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Effects of Different Cognitive Trainings on Amnestic Mild Cognitive Impairment in the Elderly: A One-Year Longitudinal Functional Magnetic Resonance Imaging (MRI) Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1 Wei Feng
BCD 2 Dan Wang
BCD 3 Long Tang
BCD 4 Yan Cheng
BCD 2 Guopu Wang
CD 5 Gengdan Hu
BCD 6 Xiaoliang Gong
BCD 7,8,9 Xinyi Cao
BCD 7,8,9 Lijuan Jiang
ABDEG 7,8,9 Chunbo Li

1 Department of Psychological Medicine, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China
2 Department of Physical Education, Tongji University, Shanghai, P.R. China
3 School of Human Cultures, University of Shiga Prefecture, Hikone, Shiga, Japan (present address: Osaka University, Suita, Osaka, Japan)
4 Department of Psychiatry, Tongji Hospital, Tongji University School of Medicine, Shanghai, P.R.China
5 Center for Psychical and Cognitive Science Research and Department of Psychology, Tongji University, Shanghai, P.R. China
6 Key Laboratory of Embedded System and Service Computing (Ministry of Education), Tongji University, Shanghai, P.R. China
7 Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China
8 Brain Science and Technology Research Center, Shanghai Jiao Tong University, Shanghai, P.R. China
9 Bio-X Institute, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders, Ministry of Education, Shanghai Jiao Tong University, Shanghai, P.R. China

Corresponding Authors: Wei Feng, e-mail: ffww06@163.com and Xiaoliang Gong, e-mail: gxllshsh@163.com

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Background: Cognitive training has been focused on the interventions of amnestic mild cognitive impairment (aMCI) in recent years, with poor understanding.

Material/Methods: The study participants with aMCI were screened in a previous intervention trial. Functional magnetic resonance imaging (fMRI) was adopted to investigate effects of single-domain cognitive training (SDCT) and multi-domain cognitive training (MDCT) on aMCI and to explore potential mechanisms.

Results: There were significant differences in the grey matter volume of the middle frontal gyrus, superior parietal lobule, inferior temporal gyrus, fusiform gyrus, and ventral V3 between the MDCT/SDCT group and the control group ($P<0.05$). Regional homogeneity (ReHo) increased significantly in the right and left inferior frontal gyrus as well as in the left and right precentral gyrus after intervention in the MDCT group and the SDCT group. ReHo increased significantly in the right and left lingual gyrus of the MDCT group and the control group. ReHo reduced significantly in the right middle temporal gyrus of the MDCT group but increased significantly in the left middle temporal gyrus in the SDCT group and the control group. The voxel of grey matter in the precuneus was positively related to the language scores on RBANS (Repeatable Battery for the Assessment of Neuropsychological Status), and amygdala, fusiform gyrus, and hippocampus also had a positive relationship with delayed memory scores in RBANS of the MDCT group. In the MDCT group, the attention and reasoning scores were also positively related to the ReHo of middle temporal gyrus.

Conclusions: Both MDCT and SDCT may improve the aMCI at brain functional and structural levels; however, the MDCT group exhibited higher ReHo values in middle temporal gyrus and superior occipital gyrus. Also, it was confirmed that MDCT leads to better results than SDCT, showing a significant correlation of cognitive functions such as attention, memory, reasoning, and visual-spatial ability.

MeSH Keywords: Cognitive Therapy • Magnetic Resonance Imaging • Mild Cognitive Impairment

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Background

Mild cognitive impairment (MCI) is an intermediate state between normal aging and dementia [1,2]. Of note, patients with amnestic MCI (aMCI), which is characterized by memory impairment, are more likely to develop to Alzheimer disease (AD) [3]. Studies have revealed that auditory language, attention, working memory, and spatial memory are impaired to different extents in aMCI patients, but findings about executive function are still controversial in these patients. Zhang et al. [4] found the inhibition capability was preserved, but the planning capacity was significantly damaged. There is evidence showing that patients with aMCI had extensive damage to the executive function, and working memory, and response inhibition and task switching (3 main components of executive function) were damaged [5]. However, symptoms of executive dysfunction are usually not as prominent as those of memory impairment in complaints of these patients, while it is a major factor affecting the daily activity in aMCI patients. Thus, it is imperative to prevent the progression of aMCI into AD and improve the quality of life in the elderly of our aging population.

Currently, the efficacy of pharmacotherapy for aMCI is not satisfactory. With respect to pathogenic factors, cognitive reserve or activation may become a strategy in the prevention of occurrence and development of aMCI. In recent years, cognitive training has been one of the important methods in preventing and delay cognition dysfunction and AD [6–8]. Greenaway et al. found cognitive training could effectively improve the activities of daily living as well as the memory self-efficacy in MCI patients [9]. In a randomized, controlled trial focusing on the single-domain cognitive training (SDCT), elderly participants who were living independently in good functional and cognitive status received memory training, reasoning training, or speed-of-processing training [10]. After 12 months of training, the cognition function in the 3 groups was significantly improved, as demonstrated during the follow-up period. However, SDCT neglects the complicated interactions between multiple mental processes required to create and preserve a viable and healthy mental state capable of the flexible thinking necessary to interact appropriately with one's world [11].

