



Multi-component exercise training improves the physical and cognitive function of the elderly with mild cognitive impairment: a six-month randomized controlled trial

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Background: This study explored the effects of multi-component exercise training on the physical and cognitive function of the elderly with mild cognitive impairment (MCI).

Methods: A total of 90 older adults with MCI were chosen from screened volunteers and randomly assigned into 2 groups (n=45), and 84 completed the 6-month follow-up. Participants in the control group received general community health instruction, while the multi-component exercise training performed on the other group. The multi-component exercise training performed on these participants was designed to suit Chinese elderly based on advice from the nursing specialist and sports medicine specialist after the preliminary experiment. The Chinese version Mini-Physical Performance Test (CM-PPT), the Mini-Mental State Examination (MMSE), and the Montreal Cognitive Assessment (MoCA) scores were examined by repeated measures analysis of variance to evaluate the physical and cognitive function of adults with MCI before and at 3 and 6 months after the intervention. The follow-up data collectors were blinded to group allocation. $P < 0.05$ was considered statistically significant.

Results: (I) The average score of CM-PPT was increased from 11.36 ± 2.69 to 11.88 ± 2.40 and 12.83 ± 2.19 in 3 and 6 months respectively after intervention, while control group was decreased from 10.79 ± 2.73 to 10.24 ± 2.62 in 3 months and 9.21 ± 2.09 in 6 months. CM-PPT scores with the main intervention effect and the interaction between intervention and time were both statistically significant ($P < 0.05$), indicating that the physical function of participants with MCI were improved after intervention. (II) The average score of MoCA was increased from 21.52 ± 2.05 to 23.48 ± 1.47 (3 months) and 25.19 ± 1.29 (6 months) after intervention, while control group was decreased from $21.14.79 \pm 1.97$ to 20.21 ± 1.88 and 19.45 ± 2.00 in 3 and 6 months. The score of MMSE showed the same trend with the score of MoCA. The MoCA score with main intervention effect and the MMSE and MoCA scores with the effect of time, the MMSE and MoCA scores with the interaction between the intervention and time were all statistically significant ($P < 0.05$), showing that the cognitive function of participants with MCI was improved by the intervention.

Conclusions: Multi-component exercise training could significantly improve physical function and cognitive function of the elderly with MCI.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2100049350.

Keywords: Exercise training; physical function; cognitive function; mild cognitive impairment (MCI); older adults

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Introduction

Dementia is a progressive neurocognitive disorder characterized by cognitive and functional decline until death, and Alzheimer's disease is the most common cause of dementia (1). The number of people suffering from dementia is anticipated to increase to 115 million by 2050 (2). Due to its increasing global prevalence, dementia has become a major public health concern worldwide, and has significantly increased health care costs and social burden (3,4). Mild cognitive impairment (MCI) often precedes dementia and is considered a transitional stage of normal aging and early dementia. A study reported that older adults with MCI develop Alzheimer's disease at a rate of 10% to 30% every year, while adults without MCI develop Alzheimer's disease at a rate of 1% to 2% annually (5). In older adults with cognitive impairment, cognitive decline may be related to a low level of education, poor health, small social network, unwholesome lifestyle, and insufficient exercise (6).

Although anticholinesterase therapies have been commonly used to treat the symptoms of MCI and dementia (7), they cannot delay disease progression and preserve the physical function of people with MCI. Furthermore, the side effects of anticholinesterase therapies that potentially lead to death, such as nausea, vomiting, diarrhea, abdominal cramping, and less commonly, hepatotoxicity, have created a need for non-drug treatments (8). Non-drug interventions which are effective and noninvasive, including universal access to prevention knowledge, increasing awareness of the risk of dementia, massage, cognitive training, and relaxation training, have been reported to improve the cognitive function of aged people with MCI (9,10). As cognitive dysfunction and physical problems are common and correlate in terms of the symptoms of dementia, physical function decline is related to a higher rate of cognitive decline in people with dementia. The decline of physical function which is manifested as muscle strength decline, balance loss, mobility decline and gait impairment can lead to the occurrence of falls, body function disuse, being bedridden long term, and even death (11), and can produce many issues which increase the risk of caregiver burden (12,13). Hence, to prevent worsening of the cognitive and physical dysfunction of people with MCI, effective intervention in the early stage before dementia should be urgently implemented.

