Hospital of Nanjing Medical University. Finally, 56 participants were randomly divided into a control group and an exercise group. The diagnosis of aMCI was made according to the guidelines of the National Institute of Aging and Alzheimer's Association (NIA-AA) (24). The inclusion criteria and exclusion criteria are shown in the supplementary information (Appendix 1).

Before randomization, the safety of aerobic dance training was evaluated for all participants through symptom-limited exercise tests. The maximum heart rate required for training was obtained through the modified Bruce protocol in this study (25).

Randomization

Participants were randomly assigned to an exercise and a control group by an independent statistician. The independent statistician generated a computer-based randomization sequence using simple randomization according to our previous study (26). Each participant was allocated to a group by a clinician who opened a black envelope containing the number and intervention method. The clinician conducting the randomization did not participate in the entire intervention process, including the process of dividing random numbers, cognitive assessment, and the intervention process. The cognitive evaluator who was in charge of the inclusion and the neuropsychologist who performed the outcome assessments were blinded to the group assignment. None of the participants in this study had had a long-term habit of dancing before intervention.

Revised sample size calculation was based on the primary outcome of changes in memory function (measured by the Wechsler Memory Scale-Revised Logical Memory, WMS-RLM) (27) at 3 months. In order to attain 80% statistical power at a significance level of 0.05 (2-sided) for the detection of a moderate effect size of 0.75 standard deviation, a minimum sample size of 56 (28 per group) was necessary.

Interventions

The aerobic dance intervention group

The intervention group undertook medium-to-moderate-intensity aerobic dance training, for 35 minutes each time, 3 times a week. The intervention cycle lasted for a total of 3 months. The target heart rate throughout the training process needed to reach 60–80% of the maximum heart rate. Maximum heart rate was obtained by electrocardiography exercise test completed at enrollment. The total aerobic dance time was 25 minutes. Participants wore a heart rate monitor on their left wrists during the whole dance class using the cardiotachometers (ONrhythm 50, GEONATURE). The specific aerobic dance details are available in our previous RCT study and supplementary methods (Appendix 1). The dance group also received a 120-minute health education program when they were enrolled. This health education project included the prevention of risk factors for dementia, the structure of the Mediterranean diet, how to choose a healthy lifestyle, as well as insomnia management. Participants were followed up by phone every week and were actively reminded of the key points of the education program.

The control group

The control group did not learn aerobic dance. They only received health education.

Outcome measurements

The assessment of cognitive function was conducted at baseline and after the 3-month intervention using comprehensive neuropsychological tests. Cognitive assessment included Mini-Mental State Examination (MMSE) (28), Montreal Cognitive Assessment (MoCA) (29), WMS-RLM, Trail Making Test Part A&B (TMT-A&B) (30), Symbol Digit Modalities Test (SDMT) (31), and Forward and Backward Digit Span Task (DST) Chinese version (32). Quality of life was assessed using 36-Item Short-Form Health Survey (SF-36) (33). Emotional assessment was assessed using the Geriatric Depression Scale (GDS-15) (34). The neuropsychological assessment scale was completed by a professional neuropsychological assessor who was unaware of the grouping situation.

Magnetic resonance imaging (MRI) acquisition

The MRI scanning was conducted using a 3.0T MRI System (750 W; GE Healthcare, Chicago, IL, USA) with a standard birdcage head transmit and receive coil at baseline and after the 3-month aerobic dance program. Initially, high-resolution three-dimensional (3D) T1-weighted anatomical images were obtained in the sagittal plan using a magnetization-prepared rapid gradient-echo sequence [repetition time (TR) =6.5 ms; echo time (TE) =2.3 ms; flip angle =11°; field of view (FOV) =256 mm × 256 mm; matrix size =256×256; slice thickness =1 mm; inter-slice gap =0 mm; voxel size =1×1×1 mm^3; 188 slices]. Secondly, axial fluid-attenuated inversion recovery images (time of inversion =2,500 ms; TR =9,000 ms; TE =100 ms; slice thickness =5 mm) were obtained for diagnosis. Finally, the diffusion tensor imaging (DTI) data were obtained using single shot spin echo-planar imaging with the following parameters: diffusion was measured along 30 noncollinear directions with b=1,000 s/mm^2, and an additional image without diffusion weighting with b =0, TR =7,464 ms, TE =98 ms, flip angle =140°, matrix =112×112, FOV =224 mm × 224 mm, slice thickness/gap =3/0 mm, 40 slices.