Most previous single-domain cognitive training (SDCT) methods were specified in some part of the cognitive ability testing, such as simple memory or reasoning, which would only improve the corresponding cognitive category. Thus, in recent years, some studies focused on the multi-domain cognitive training (MDCT). For example, reasoning, memory, speed of processing, and executive function trainings are integrated to improve different domains of cognitions. Studies have revealed that MDCT not only improves a single cognitive domain, but also affects multiple cognitive domains, or even leads to the generalization of the improvement as compared to SDCT [12]. In this study, MDCT and SDCT (reasoning training) were employed with aMCI patients, and efficacy of both methods was compared.

In recent years, functional magnetic resonance imaging (fMRI) has revealed that activation increased in the regions (frontal lobe, parietal lobe, and bilateral hippocampus) related to memory in healthy and aMCI individuals after cognitive training [13,14]. A recent resting state fMRI study indicated that cognitive training may induce plastic changes in neural functional connectivity of healthy older people, and these changes may underlie the positive effect of cognitive training [15]. In the resting state of fMRI studies, regional homogeneity (ReHo) is often employed to reflect the functional activation of the brain. ReHo is used to describe that the BOLD (blood-oxygen-level dependent) signal change of a given voxel over time is similar to that of its nearest neighbors in a specific functional region of the brain. To weigh the similarity of time series of different voxels in a specific functional region of the brain, ReHo method is used to determine the Kendairs coefficient of concordance of 3 or more voxels which is then endowed with the selected voxel. These procedures are repeated to achieve the ReHo of each region in the brain [16,17]. In the present study, ReHo was employed to evaluate the functional status of each region of the brain, and the effects of different cognitive trainings on the volume and function of grey matter were investigated in aMCI patients.

We hypothesized that both MDCT and SDCT may alter the function or structure of the aMCI brain as compared to a control group but features in the improvement would be different after MDCT and SDCT.

Material and Methods

Ethics

This study was approved by the Ethics Committee of Shanghai Tongji Hospital, and written informed consent was obtained before study (LL[H]-09-04).

Participants

Elderly individuals from 3 communities of Shanghai were recruited and divided into 3 groups: the MDCT group, the SDCT group, and the control (CON) group; and participants were screened for aMCI [18]. Patients with aMCI further received MRI examination.

The inclusion criteria were as follows: 1) patients aged 65–75 years; 2) patients received education for ≥1 year; 3) patients complained of memory impairment of at least 3 months or

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Table 1. Characteristics of participants in this study.

Characteristics	MDCT	SDCT	CON	F/χ^2 value	P
Female/male	4/4	4/4	5/4	0.071	0.965
Age (years)	69.63±3.54	72.13±3.56	68.13±2.80	1.92	0.17
Education (years)	10.75±3.54	10.35±4.33	11.00±2.78	1.83	0.63
RBANS	85.75±8.45	79.88±9.01	86.56±11.79	1.10	0.35
CWST-word	36.38±6.57	35.00±8.90	40.44±13.34	0.67	0.52
Reasoning	5.00±1.07	4.13±2.10	4.67±2.50	0.39	0.68

RBANS – the Repeatable Battery for the Assessment of Neuropsychological Status; CWST-word – word-interference time of the Color Word Stroop Test; Reasoning – the visual reasoning test of the World Health Organization Neuropsychological Battery of Cognitive Assessment Instruments for the elderly (WHO-BCAI).

the insiders speculated that the memory impairment last for more than 3 months; 4) the score of memory in the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was ≤ mean −1.0 standard deviation (the mean is calculated according to the norm on the basis of age and education level); 5) the score of Clinical Dementia Rating Scale (CDRS) was 0.5, while there was no evident cognition impairment (score of Mini Mental State Examination [Chinese edition] ≥17 [19]); 6) patients had no severe impairment to vision and hearing; no physical disability, no severe physical diseases, and no severe mental disorders, and were living independently.

A total of 25 patients with aMCI were recruited into the present study. The demographics of these patients are shown in Table 1. All these patients received resting state MRI (MDCT: SDCT: CON=8: 8: 9); brain structural analysis was performed in 23 patients due to concern on data matching (MDCT: SDCT: CON=7: 8: 8).

Study design

This was a single blind, prospective study aiming to investigate the effects of different cognitive training methods on the structure and function of the brain in aMCI. The cognitive function was evaluated, and MRI examination was conducted before the study intervention and 1 year after the intervention.

Cognitive training

The cognitive training used into the present study included 4 components: repeated exercises, training focusing on the problem-solving ability, standardized training, and training targeting one or more cognitive domains.

MDCT focuses on the memory, reasoning, problem-solving ability, and visual-spatial reading skills. In these dimensions, the validity of each dimension has been confirmed by previous studies [19,20]. Moreover, studies have also confirmed the effectiveness of interventions with each dimension. SDCT focuses on reasoning, including picture arrangement, digital reasoning, and the Raven reasoning test [15,19,21,22].