Since physical dysfunction is related to a higher rate of cognitive decline, it is important to detect the effects

of non-drug interventions on physical and cognitive improvement. To explore the new approach alone or in combination with the other therapy to improve cognitive function can make more benefit for the elderly with MCI. Systematic reviews have pointed out that general exercise training can give rise to small to moderate improvements in cognitive function. So, aerobic exercise, strength training, balance training, coordination training, and sensitivity training might be one approach to improve the cognitive function of the elderly with MCI.

New evidence has shown that multi-component exercise training (14), which is based on a broad definition of fitness that includes motor (balance, co-ordination, agility, proprioception, flexibility, and reaction time) and physical (cardiovascular and resistance) components, can improve cognitive performance in later life. Recent research developments suggest that a multi-modal exercise intervention that includes motor as well as physical training, and that requires sustained attention and concentration, may better elicit the actual potency of exercise to enhance cognitive performance. Although the exercise-induced benefits on cognitive function in elderly with cognitive dysfunction are increasingly, the multi-component exercise training which against muscle strength decline, balance loss, mobility decline and gait impairment have not been studied in Chinese adults.

Therefore, our research aimed to explore the effects of multi-component exercise training on the physical function and cognitive function of older adults with MCI. This intervention may prevent older adults with MCI from progressing to dementia, and may provide a new strategy to decrease the health care costs and societal burden of caring for aged people.

Aims

The purpose of this study was to explore the effects of multi-component exercise training on the physical function and cognitive function of elderly participants with MCI.

We present the following article in accordance with the CONSORT reporting checklist (available at <https://dx.doi.org/10.21037/apm-21-1809>).

Methods

Design and participants

This experiment was a randomized, controlled, quantitative,

two-parallel study. The research was approved by the Ethics Committee of Central South University. Research complied with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration (as revised in 2013). Informed consent was obtained from all participants included in the research. A total of 90 older people with MCI were chosen in Wang Yuehu community in Changsha, China. The inclusion criteria were as follows: 60 years old or over with no hearing or visual dysfunction; based on educational levels of illiteracy, primary school, and middle school and above, the scores on the Montreal Cognitive Assessment (MoCA) were 17–23, 20–24, and 20–25, respectively. The diagnostic criteria of MCI proposed by Petersen *et al.* (15): (I) the subjective report of memory decline; (II) impaired memory function (or other cognitive function) on objective tests that is not consistent with age and education level; (III) general cognitive function is relatively intact; (IV) functions of daily life were not affected; (V) no dementia. The exclusion criteria were as follows: Older adults who have serious physical disease, severe weakness, long-term bed are excluded; Those who had trouble completing the multi-component exercise training or who had Performed regular exercise in the recent 6 months were excluded. A study on the effects of physical activity on cognitive function provided the basis to estimate the sample size. According to the formula of comparing 2 means, a sample size of 34 participants per group was necessary to detect statistically significant differences. In consideration of subject dropout, 90 participants were recruited in this study, and participants were randomly divided into the experimental group (n=45) and control group (n=45). Participants were randomly assigned to either the experimental or control group using an independent randomization service (randomization with a 1:1 ratio). Participants and researchers could not be blinded due to the nature of the intervention. The follow-up data collectors were blinded to group allocation. The control group received general community health instruction while the experimental group received multi-component exercise training based on general community health instruction. Participants and instructors could not be blinded due to the nature of the intervention.

Recruitment

All members of the study team accepted the training from the primary investigator before the study to make sure that the measures were consistent and accurate. With permission

and support from the community leaders, prior eligibility screening was applied. Participants who met the criteria were informed of the details of the whole research and written informed consent. A total of 98 elderly participants from an original 425 met the inclusion criteria during screening. Subsequently, 90 of these 98 people participated in this research and were divided into the experimental group and control group equally by the random number table method. During the 6-month training, 3 participants from each group quit from the study with reasons including hospitalization, moving out from the community, or their own will. A total of 84 cases completed the study. The information of the participants, including average age, marital status, education, income, and living status, among others, are shown in *Table 1*. The differences between the 2 groups in terms of age, marital status, education level differences, and living status were not statistically significant ($P>0.05$).

Interventions

Participants in the control group received regular community health instruction, such as receiving lessons lasting 1 hour every month including how to keep fit. Participants in the experimental group received multi-component exercise training based on the control group. Multi-component exercise training involved comprehensive exercise including aerobic exercise, strength training, balance training, coordination training, and sensitivity training in reference to Vaughan *et al.*'s research (14). The multi-component exercise training performed on these participants was adjusted to suit the Chinese elderly based on advice from the nursing specialist and sports medicine specialist after the preliminary experiment.