The images were all gathered by a single imaging radiographer and reviewed by a seasoned radiologist in order to rule out patients with evident brain lesions, such as cerebral infarction, moderate-to-severe white matter lesions, brain tumor, and other brain damage.

MRI preprocessing

The DTI data underwent preprocessing with the FMRIB Software Library (FSL). The b0 image was initially corrected for head motion artifacts and eddy current distortions using diffusion-weighted transformation. Then, the diffusion tensor matrix was calculated based on the Stejskal and Tanner equation. Subsequently, by diagonalization of the tensor matrix, 3 eigenvalues and eigenvectors to the main direction of diffusion and diffusivity were acquired, and then fractional anisotropy (FA) maps were estimated. Finally, we utilized DiffusionKit to align each b0 image with the Montreal Neurological Institute (MNI) space using the individual T1 image (http://diffusion.brainnetome.org/en/latest/tutorials.html). The matrix for converting from the diffusion space to the MNI space has been stored for future reference.

For the fiber tractography, the diffusion toolkit by the Fiber Assignment by Continuous Tracking (FACT) algorithm was utilized, in which fiber tracking was terminated when the turning angle between adjacent voxels became larger than 50° or the FA fell below 0.2. At last, the streamlines of each individual were transformed into MNI space using a transformation matrix in order to analyze the streamlines of each sample at a group level.

Fractional anisotropy structural connectivity (FASC)

We identified the specific areas of interest within the DMN using the automated anatomical labeling (AAL) atlas, which includes 24 cortical and subcortical regions (*Table 1*). Therefore, we obtained a 24*24 FASC matrix for each participant. Reversing the transformations, we registered the AAL atlas from the MNI space to the individual's native space. We defined region (i) and region (j) as structurally connected if there was an edge e = (i, j) with passing fibers longer than 10 mm and at least 2 streamline counts in the native space. For each edge, we computed the mean FA values of all fibers as their weights. To regress out the effects of age, sex, and years of education, we used a general linear model (GLM) on all participants' FASC data.

Statistical analysis

The software SPSS 27.0 (IBM Corp., Armonk, NY, USA) was used to analyze the demographic and neuropsychological characteristics. The comparison of gender between the 2 groups was conducted by using the χ^2 test. The independent sample *t*-test was used for the comparison of age, years of education, and neuropsychological assessment between the 2 groups. The comparison before and after the intervention in each group was conducted by using the paired sample *t*-test. A P value of <0.05 was considered indicative of statistical significance.

Table 1 Abbreviations for the 24 ROI used in this study

Regions	Abbreviations	
	Left hemisphere	Right hemisphere
Superior frontal gyrus, dorsolateral	SFG.L	SFG.R
Supplementary motor area	SMA.L	SMA.R
Superior frontal gyrus, medial orbital	MFG.L	MFG.R
Gyrus rectus	REC.L	REC.R
Anterior cingulate and paracingulate gyri	ACC.L	ACC.R
Posterior cingulate gyrus	PCC.L	PCC.R
Hippocampus	HIP.L	HIP.R
Parahippocampal gyrus	PHG.L	PHG.R
Fusiform gyrus	FFG.L	FFG.R
Angular gyrus	ANG.L	ANG.R
Precuneus	PCUN.L	PCUN.R
Temporal pole: middle temporal gyrus	MTG.L	MTG.R

ROI, regions of interest.

The significant FASC between different groups was evaluated using the network-based statistic (NBS). NBS is a method that controls the family-wise error rate when mass-univariate testing is performed at every connection comprising the graph, based on classical cluster-based thresholding of statistical parametric maps. When comparing the FASC differences between MCI and controls at baseline, *t*-test was conducted on every connectivity value. Relevant connections with *t*-values surpassing the main threshold were chosen to create topological clusters, where the quantity of connections within each cluster was designated as the observed cluster score. Actually, there is no widely accepted standard of the criterion. Here, according to our experience and the manual, we established the primary threshold and set the $P=0.001$ level in order to rigorously control for Type I error. The FA matrix was randomized 5,000 times across groups to obtain the reference cluster distribution for the NBS. The reference distribution was formed by selecting the maximum number of connections across all clusters for each randomization. When comparing the FASC differences between patients with aMCI before and after aerobic dance, the paired-sample *t*-test was selected. The structural connection and cognitive assessment scores were statistically analyzed by Pearson's correlation analysis.