Cognitive training was performed in a face-to-face manner for 1 hour twice weekly for a total of 12 weeks. The in-home practice was administered once weekly, and the completion of homework was checked in a timely manner. In the control group, cognitive training was not administered.

Methods for evaluation

In the present study, the comprehensive cognitive assessment tool and the Elderly Community Health Assessment Questionnaire of Shanghai were employed to evaluate the cognitive function and health status. Evaluations were performed in a blinded manner to assure the accuracy of results. All the evaluators received consistency test with Kappa value of >0.8 and intergroup correlation coefficient was >0.75.

The RBANS [23], the Color Word Stroop test (CWST) [24], the visual reasoning test [25] and trail making test [26] of the World Health Organization Neuropsychological Battery of Cognitive Assessment Instruments for the elderly were employed for the evaluation.

Data acquisition of MRI

MRI was performed with Siemens Magnetom Trio 3.0T in the Shanghai East China Normal University. Patients were in a supine position and wore noise-canceling headphones, and their head was fixed with a sponge mat. The patients were asked to keep calm and minimize the movement of the head. Resting state MRI was performed with Echo Planner Imaging (EPI) sequence; scanning was done at the plane parallel to the posterior-anterior line with the following parameters:

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Table 2. Grey matter volume of the brain after interventions in different groups.

Region	Hemisphere	F Value	P	Cluster size	Coordinates (mm)		
					X	Y	Z
Middle frontal gyrus	R	37.43	0.001	123	40.5	43.5	15.0
Superior parietal lobule	R	26.17	0.011	25	21.0	–49.5	66.0
Inferior temporal gyrus	R	25.42	0.003	59	48.0	–43.5	–28.5
Fusiform gyrus	R	25.35	0.002	74	34.5	–7.5	–36.0
Ventral V3	L	24.36	0.000	178	–25.5	–99.0	–18.0

P<0.05 (FWE-corrected). Cluster size at least 18 voxels.

time of repetition=2000 ms; time of echo=25 ms; flip angle=90°; FOV=240 mm; matrix=64×64; slice thickness=5 mm; slice number=32.

T1 weighed scanning was performed with spin echo sequence at the sagittal plane with the following parameters: time of repetition=1900 ms; time of echo=3.43 ms; flip angle=90°; FOV=256 mm; matrix=256×256; slice thickness=1 mm; slice number=160.

Data processing

Data processing of brain structure

SPM12 (*http://www.fil.ion.ucl.ac.uk/spm/*) software was used for data processing, and DARTEL for the Voxel based morphometry (VBM) analysis of brain structure as follows: 1) T1 weighed images were standardized into a 3-dimensional space; 2) the standardized brain images were divided into grey matter part, white matter part, and cerebral spinal fluid part; 3) DARTEL was used for space standardization of 3 parts; (4) data smoothening was done for 6-mm 3-dimensional Gaussian kernel with full width half maximum (FWMH).

Data processing of resting state fMRI

Convert software was used to transform the data of DICOM format into those of NIFTI format, followed by pre-treatment as follows: the first 4 images were removed considering the adaptation of participants, followed by adjustment for head movement, space standardization, removal of linear drift and wave filtering in which the data were sampled into 3×3×3 mm^3 area. Rest software (REST Version: 1.8) [27] was used to calculate ReHo which was then smoothened. The 4-mm FWHM Gaussian kernel was used to space smoothening, aiming to reduce spatial noise and anatomical difference between individuals. After smoothening, data in different groups were tested with analysis of variance and paired *t*-test. In addition, correlation of these parameters with the behaviors was also evaluated.

Results

Characteristics of participants

As shown in Table 1, there were no significant differences in the age, gender, education level, and scores of 3 scales among the 3 groups.

Data analysis of brain structure

Age and gender served as covariates and 2-way-ANOVA was employed for statistical analysis. Results showed significant differences among 3 groups in the middle frontal gyrus, superior parietal lobule, inferior temporal gyrus, fusiform gyrus, and ventral V3 (Table 2, Figure 1A), which were more obvious in the right hemisphere.

Comparisons between 2 groups showed the grey matter volume of the middle frontal gyrus, superior parietal lobule, and inferior temporal gyrus in the MDCT group was significantly higher than in the SDCT group (*P*<0.05; Figure 1, B1–B3 respectively). This suggests that the effect on the MDCT and the SDCT group was different in grey matter volume, especially in the right cerebellum (Table 3).

Resting state fMRI

Intergroup comparison of ReHo before and after intervention

The ReHo value was compared before and after the intervention among the groups. Results showed significantly differences in the ReHo of cerebellum (peak voxel of MNI: x=–36, y=–42, z=–30, F score11.3417, corrected *P*=0.05), right fusiform (peak voxel of MNI: x=36, y=–36, z=18, F score=14.0737, corrected *P*=0.05), left pars triangularis inferior frontal gyrus (peak voxel of MNI: x=–51, y=–30, z=3, F score=7.5399, corrected *P*=0.05), left postcentral gyrus (peak voxel of MNI: x=–18, y=–33, z=75, F score=6.9578, corrected *P*=0.05) among the 3 groups. Paired comparison showed the ReHo of putamen,

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calcarine and inferior temporal gyrus in the MDCT group was significantly higher than in the SDCT group, while that of superior parietal lobule and postcentral gyrus was markedly lower than in the SDCT group. This suggests that MDCT and SDCT may differentially affect the brain function of several regions.