Specific content

- (I) Warming up : the participant was guided to march on the spot, static stretches on the floor, lasting for 5 minutes, 3–4/10 rating of perceived exertion (RPE).
- (II) Aerobic exercise training: shoulder range of motion (shoulders rotating clockwise and counterclockwise), clapping hands, toe side pointing and knee lifting motion, lasting a total of 5 minutes, 4–5/10 RPE.
- (III) Strength training: half squats, bend standing, elbow and knee bend motion lasting for 5 minutes, 4–5/10 RPE.
- (IV) Balance training: supported standing on one leg,

Table 1 Comparison of the experimental group and control group at baseline (n=84)

Variables	Experimental group (n=42)		Control group (n=42)		Chi-squared ^a	P
	N	%	N	%		
Gender					0.449	0.503
Male	15	35.7	18	42.9		
Female	27	64.3	24	57.1		
Age, years					0.411	0.887
60–69	20	47.6	18	42.9		
70–79	20	47.6	21	50.0		
80 and above	2	4.8	3	7.1		
Family history					1.000	0.753
No	41	97.6	41	97.6		
Dementia	1	2.4	1	2.4		
Marital status					0.985	0.321
Married	33	78.6	29	69.0		
Divorced or widowed	9	21.4	13	31.0		
Education					4.514	0.874
None	3	7.1	2	4.8		
Primary school	9	21.4	14	33.3		
Middle school and above	30	71.5	26	61.9		
Income, Yuan					1.418	0.701
1,000 and below	7	16.6	5	11.9		
1,000–2,000	17	40.5	22	52.4		
2,000–3,000	12	28.6	11	26.2		
3,000 and above	6	14.3	4	9.5		
Living status					0.217	0.897
Living alone	7	16.6	6	14.3		
Couple	18	42.9	17	40.5		
Others	7	40.5	19	45.2		
Smoking					0.309	0.782
Yes	7	16.7	9	21.4		
No	35	83.3	33	78.6		
Drinking					0.105	0.746
Yes	6	14.3	5	11.9		
No	36	85.7	37	98.1		

Table 1 (continued)

Table 1 (continued)

Variables	Experimental group (n=42)		Control group (n=42)		Chi-squared ^a	P
	N	%	N	%		
Chronic disease					0.074	0.786
Yes	33	78.6	34	81.0		
No	9	21.4	8	19.0		
Health condition					2.597	0.273
Good	7	16.7	10	23.8		
General	30	71.4	23	54.8		
Bad	5	11.9	9	21.4		
CM-PPT, mean ± SD	11.36±2.69		10.79±2.73		0.963 (t ^b)	0.338
MMSE, mean ± SD	26.50±1.33		26.62±1.46		0.393 (t ^b)	0.694
MoCA, mean ± SD	21.52±2.05		21.14±1.97		0.866 (t ^b)	0.389

^a, independent chi-squared test; ^b, independent two-sample *t*-test. CM-PPT, Chinese version Mini-Physical Performance Test; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

kicking motion (leg and right kicking forward and backward with trunk straightened), lasting for 5 minutes, 4–5/10 RPE.

- (V) Coordination training: three steps forward and back, zig zag movements, weaving in and out of chairs, circuit, lasting for 5 minutes, 4–5/10 RPE.
- (VI) Sensitivity training: fast, fixed-pattern foot tapping, walking ball bounces, lasting for 5 minutes, 4–5/10 RPE.

Intensive training

The multi-component exercise group were gathered together to receive the intervention. Researchers explained and demonstrated exercise techniques to the participants, ensuring that they mastered the correct exercise methods. After the intensive training session, the exercise training group was subdivided into 5 groups, and participants who exhibited skillful use of the techniques and organizational ability were selected to lead the team in focusing on exercises 5 mornings a week, 30 minutes each time. All of the exercise trainings were performed under the same 2 instructors to maximize the intervention compliance. A pamphlet and videotape which explained the mechanisms and benefits of the multi-component exercise training were given to the participants to guide their training at home. The training lasted for 6 months.

Intervention fidelity

Two research members were present in each class. At random intervals, another research member recorded content consistency using a check-list based on multi-component exercise training. Class attendance was also monitored. The experimental group members were required to attend at least 80% of classes and were followed up by telephone if they were absent for 2 consecutive classes. The researchers urged the participants to finish the whole experiment by the way of checking the completion of training materials, training diaries, telephone follow-up and home visit. Regularly distributing small gifts to the subject participants to encourage their enthusiasm for participation. For those who did not complete well, the researchers strengthened supervision. While the controls received their intervention in a similar way.