Results

A total of 112 elderly people (age ranging from 50 to 85 years) signed up for this program in this study. Among them, 2 cases were excluded from the analysis due to death or request, and 42 cases were not included in the study because they did not meet the requirements. Finally, a total of 56 participants were randomly assigned to either the exercise group (n=28) or the control group (n=28) for the study. However, only 19 participants in each group successfully completed the MRI assessment. A total of 18 individuals were unable to complete the entire scan at baseline. We did not include patients who had taken medications, such as donepezil, and memantine, that may affect cognitive function, during the past 6 months. No medication was given to any of these patients during the intervention. After 3 months of intervention, 16 people in each group completed cognitive assessment and MRI assessment. A diagram in *Figure 1* illustrates the entire process of this study in detail.

Baseline demographic and clinical characteristics

The baseline demographic and neuropsychological characteristics of the exercise and control groups are outlined in *Table 2*. There were no statistically significant differences in gender, age, educational level, and neuropsychological assessment at the baseline level between the 2 groups.

Neuropsychological assessment of intervention effects

After having completed the 3-month aerobic dance program, the exercise group demonstrated significant improvement in their cognitive functions. As shown in *Table 3*, there were significantly increased scores of MMSE, MoCA, WMS-RLM, and SDMT ($P<0.05$) whereas the score of TMT-A was significantly decreased ($P<0.05$) at 3 months compared to the baseline. However, we found no statistical difference between neuropsychological measures in controls at baseline and at 3 months. Moreover, we found significantly higher changes of the WMS-RLM from baseline to 3 months between the 2 groups ($P<0.05$), implying improved logical memory function after the 3-month intervention.