Intragroup comparison of ReHo before and after intervention

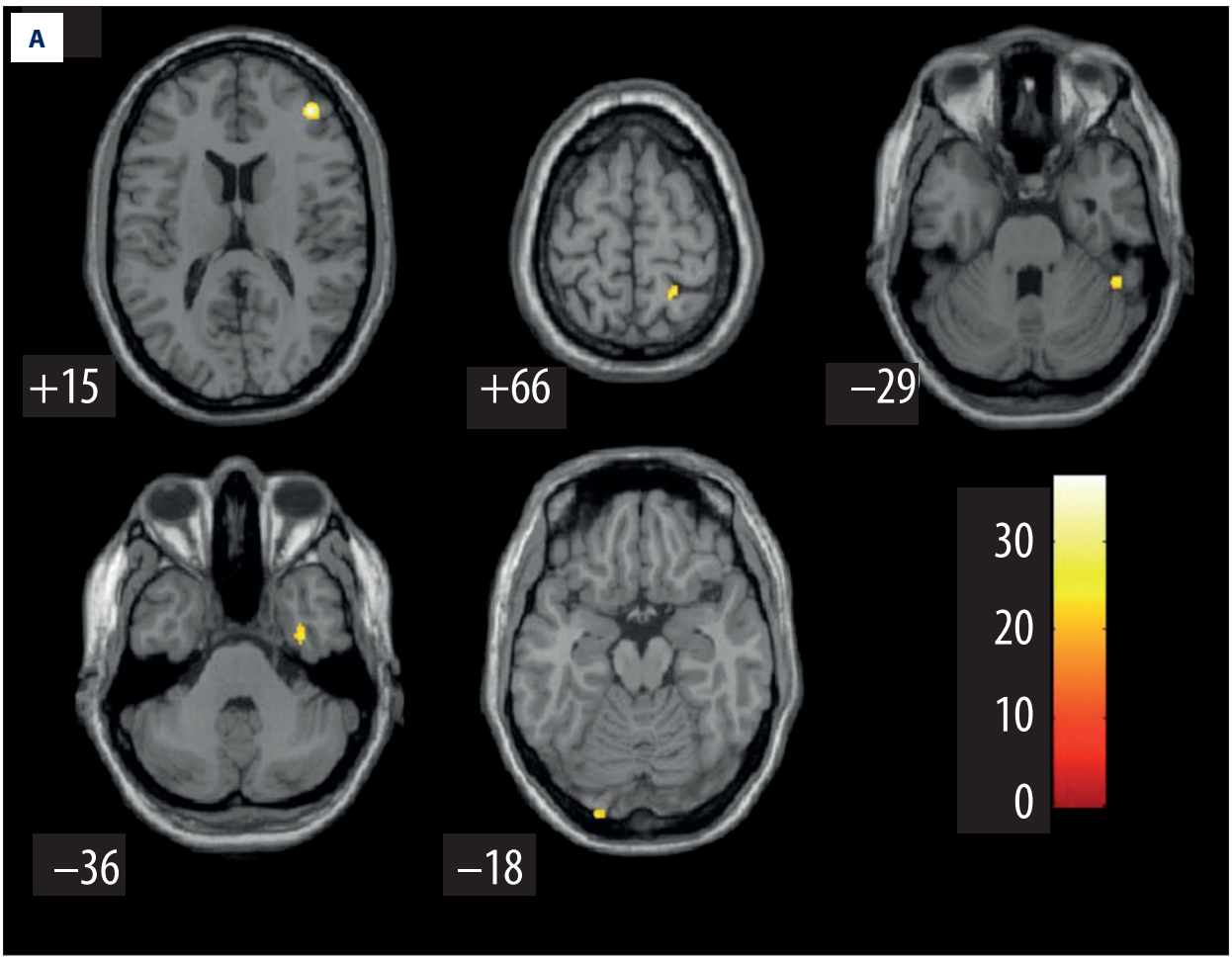
As shown in Table 4, the ReHo of the precentral gyrus, superior temporal gyrus, inferior frontal gyrus, and lingual gyrus increased significantly in the MDCT group, while ReHo of the superior temporal gyrus and lingual gyrus increased in the control group. The ReHo of superior frontal gyrus remained unchanged in the MDCT group but reduced in the control group. The ReHo of the middle temporal gyrus and superior occipital gyrus reduced significantly in the MDCT group but increased in the control group.