Measures

The basic situation of the elderly was measured with a self-designed questionnaire including name, gender, age, education level, marital status, occupation, income, living conditions, disease history, and family history, among others. The primary endpoints of this study are the Chinese version Mini-Physical Performance Test (CM-PPT), the Mini-Mental State Examination (MMSE), and the Montreal

Cognitive Assessment (MoCA) scores.

Chinese version Mini-Physical Performance Test (CM-PPT)

The CM-PPT (16) was applied to evaluate the subjects' physical function in 4 areas, including standing static balance (feet together, semi-tandem, tandem, and one-leg position), 6 meter timed walk (time of 3 meters forward and back), chair-stand time (time to sit in and rise from a chair with arms folded across their chest 5 times), and picking up a penny from the floor (placing a penny approximately 0.3 meters from the participant's foot on the dominant side and measuring the time used by the participant to pick up the penny from the floor and stand up). Five grades (0–4) were used to score each subscale, and scores for the CM-PPT ranged from 0 to 16. A higher score represented better physical function. Xu *et al.* (16) confirmed that the Cronbach's coefficient of the CM-PPT was 0.868, and the test-retest and inter-rater reliability were 0.96 and 0.99, respectively ($P < 0.001$).

Mini-Mental State Examination (MMSE)

The MMSE (17) was applied to evaluate the subjects' cognitive function in 5 areas, including orientation, memory, attention and calculation, language, and graphic simulation. The scores of the MMSE including 30 items ranged from 0 to 30. Participants who answered or operated correctly got 1 score, while errors, refusal to answer, or saying "no" were marked as 0. Based on the educational levels of illiteracy, primary school, and middle school and above, the cut-off scores of cognitive dysfunction were 17, 20, and 24, respectively. The reliability of 0.91 and validity of 0.99 of the MMSE have been widely accepted.

MoCA

The MoCA is an MCI screening tool including visual-spatial executive ability, naming, memory, attention, language fluency, abstract thinking, delayed memory, and orientating function. Scores for the MoCA ranged from 0 to 30. A higher score represented better cognitive function. Kappa consistency test showed that Kappa value was 0.763 with good consistency (18). Based on the educational levels of illiteracy, primary school, and middle school and above, the scores of cognitive dysfunction were 17–23, 20–24, and

20–25, respectively (18).

Data collection

The scores of the physical and cognitive function of the participants in our study groups were evaluated with the above questionnaires before the intervention and at 3 and 6 months after the intervention.

Statistical methods

A database was established with the statistical software SPSS 17.0, and data was presented as the mean \pm SD. Repeated measures analysis of variance was applied to determine the effects of multi-component exercise training. Differences between group characteristics were compared, and the *t*-test or chi-squared test was adopted to analyze and compare information such as demographic features and physical and cognitive functions before the intervention. The α value was set at 0.05, and *P* values were two-sided.

Results

Description of the groups

All members of the study team accepted the training from the primary investigator before the study to make sure that the measures were consistent and accurate. A total of 98 elderly participants who met the criteria from an original 425 were informed of the details of the whole research and written informed consent; 90 of these 98 people participated in this research and were divided into 2 groups equally by the random number table method. During the 6-month training, a total of 84 cases completed the study and 3 participants from each group quit from the study for some reasons (*Figure 1*).

Before the intervention, no significant group differences in socio-demographic variables were revealed with the chi-squared test ($P > 0.05$). Furthermore, no significant group differences in the scores of the CM-PPT, MMSE, and MoCA, which represent physical and cognitive function, were revealed with the *t*-test ($P > 0.05$), as shown in *Table 1*.