MRI measures of intervention effects

First, we examined the FASC network differences between

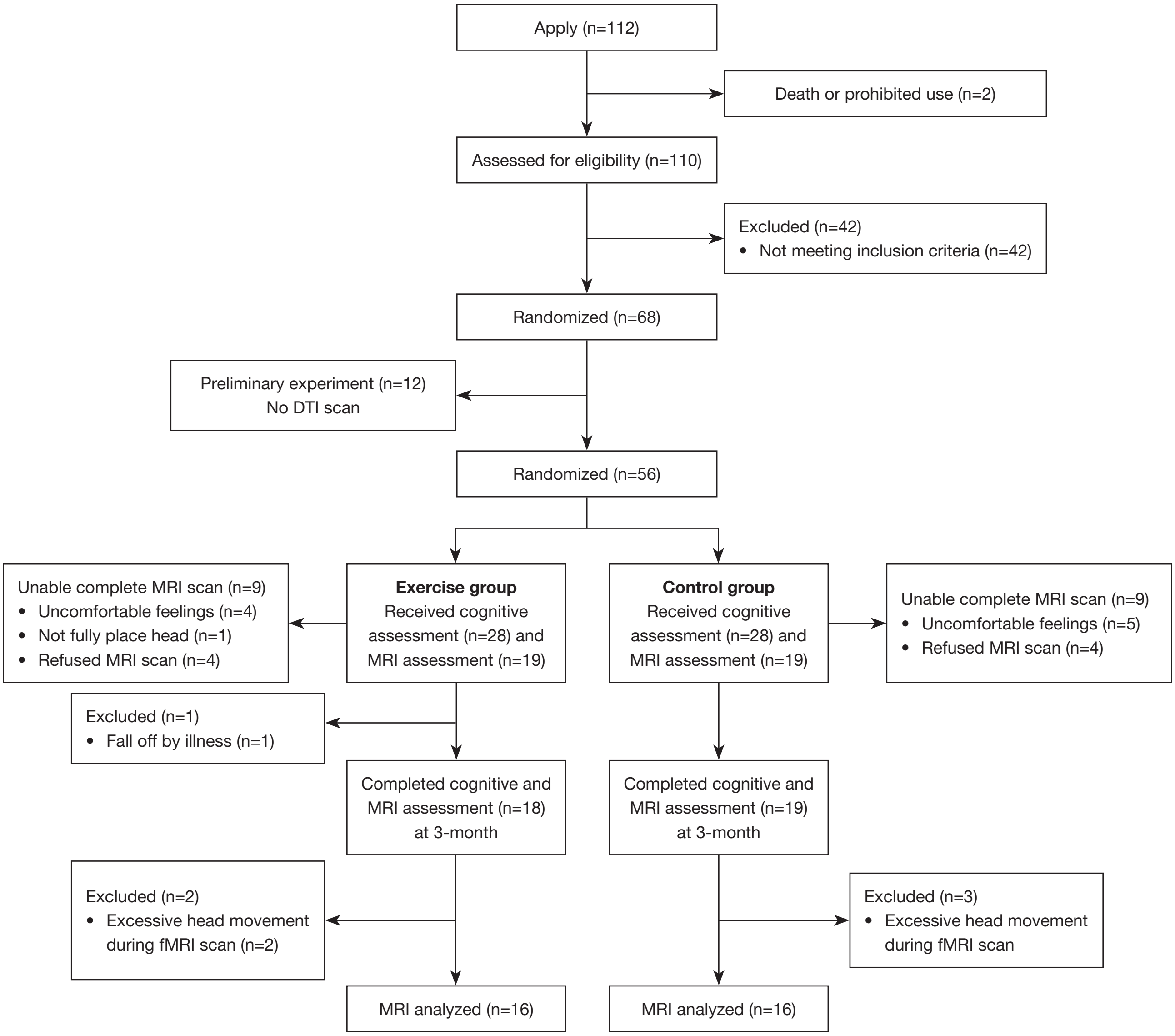

Figure 1 A flow chart of the recruitment and exclusion of participants. DTI, diffusion tensor imaging; fMRI, functional MRI; MRI, magnetic resonance imaging.

the exercise group and the control group at baseline. We found no significant FASC network differences between them. In addition, we found no significant FASC network changes in the control group after the 3-month intervention. However, paired-sample NBS revealed a significantly increased FASC in the hippocampus and temporal network of exercise group (*Figure 2*). This network consisted of 6 regions and 5 connections, involving the hippocampus, para-hippocampal cortex, fusiform gyrus, SMA, precuneus, and MTG. Interestingly, these regions are located in the right hemisphere, indicating a lateralization process of strengthening brain structural connections after aerobic dance. More specifically, the hippocampus was the hub of the altered FASC network. We also compared the FASC changes of this network between the exercise group and the control group. We found that the increased mean FASC was much higher in the exercise group than the control group (U=60, P=0.0096). The dance intervention would have effects on gray matter volume (22,35). Therefore, we performed a complementary analysis using gray matter volume of the 6 regions as regressor during statistical analysis on FASC changes; consistent findings were yielded.

Table 2 Baseline demographic and clinical characteristics

Characteristics	The exercise group (n=16)	The control group (n=16)	t value	P value
Sex (male:female)	5:11	4:12		0.69
Age (years)	70.56 (6.21)	69.13 (8.09)	0.564	0.58
Education (years)	12.94 (2.72)	13.00 (2.28)	–0.070	0.94
Mini-Mental State Examination	27.25 (1.34)	27.06 (1.24)	0.411	0.68
Montreal Cognitive Assessment	22.63 (2.12)	22.94 (1.69)	–0.460	0.65
Wechsler Memory Scale-Revised Logical Memory	14.13 (5.93)	16.69 (5.40)	–1.278	0.21
Digit Span Test	16.38 (2.94)	18.06 (3.36)	–1.513	0.14
Trail making test part A	107.25 (97.06)	72.19 (23.34)	1.316	0.20
Trail making test part B	190.56 (59.23)	182.19 (57.73)	0.405	0.69
Symbol digit modalities test	31.75 (9.57)	34.06 (10.88)	–0.639	0.53
Geriatric Depression Scale	13.13 (6.85)	14.19 (7.55)	–0.417	0.68
36-Item Short-Form Health Survey	107.75 (17.19)	108.94 (13.19)	–0.219	0.83

Data are expressed as n or mean (standard deviation).