As shown in Table 5, the ReHo of the inferior frontal gyrus and precentral gyrus increased significantly in the SDCT group but remained unchanged in the control group. The ReHo of the lingual gyrus remained stable in the SDCT group but increased dramatically in the control group. The ReHo of middle temporal gyrus, superior temporal gyrus, superior occipital gyrus, and superior frontal gyrus showed similar trend in both the SDCT group and the control group, but it was more obvious in the control group. These findings suggest that SDCT and MDCT have differential effects on the brain function, which are more evident after MDCT.

Correlation between MRI findings and behaviors

Correlation between grey matter volume and behaviors

The correlation between grey matter volume and the behavioral score was evaluated in the MDCT group. Results showed the voxel of the precuneus was positively related to language section in RBANS, but that of the amygdala, fusiform gyrus, and hippocampus had a positive relationship with delayed memory section in RBANS in the MDCT group (Table 6). However, there was no significant correlation between grey matter volume and behavioral score in the SDCT group.



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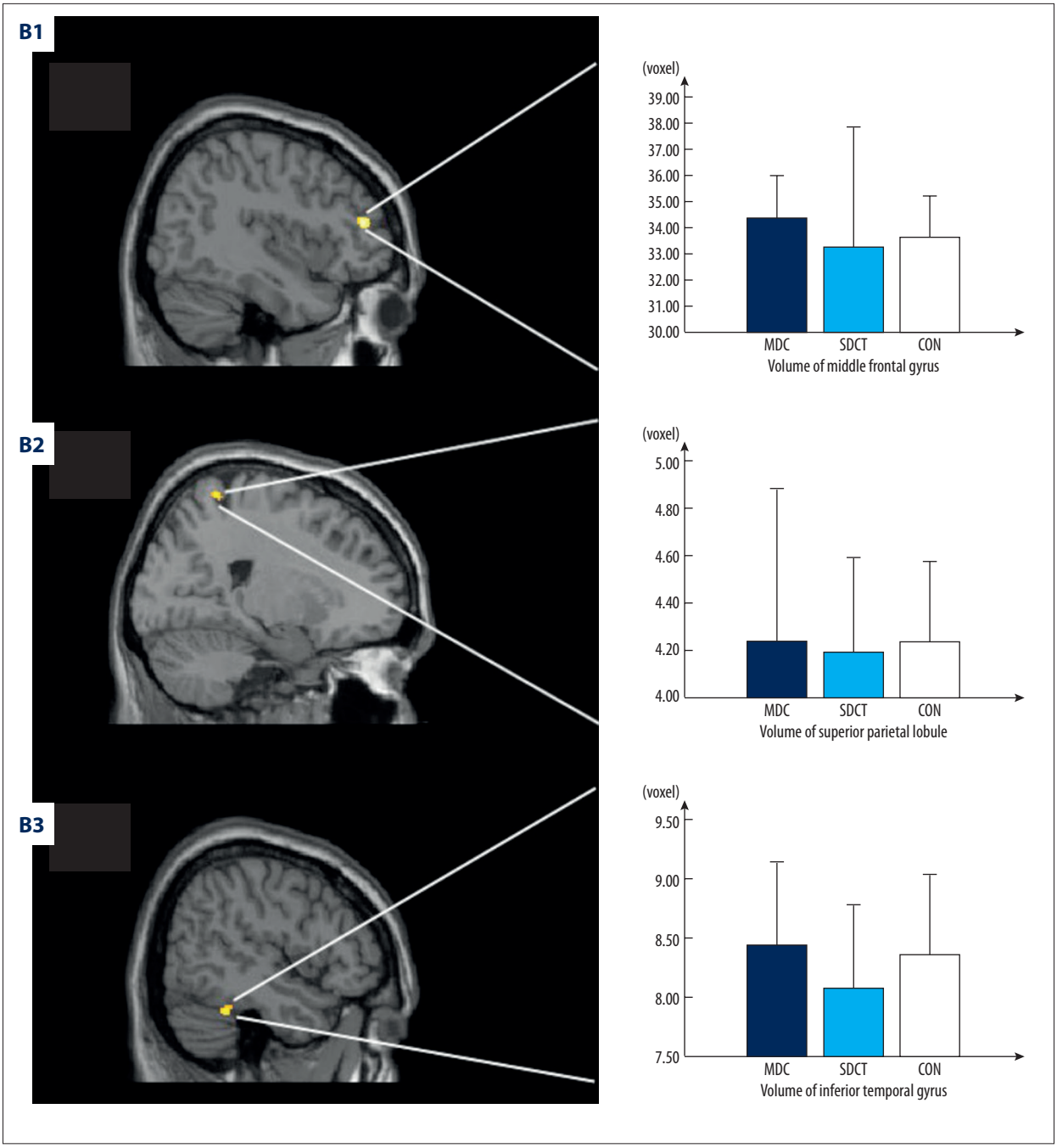

Figure 1. Brain morphology differences based on volume pixel in the MDCT group and the SDCT group. MDCT – multi-domain cognitive training; SDCT – single-domain cognitive training.