Physical and cognitive function before and after the intervention

The scores of the CM-PPT, MMSE, and MoCA before and

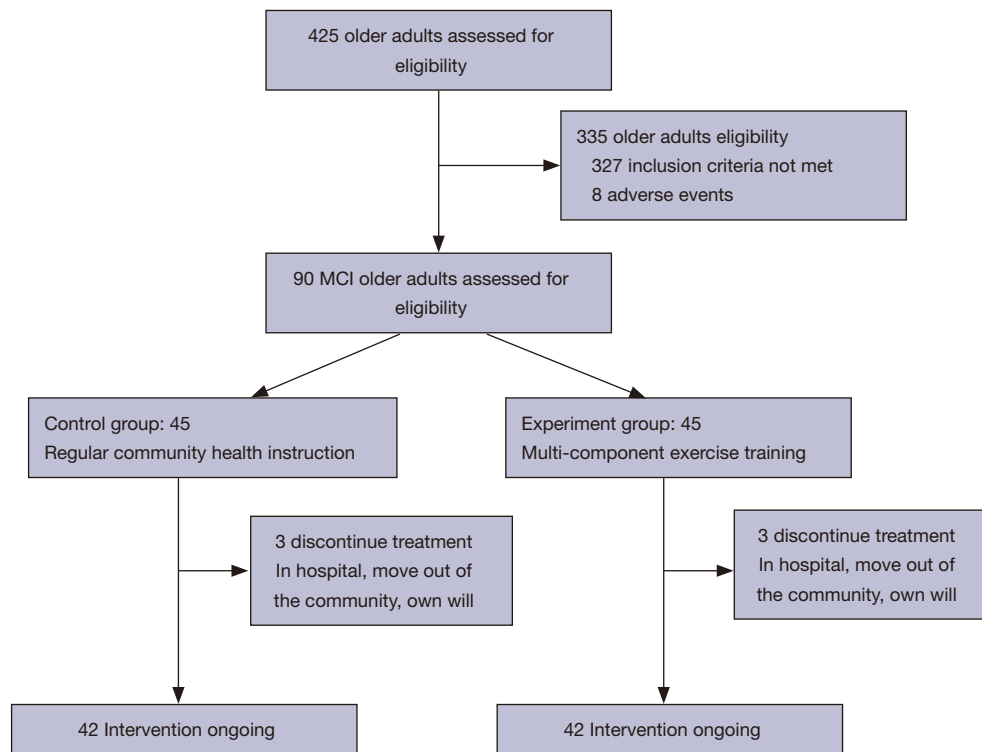


Figure 1 Participants flow. MCI, mild cognitive impairment.

Table 2 Physical and cognitive function before and after the intervention

Variables	Experimental group (n=42)			Control group (n=42)		
	Before intervention	3 months	6 months	Before intervention	3 months	6 months
CM-PPT	11.36±2.69	11.88±2.40	12.83±2.19	10.79±2.73	10.24±2.62	9.21±2.09
MMSE	26.50±1.33	27.00±1.25	27.79±1.18	26.62±1.46	25.90±1.45	25.42±2.28
MoCA	21.52±2.05	23.48±1.47	25.19±1.29	21.14±1.97	20.21±1.88	19.45±2.00

CM-PPT, Chinese version Mini-Physical Performance Test; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

after 3- and 6-month training are presented in *Table 2*.

The effects of multi-component exercise training and time on physical function

Repeated measures analysis of variance was used to measure the scores of the CM-PPT before and after the intervention. As shown in *Table 3*, only the effect of time on the 6-meter timed walk score was statistically significant ($P<0.05$). The main effect of the intervention represented with the scores of the CM-PPT and its 3 subscales (standing static balance, chair-stand time, 6-meter timed walk) before

and after the intervention were statistically significant ($P<0.05$). The interaction between the intervention and time before and after the intervention was also statistically significant ($P<0.05$), indicating that the physical function of the intervention group was improved compared with the control group.

The effects of multi-component exercise training and time on cognitive function

In the repeated measures analysis of variance as shown in *Table 4*, the main effects of time on the MoCA and all

Table 3 Intervention effect on physical function in the repeated measures analysis of variance

Physical function	Time main effect		Intervention main effect		Interaction effect	
	F	P	F	P	F	P
CM-PPT	0.057	0.922	14.348	0.000	111.595	0.000
Standing static balance	1.601	0.210	4.068	0.047	17.254	0.000
Chair-stand time	0.125	0.853	41.438	0.000	8.002	0.006
6-meter timed walk	255.392	0.000	7.024	0.010	24.773	0.000
Picking up a penny from the floor	0.034	0.953	2.334	0.130	30.977	0.000

CM-PPT, Chinese version Mini-Physical Performance Test.