Table 3 Comparison of neuropsychological tests at baseline and at 3-months of intervention in aMCI

Neuropsychological testing	EG (n=16)			CG (n=16)			EG *vs*. CG post-intervention		
	Pre-intervention	Post-intervention	P value	Pre-intervention	Post-intervention	P value	Difference changes in EG	Difference changes in CG	P value
Mini-Mental State Examination	27.25 (1.34)	28.19 (0.98)	0.006[a]	27.06 (1.24)	27.25 (1.69)	0.723	0.94 (1.18)	0.19 (2.07)	0.218
Montreal Cognitive Assessment	22.63 (2.12)	24.25 (2.18)	0.009[a]	22.94 (1.69)	23.69 (1.69)	0.090	1.63 (2.19)	0.75 (1.65)	0.212
Wechsler Memory Scale-Revised Logical Memory	14.13 (5.93)	17.94 (4.43)	0.005[a]	16.69 (5.40)	15.19 (3.25)	0.208	3.81 (4.65)	–1.56 (4.62)	0.003[b]
Digit Span Test	16.38 (2.94)	16.44 (2.63)	0.948	18.06 (3.36)	17.13 (2.90)	0.105	0.06 (3.80)	–0.88 (2.13)	0.396
Trail Making Test Part A	83.80 (25.80)	67.27 (26.15)	0.007[a]	72.19 (23.34)	68.81 (19.10)	0.573	–16.53 (20.35)	–3.38 (23.42)	0.107
Trail Making Test Part B	190.56 (59.23)	161.63 (53.81)	0.147	182.19 (57.73)	181.63 (46.69)	0.956	–28.94 (75.69)	–0.69 (39.92)	0.197
Symbol Digit Modalities Test	31.75 (9.57)	34.50 (9.27)	0.025[a]	34.06 (10.88)	33.50 (10.49)	0.824	2.75 (4.41)	–0.56 (9.91)	0.231
Geriatric Depression Scale	13.13 (6.85)	11.31 (6.36)	0.162	14.19 (7.55)	11.44 (7.19)	0.062	–1.81 (4.93)	–2.75 (5.46)	0.614
36-Item Short-Form Health Survey	107.75 (17.19)	110.50 (16.28)	0.439	108.94 (13.19)	114.56 (16.75)	0.080	2.94 (14.28)	5.63 (11.98)	0.568

Data are expressed as mean (standard deviation). [a], within-group change is calculated as the outcome measure after the 3-month aerobic dance program; [b], between-group change is calculated as the outcome measure after 3 months of aerobic dance. aMCI, amnestic mild cognitive impairment; CG, the control group; EG, the exercise group.

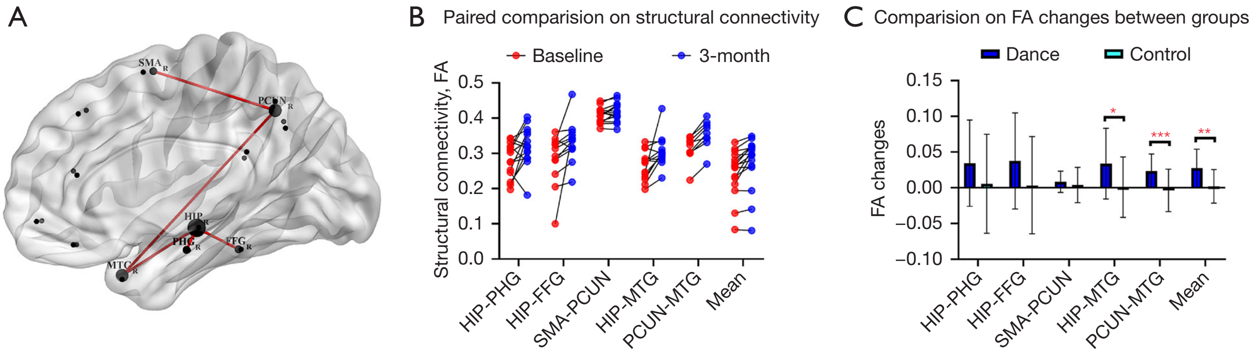

Figure 2 Increased structural connections over the aerobic dance period. After the 3-month aerobic dance intervention, patients with aMCI showed significantly increased structural connections of hippocampus-hub temporal network. This network consisted of 6 regions and 5 connections (A). (B) Paired-sample structural connection changes were shown. (C) Comparisions of FA changes between groups were illustrated. *, P<0.05; **, P<0.01; ***, P<0.001. Please refer to *Table 1* for the definitions of ROI abbreviations. aMCI, amnestic mild cognitive impairment; FA, fractional anisotropy; ROI, regions of interest.