Correlation between ReHo and behavioral score

The correlation between ReHo and behavioral score was further evaluated in the brain regions with significant difference in ReHo of MDCT. Results showed the attention score of RBANS and reasoning score had positive relationship with the ReHo of middle temporal gyrus; word interfere score of the CWST was positively related to the ReHo of the precentral gyrus; visuospatial score of RBANS was negatively associated with the ReHo of the lingual gyrus. These findings suggest that the ReHo of some brain regions was related to the behavioral scores (such as reasoning and attention) in aMCI patients after MDCT (Figure 2).

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Table 3. ReHo in MDCT group and SDCT group before and after intervention.

Region	Hemisphere	Cluster size	Coordinates (mm)			t Value
			X	Y	Z	
Putamen	R	154	30	–6	–3	3.96
Calcarine	R	232	27	–60	12	4.44
Postcentral gyrus	R	111	57	–21	18	–3.77
Superior parietal lobule	R	125	24	–51	57	–3.69
Inferior temporal gyrus	L	119	–48	–21	–18	4.41
Superior parietal lobule	L	235	–33	–48	60	–4.22

P<0.05 (Alphasim corrected). Cluster size at least 85 voxels.

Table 4. ReHo in MDCT group and control group before and after intervention.

Brain Regions	Hemisphere	Group	Cluster size	Coordinates			t Value
				X	Y	Z	
Precentral gyrus	L	MDCT	162	–9	–30	69	–7.74
		CON	–	–	–	–	–
Superior frontal gyrus	L	MDCT	–	–	–	–	–
		CON	7091	–18	24	51	10.53
Inferior frontal gyrus	R	MDCT	993	51	27	0	–8.26
		CON	–		–	–	–
Lingual gyrus	R	MDCT	149	3	–78	–3	–9.05
	L	CON	123	–21	–57	–9	–4.21
Superior temporal gyrus	R	MDCT	115	33	15	–27	–4.71
	R	CON	2322	60	3	–6	–11.21
Middle temporal gyrus	L	MDCT	1159	–45	–48	9	13.76
	R	CON	262	51	–63	3	–10.93
Superior occipital gyrus	R	MDCT	380	27	–69	21	9.97
	R	CON	899	15	–54	6	–6.28

x, y, z – coordinates of primary peak locations in the space of MNI; t – statistical value of peak voxel showing ReHo before and after intervention (positive t value means decreased ReHo). *P*<0.05 (Alphasim corrected). Cluster size at least 85 voxels.

Discussion

In this study, the grey matter volume and resting state of specific brain regions were investigated. After the intervention, the grey matter volume was significantly different in the right middle frontal gyrus, right inferior temporal gyrus, and temporal fusiform gyrus among the 3 groups, and the grey matter volume in the MDCT group was significantly higher than in the SDCT group and the control group. In addition, from the discussion of the resting state results and the correlation with behavioral data described, it can be assumed that the MDCT group and the SDCT group leads to better results than in the control group before and after the intervention. This indicates that SDCT and MDCT may affect aMCI at both structural and functional levels of the brain. This study, for the first time, elucidates the beneficial effects of SDCT and MDCT on aMCI from the structural and functional levels of the brain and identifies the difference in the effectiveness on aMCI between SDCT and MDCT, which provides reference for the prevention and therapy of aMCI.

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Table 5. ReHo in SDCT group and control group before and after intervention.

Brain Regions	Hemisphere	Group	Cluster size	Coordinates			t Value
				X	Y	Z	
Inferior frontal gyrus	L	SDCT	87	–54	39	–3	–4.07
		CON	–	–	–	–	–
Precentral gyrus	R	SDCT	114	54	12	42	–5.39
		CON	–	–	–	–	–
Lingual gyrus		SDCT	–	–	–	–	–
	L	CON	123	–21	–57	–9	–4.21
Middle temporal gyrus	R	SDCT	139	54	–72	15	–4.08
	R	CON	262	51	–63	3	–10.93
Superior temporal gyrus	R	SDCT	997	63	6	0	–11.03
	R	CON	2322	60	3	–6	–11.21
Superior occipital gyrus	R	SDCT	89	21	–72	48	–4.86
	R		993	18	–81	18	–6.07
	R	CON	899	15	–54	6	–6.28
Superior frontal gyrus	L	SDCT	4435	–21	–3	72	8.32
	L	CON	7091	–18	24	51	10.53

P<0.05 (Alphasim corrected). Cluster size at least 85 voxels.

Table 6. Correlation between grey matter volume and behavioral score after intervention in MDCT group.

Behavior score	Region	Hemisphere	t Value	*P*	Cluster size	Coordinates (mm)		
						X	Y	Z
Delayed Memory	Amygdala	R	23.98	3.45×10^{-7}	948	24.0	–4.5	–25.5
		R	22.72	4.76×10^{-7}		28.5	–7.5	–19.5
		R	13.44	1.05×10^{-5}		30.0	–9.0	30.0
	Fusiform gyrus	L	9.55	7.53×10^{-5}	907	–36.0	–4.5	–39.0
		L	8.38	1.57×10^{-4}		–31.5	–4.5	–30.0
	Hippocampus	L	8.27	1.69×10^{-4}		–25.5	–9.0	–22.5
Language	Precuneus	L	14.70	6.23×10^{-6}	169	0.0	–66.0	27.0

Delayed Memory: *P*<0.001, FWE-corrected. Cluster size at least 23 voxels. Language: FWE-corrected. Cluster size at least 27 voxels.