Table 4 Intervention effect on cognitive function in the repeated measures analysis of variance

Cognitive function	Time main effect		Intervention main effect		Interaction effect	
	F	P	F	P	F	P
MMSE	0.441	0.555	14.964	0.000	56.485	0.000
MoCA	78.116	0.000	66.906	0.000	574.892	0.000
Visual-spatial executive	21.865	0.000	18.669	0.000	74.473	0.000
Naming	6.271	0.002	0.191	0.063	6.271	0.002
Attention	8.537	0.001	16.420	0.000	53.356	0.000
Language	5.002	0.015	0.035	0.853	7.688	0.002
Abstract	15.769	0.000	1.569	0.214	15.769	0.000
Delayed memory	27.466	0.000	30.726	0.000	79.048	0.000
Orientating	2.885	0.059	0.176	0.676	5.301	0.015

MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

subscales, except orientating and the MMSE, and the main effects of the intervention on the MMSE, MoCA, and the 3 subscales (visual-spatial executive, attention, delayed memory) were statistically significant ($P < 0.05$). The interaction between the intervention and time before and after the intervention was significant for MMSE, MoCA, and the 3 subscales ($P < 0.05$, *Table 4*), indicating that the cognitive function of the intervention group was improved compared with the control group.

Discussion

In the present study, we investigated physical and cognitive functional changes after multi-component exercise training in older adults with MCI. Our results showed that: (I) the physical function of MCI adults was improved after multi-component exercise training for 3 and 6 months, and (II)

the cognitive function of older adults with MCI was also improved after multi-component exercise training at the same time. These results suggest that multi-component exercise training is a new strategy to improve the physical and cognitive function of adults with MCI.

The MMSE and MoCA tests were used to evaluate cognitive function (19). This study revealed that multi-component exercise training improved visual-spatial executive ability, attention, and delayed memory in elderly participants with MCI, while naming, language fluency, and abstract thinking also improved over time. The specific mechanisms underlying the improvement in cognitive function after multi-component exercise training in the elderly with MCI is still being explored. Vaughan *et al.* (14) showed that the improvement in cognitive function after multi-component exercise training could be related to elevated brain nutritional factors in the serum.

Erickson *et al.* (20) found that aerobic exercise can increase hippocampal volume, significantly improving spatial memory.

The CM-PPT is commonly used to evaluate the physical function of the Chinese population. This study revealed that multi-component exercise training improved physical function in elderly participants with MCI, which is consistent with research by Locks *et al.* (21). Moderate exercise training can enhance older people's body metabolism, breathing in more oxygen, and the release of more carbon dioxide and other metabolic toxins. It can also improve heart, lung, and digestive function and promote cell metabolism, which can effectively prevent diseases that affect the elderly and delay the aging process. Pereira *et al.* (22) reported that exercise training can slow the accumulation of chronic inflammatory mediators such as TNF- α , IL-10, and IL-6, and decrease the intensity of inflammatory responses and sensitivity to disease, thus enhancing the physical function of the elderly.

Cognitive function impairment and poor physical function are critical issues among older adults. With aging, people's physical function declines. Physical function decline in older people manifests as decreasing strength, balance dysfunction, slow walking, and gait impairment (23). Physical function decline can lead to the occurrence of falls, body function disuse, being bedridden long term, and even death (24). Improving the cognitive and physical function of adults with MCI in the early stage via multi-component exercise training is a novel strategy to delay the progression from MCI to dementia. In the multi-component exercise training, sensitivity training such as fast, fixed-pattern foot tapping and pat ping-pong were used to improve participants' attention and hand-eye coordination, and consequently, attention and visual-spatial executive ability (25). Strength training such as elbow and knee bend motion can improve selective attention ability. Coordination training such as 3 steps forward and back and zig zag movements integrate visual-spatial executive ability. Clapping hands can improve brain reaction times, thus improving older adults' cognitive function.

Furthermore, biological, psychological, cultural, and even environmental factors, such as aging, not participating in sports activities, chronic diseases, low level of education, and living with children, can affect the physical function of the elderly (26). Thus, multi-component exercise training can be used as an alternative or adjunctive way of reversing the cognitive and physical dysfunction of adults with MCI

and prevent progression to dementia.

Limitations

In this study, the 2 groups of elderly adults came from the same community. Although they were told not to communicate with members of the other group prior to the intervention, the possibility of experimental pollution cannot be ruled out.

Conclusions

Our results showed that multi-component exercise training could not only improve physical function but also protected or improved cognitive function. The multi-component exercise training used in this study is a safe, economical, and simple intervention which is easy for the elderly to learn and can be popularized to promote healthy aging.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at <https://dx.doi.org/10.21037/apm-21-1809>

Data Sharing Statement: Available at <https://dx.doi.org/10.21037/apm-21-1809>

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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 research was approved by the Ethics Committee of Central South University (No. 2020-649). Research complied with the ethical standards of the institutional and/or national

research committee and with the Helsinki Declaration (as revised in 2013). Informed consent was obtained from all participants included in the research.

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