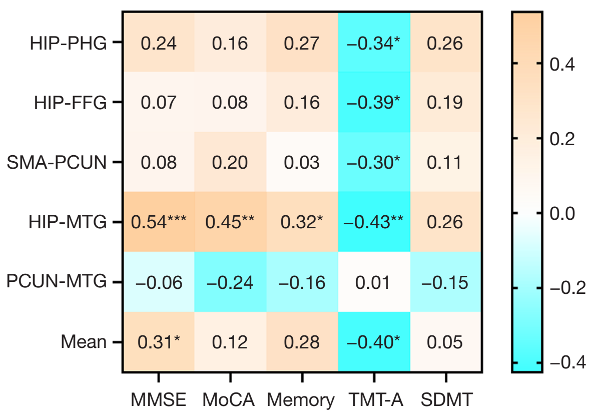

Figure 3 Correlation heatmap of structural connections strength and cognition performance. We performed correlation analyses between neuropsychological tests and structural connections in which significant changes after aerobic dance were detected. There were significant positive and negative correlations between mean structural connections with MMSE (R=0.31, P=0.04) and TMT-A (R=−0.40, P=0.011), respectively. *, P<0.05; **, P<0.01; ***, P<0.001. Please refer to *Table 1* for the definitions of ROI abbreviations. MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; ROI, regions of interest; SDMT, Symbol Digit Modalities Test; TMT-A, Trail Making Test Part A.

In addition, there were no significant relationships observed between increased structural connections and volume changes (R=−0.34, P=0.192), which may argue against a significant influence of the volume changes on structural connections after aerobic dance intervention.

Correlation between structural connectivity and cognitive function

Finally, Pearson correlation analyses were performed between neuropsychological tests and FASC in which significant changes after aerobic dance were detected. *Figure 3* shows the results of the correlation analysis of differential FASC with neuropsychological tests in the exercise group. Hippocampus -middle temporal gyrus connections were significantly correlated with MMSE (R=0.54, P<0.001), MoCA (R=0.45, P=0.005), memory (R=0.32, P=0.036) and TMT-A (R=−0.43, P=0.008). TMT-A was significantly negatively correlated with hippocampus-para-hippocampal cortex (R=−0.34, P=0.030), hippocampus-fusiform gyrus (R=−0.39, P=0.014), SMA-precuneus (R=−0.30, P=0.045), and hippocampus-middle temporal gyrus (R=−0.43, P=0.008). We added the results of the correlations between FA and neuropsychological tests of the whole group at baseline and 3 months, and the results of the correlations between FA and neuropsychological tests of the control group at 3 months in the supplementary information (Figure S1).

Discussion

Early interventions for aMCI are crucial in order to delay its progression to AD. Dance, synchronizing music and movement, which essentially constitutes a "pleasure double play", are being used to treat people with AD and MCI. In the current study, we demonstrated that a 3-month aerobic dance program could increase structural connectivity in the hippocampus and temporal network in aMCI, which is positively correlated with the improved cognitive function.

Our dance routine involved cognitive training and aerobic exercise. Learning how to combine dance movements together requires practice (repetition) and cognitive effort, which includes attention, awareness and, especially importantly, episodic memory. Compared with the control group, the cognitive function of the exercise group improved significantly after 3 months of aerobic dance intervention, mainly reflected in logical memory function and executive function. This result is consistent with those of other studies. Recent meta-analyses have found that dance may improve MCI and the cognitive functions of healthy elderly people, such as global cognitive function, executive function, attention, and so on (20,36). One possible cause is that our dance requires participants to maintain a high degree of concentration during the intervention process in order to successfully complete each session compared with other dance types. Therefore, aerobic dance may produce a reliable and significant curative effect on cognitive improvement in aMCI complicated by neuropathological changes. However, no active control group was established in this study; we were unable to distinguish the roles of cognitive and physical functions throughout the aerobic dance process. A 2020 analysis showed that dance improved cognitive function in older adults with aMCI compared with physical therapy (37). Future studies would involve designing an aerobic dance program, as a dual task intervention, to be compared with a single aerobic exercise task and a single cognitive task intervention.