There were similarities between the findings of our study and previous studies. 1) the change of grey matter volume of the right middle frontal gyrus, right inferior temporal gyrus, and temporal fusiform gyrus was significantly different among the 3 groups (Table 2). The grey matter volume of these regions in the MDCT group was significantly higher than in the SDCT group and the control group. Available findings suggest that memory training is able to increase the cortical thickness of some brain regions, especially those related to cognitive impairment and AD, such as temporal lobe, supramarginal gyrus, and entorhinal gyrus, as well as cortex of the frontal and prefrontal lobes [28–30], which also explains the elevated grey matter volume of the inferior temporal gyrus and temporal fusiform gyrus after intervention in the MDCT group. 3) Brain resting state analysis showed ReHo of the inferior frontal gyrus and precentral gyrus increased significantly in both the SDCT group and the MDCT group after intervention, but it remained unchanged in the control group. When compared with healthy individuals,

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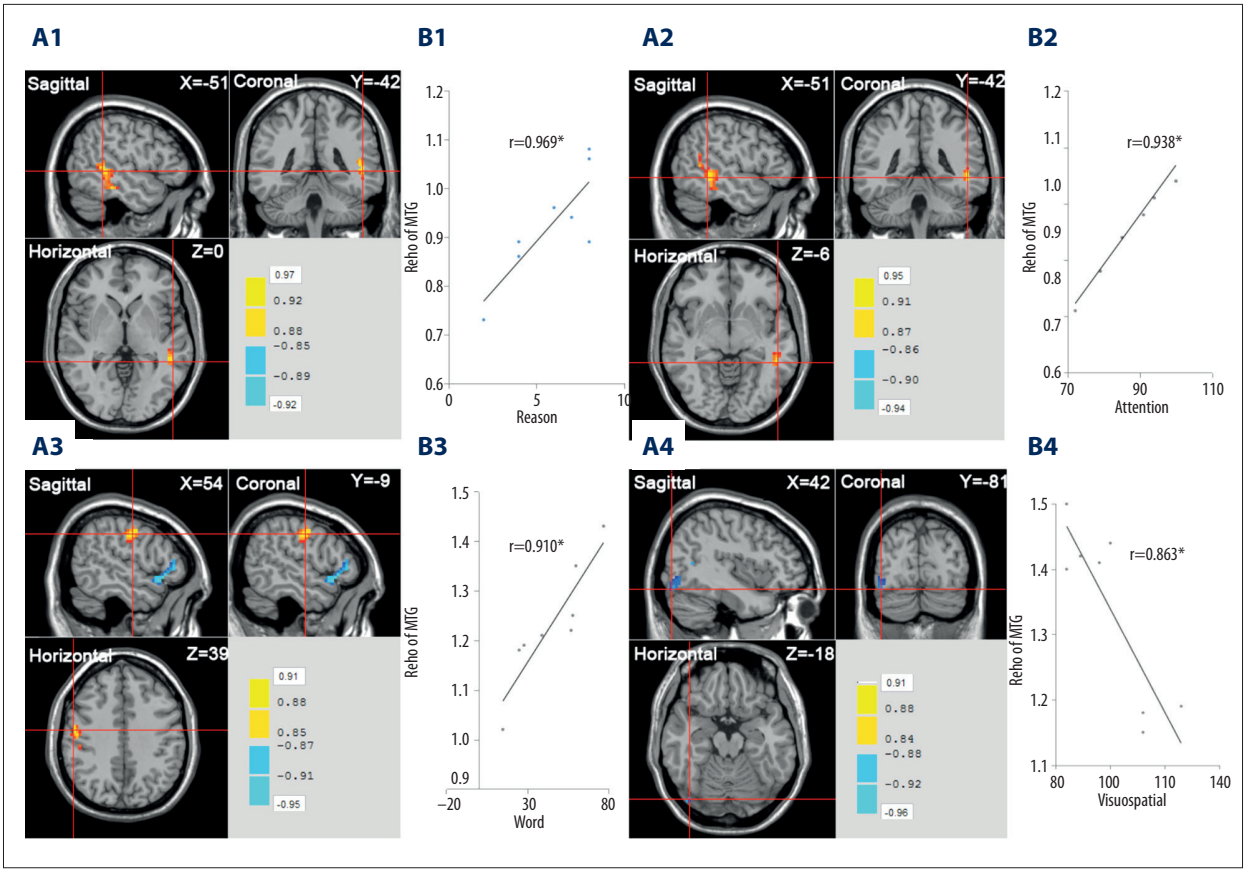

Figure 2. Correlation between behavioral score and ReHo of different brain regions in the MDCT group. * r: *P*<0.05. (**A1**) Correlation between reasoning score and ReHo of middle temporal gyrus (r=0.969); (**A2**) correlation between attention score of RBANS and ReHo of middle temporal gyrus (r=0.938); (**A3**) correlation between word interfere score of the CWST and ReHo of precentral gyrus (r=0.910); (**A4**) correlation between visuospatial of RBANS score and ReHo of lingual gyrus (r=–0.863). MDCT – multi-domain cognitive training; SDCT – single-domain cognitive training; ReHo – regional homogeneity; RBANS – Repeatable Battery for the Assessment of Neuropsychological Status; CWST – Color Word Stroop Test.