In the present study, our results showed the increased SC in MCI patients after a 3-month aerobic dance program, including the connection between hippocampus and para-hippocampus, hippocampus and fusiform gyrus, hippocampus and middle MTG, and precuneus and MTG. A previous study showed that MCI is characterized by atrophy of the MTG and hippocampus structures (38). Furthermore, the white matter damage in para-hippocampal tracts is highly correlated with memory decline in patients with AD (39,40). Another study showed that global cognitive function and delayed memory was also correlated with right fusiform gyrus (41). Compared with healthy adults, structural connections in MCI are reduced and strongly associated with declines in cognitive function (42). Our previous study and research by others have shown that dance increased hippocampal volume and the cortical thickness of the right inferior temporal, fusiform, and lateral occipital regions (22,43). The functional connection (FC) of the DMN has been shown to be significantly increased after aerobic exercise (including dance, walking) in MCI participants (44-46). In addition, we found increased structural connections between the SMA and precuneus. SMA is primarily involved in production and control of movement (47). One study showed that the motor cortices increased involvement during the memory task after a 6-week dance exercise program in healthy older adults (48). Another study showed that 12-week training increased electrical activity of SMA in MCI and mild AD (49). The increased SC between SMA and the precuneus may suggest that aerobic dance can increase the association between exercise-related brain area and cognitively related brain area. In the present study, we demonstrated that the internal structural connection of default network were increased in aMCI after 3-month aerobic dance. This result is consistent with the direction of previous research results. In this context, our results may provide further evidence that aerobic dance may enhance structural connectivity in MCI patients.

In this study, we found that the increased SC between the hippocampus and para-hippocampus, hippocampus and fusiform gyrus, SMA and precuneus, and hippocampus and MTG was positively correlated with the improvement of TMT-A. Increased SC between the hippocampus and MTG was positively correlated with the improvement of MMSE, MoCA, WMS-RLM, and TMT-A. TMT-A mainly evaluates processing speed, and the higher the score, the slower the reaction speed (30). A systematic review had shown that dance may increase hippocampal volume, gray matter volume in the left precentral and para-hippocampal gyrus, and white matter integrity (50). Our results are consistent with those of previous studies. Although the present study may provide more evidence that aerobic dance can improve cognitive function underlying the increase of structural connectivity, the limited sample size might have a certain influence on the feasibility of our research findings. Given the current results indicating that aerobic dance may enhance the structural connectivity of the default network, we will expand the sample size in future studies to further validate the results.

Interestingly, we also found that the enhanced FASC of the brain after 3 months of aerobic dance was mostly located in the right hemisphere. One possible interpretation is that the right hemisphere plays an important role in tasks with higher comprehension demands compared with the left hemisphere (51). In addition, the right hemisphere is particularly involved in emotion regulation, attention, and arousal (52), whereas the left hemisphere is involved in processing of consistent information (53). As another study reviewed that the right hippocampus was more atrophic than its left counter-part in MCI compared with AD (54), the right hippocampus is related to immediate and delayed recall, visuospatial memory, fluency task performance, and spatial memory. In contrast, the left hippocampus plays a greater role in episodic verbal memory (55-59). The aerobic dance routine in our study included variable movements of upper and lower extremities, which evoke learning and memory processing of spatial information. MCI patients need to maintain a high level of concentration throughout the training process to avoid errors during the whole training. Therefore, after dance exercise, the global cognitive function, memory, and execution are significantly increased in MCI compared with the control group, and the SC between the right hippocampus and other right regions significantly increased after the 3-month aerobic dance training in MCI.

Limitations

The present study had several limitations. Firstly, the main limitation of this experiment is the relatively small sample size. This study set 28 participants in each group based on the Wechsler Logical Memory Scale. However, only 16 participants in each group were ultimately included in the analysis, which might influence the validity of the results. Our results should be further validated by larger cohorts together with multimodal data and other intervention strategies. Secondly, the effect of aerobic dance on physical function was not demonstrated in this study. We will explore the interaction of exercise with cognition and brain function in future studies. Thirdly, this study only adopted the blank control group and did not use the active control group for comparison. In future studies, we will compare the groups of simple aerobic exercise or simple cognitive training with the aerobic dance group. Finally, the study did not evaluate the long-term effects of the aerobic dance. Fiber integrity is a physical structure that is relatively stable, implying that cognitive improvement of dance training would last for a certain period of time, but follow-up studies are needed to confirm this. In addition, follow-up research would be designed to investigate how aerobic dance effect be maintained and reinforced and at what frequency.

Conclusions

A 3-month aerobic dance program significantly increases the structural connectivity within DMN and SMA, and efficiently improves cognitive function in elderly individuals with aMCI, especially memory and executive function. Revisions in the structural connections may serve as a measurable indicator for assessing the impact of aerobic dance on cognitive function.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The primary study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (No. 2012-SR-098). All the participants of this project signed the informed consent form.

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