ReHo was reduced significantly in the inferior frontal gyrus and precentral gyrus of aMCI. This indicates that both MDCT and SDCT may improve aMCI to a certain extent. For the middle temporal gyrus and superior occipital gyrus, 2 regions with significant difference in ReHo, the ReHo in the SDCT group and the control group consistently was increased, but that in the MDCT group it was reduced. This suggests that intervention may reduce ReHo, which was also observed in the studies of Machulda et al. and Yetkin et al. several brain regions (such as middle temporal gyrus and fusiform gyrus) were activated in executing an assignment in aMCI patients and thus they speculated that aMCI was characterized by memory impairment in early stages when the executive function is relatively intact and there might be compensatory mechanism [31–35].

In the present study, the correlation between fMRI findings and behaviors was further evaluated. Results showed the language score and delayed memory section of RBANS had positively relationships with the grey matter volume of the precuneus and hippocampus in the MDCT group; the attention score of RBANS and reasoning score were positively related to the ReHo of the middle temporal gyrus; after intervention, the ReHo reduced significantly at this region in the MDCT group. Thus, we speculate that the attention and reasoning were significantly improved after intervention, which was consistent with the improvement of corresponding scores. The CWST-word score was positively related to the ReHo of the precentral gyrus. This suggests that both MDCT and SDCT can improve the executive function in aMCI patients. Visuospatial score of RBANS was negatively associated with the ReHo of the lingual gyrus, but ReHo of this region increased significantly in the MDCT group and remained unchanged in the SDCT group. The ReHo values in lingual gyrus increased, based on the brain-behavior relationships between MRI and behavior data, and revealed a significant negative correlation with the visuospatial score and ReHo value in lingual gyrus. We hypothesized that the visuospatial score of the MDCT group would decrease. Excellent agreements were found with our results, i.e., the visuospatial score

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of the aMCI participants in the MDCT group was decreased, and visual-spatial ability was improved. We speculated that MDCT may confer more beneficial effects on the visuospatial capability of aMCI patients compared to SDCT.

One of major findings in this study was that changes in both grey matter volume and ReHo after intervention in the MDCT group and SDCT group were mainly found in the right hemisphere. That is, grey matter atrophy and brain function deterioration were different between left and right hemispheres at the speed and extent with the conduction of cognitive training, and the degeneration of the right hemisphere was generally slower than that of left hemisphere. Cabeza et al. and Allali et al. [36,37] found that brain activity was reduced in MCI patients, which could result in asymmetrical reduction in 2 hemispheres. The lateral development of 2 hemispheres indicated that the more advanced the hemisphere, the more evident the lateral development was. Thus, there was lateral processing in the cognitive function, a component of advanced function of the brain. Based on our study findings, the change of ReHo value after intervention was compared between the MDCT and the SDCT group. Significant differences were observed in right brain, indicating that the change in the right brain activity after intervention was more significant in the MDCT group than in the SDCT group. Thus, MDCT could attenuate the cognition degradation of right brain, keeping the asymmetry between the left and right brain. MDCT and SDCT may attenuate the degradation of the brain to a certain extent, but MDCT is more likely to preserve the laterality of the brain (Table 3). In addition, the laterality of the brain function is considered a marker of specialization of cognitive function in humans. In the elderly, studies on the influence of network laterality of the brain on cognitive training have indicated that the network laterality, including advanced cognition, is sensitive to MDCT [38]. Taken together, cognitive training, especially MDCT, has its own advantages in preventing cognitive impairment of the elderly.

There were several limitations to this study: 1) there might be systemic error (difference in the quality of brain images) in the fMRI examination before and after intervention; 2) the follow-up was conducted for 1 year, causing some patients to be lost to follow-up, and thus the small sample size was an important limitation of this study. In our future studies, more participants will be recruited to confirm our findings. As compared to previous studies, we compared the effects of MDCT and SDCT on aMCI, and fMRI was employed to evaluate them at the structural and functional levels. Thus, our findings or conclusions may be theoretically important for the clinical prevention and treatment of cognitive impairment.

Conclusions

Both MDCT and SDCT may improve the aMCI at the brain functional and structural levels, and MDCT is more likely to block the reduction of laterality. In the MDCT group, results suggest not only that memory impairment is attenuated by MDCT, but also the compensatory activation of several brain regions (such as middle temporal gyrus and fusiform gyrus) may conceal the deterioration of executive dysfunction in aMCI patients.

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