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Effects of a moderate-intensity aerobic exercise programme on the cognitive function and quality of life of community-dwelling elderly people with mild cognitive impairment: A randomised controlled trial

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ABSTRACT

Background: Individuals with mild cognitive impairment have a heightened risk of developing dementia. Physical exercise, especially moderate-intensity aerobic exercise, is a promising lifestyle intervention to improve the cognitive function of this patient group. However, the mechanisms underlying the exercise–cognition relationship are not fully understood. Whether the cognitive benefits of physical exercise can improve the overall well-being of this group remains unknown. This study aims to address these research gaps in the under-researched Chinese population.
Objectives: This study aimed to evaluate the effects of a moderate-intensity aerobic exercise programme on the cognitive function and health-related quality of life of Chinese elderly with mild cognitive impairment and to explore the mediating roles of depressive mood and sleep quality in the exercise–cognition relationship.
Design: A single-blinded randomised controlled trial.
Settings and participants: This study was conducted in two urban community healthcare centres in Hangzhou City, China. Elderly people aged over 60 years screened with mild cognitive impairment were included.
Methods: A total of 120 eligible participants were randomly assigned to receive either the group-based moderate-intensity aerobic exercise programme or the health education programme (as attention–placebo control). Montreal Cognitive Assessment, Quality of Life-Alzheimer's Disease, Geriatric Depression Scale and Pittsburgh Sleep Quality Index were administered at baseline before randomisation and immediately after the completion of the interventions. Analysis followed the intention-to-treat principle. Generalised estimating equation was used to compare the changes in the cognitive function and health-related quality of life over the pre-test and post-test periods between the groups. The mediating roles of depressive mood and sleep quality in the exercise–cognition relationship were examined with the PROCESS macro.
Results: Participants in the intervention group had a significantly greater improvement in terms of cognitive function ($\beta = 1.895$; 95% confidential interval [CI] = 1.421, 2.368; $p < 0.001$) and health-related quality of life ($\beta = 0.605$; 95% CI = 0.295, 0.914; $p < 0.001$) compared with the control group over the pre-test and post-test periods. The exercise–cognition relationship was significantly mediated by reduced depressive symptoms (indirect effect: $\beta = -0.705$; 95% CI: −1.028, −0.382) and improved sleep quality (indirect effect: $\beta = -0.205$; 95% CI: −0.122, 0.831).
Conclusions: This study revealed the benefits and outlined the underlying mediating mechanism of an aerobic exercise programme to the cognitive function and health-related quality of life of Chinese elderly people with mild cognitive impairment. The findings provided insights into the development of public health initiatives to promote brain health amongst the elderly with mild cognitive impairment.

What is already known about the topic?

- Individuals with mild cognitive impairment have an increased risk of developing dementia. Timely and effective interventions at this stage are crucial to prevent cognitive deterioration.

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- Physical exercise, particularly moderate-intensity aerobic exercise, can potentially improve the cognitive function amongst individuals with mild cognitive impairment.
- Given the benefits of physical exercise on depressive mood and sleep quality, the exercise–cognition relationship could possibly be mediated by improving these risk factors for cognitive decline.

What this paper adds

- A 16-week moderate-intensity aerobic exercise programme was administered to improve the cognitive function and health-related quality of life of Chinese community-dwelling elderly people with mild cognitive impairment.
- Delivering the exercise programme in a group format with the integration of movements to assimilate daily activities was feasible and with satisfactory adherence amongst elderly people with mild cognitive impairment.
- The exercise–cognition relationship was mediated by reduced depressive symptoms and improved sleep quality.

1. Introduction

Dementia is a major public health problem that imposes a high level of health and social care burden in the aging society worldwide (Wimo et al., 2017) and has been exacerbated by population ageing. Preventive interventions for this disease have been widely explored. Individuals with mild cognitive impairment have a heightened risk of developing dementia (Petersen et al., 2014). The annual conversion rates from mild cognitive impairment to dementia are estimated from 10% to 15%, whereas the annual incidence rate of dementia in the overall elderly population is estimated from 1% to 3% (Doblhammer et al., 2015; Satizabal et al., 2016). Mild cognitive impairment is prevalent amongst the elderly with an estimated global prevalence range of 9.6% to 21.6% (Jia et al., 2014; Lara et al., 2016; Petersen et al., 2010). The high prevalence and progression rates to dementia amongst patients with mild cognitive impairment emphasise the need to identify effective treatments at this stage to reduce the burden associated with further cognitive decline.

Nonpharmacological intervention remains the mainstay treatment for elderly with mild cognitive impairment (Petersen et al., 2014). Amongst various therapies, physical exercise as a low-cost, low-risk and readily available lifestyle intervention has been extensively investigated because of its well-known benefits to brain health promotion in elderly care practice (Angevaren et al., 2008). The cognitive benefits of different exercise modalities amongst the individuals with mild cognitive impairment have been reported. According to a recently conducted systematic review of 11 randomised controlled trials (Song et al., 2018a,b) physical exercise, including aerobics and resistance training, exhibits low to moderate effects on the cognitive function of this population. Sensitivity analysis has further revealed the outweighed cognitive benefit and high acceptability of moderate-intensity aerobic exercise interventions compared with other exercise-based interventions (Song et al., 2018a,b). However, the cognitive benefit of physical exercise were still under investigated among Chinese elderly people with mild cognitive impairment. In addition, although this condition poses considerable challenges to a patient's daily life, the effect of physical exercise on the health-related quality of life of this patient group has been seldom studied. Limited evidence related to this phenomenon has reported negative findings (Lautenschlager et al., 2008; van Uffelen et al., 2007), thereby causing queries on the transferability of the cognitive gains of exercise interventions to the general well-being of people with mild cognitive impairment.

Despite evidence supporting the cognitive-enhancing effects of physical exercise, studies that examine the mediating mechanisms underlying the exercise–cognition relationship are still lacking. Addressing this research gap is important for further theoretical understanding of the cognitive benefit of physical exercise and to provide insights into developing exercise interventions that can optimise the changes on the mediators. Amongst the possible mediating pathways, the most widely recognised one is the improved cardiovascular function associated with physical exercise, which increases cerebral blood flow and oxygenation to the brain tissue and thus enhances the neurotransmitter availability and neural efficiency (Ainslie et al., 2008) and promotes cognitive function (Donley et al., 2014). The mediating mechanism related to the risk factors of cognitive decline, which are modifiable by physical exercise, has been poorly studied. Recent large-scale longitudinal studies identified depressive symptoms and poor sleep as prominent risk factors predicting cognitive decline (Diniz et al., 2013; Shi et al., 2018). The risk is increased because depressive symptoms and poor sleep induce fatigue, thereby compromising the optimal cognitive performance. Neurobiological studies have also explained that the cognitive decline associated with depressive symptoms and poor sleep is also connected to hippocampus shrinkage (Molendijk et al., 2014) and deficits in prefrontal cortical functionality (Kincheski et al., 2017). Considering that physical exercise reduces depressive symptoms by boosting self-efficacy, causing distraction, increasing endorphin secretion (Silveira et al., 2013) and elicits a sleep-inducing effect by creating a state of energy exhaustion and enhancing basic metabolic rate (Yu et al., 2018); the exercise–cognition relationship could possibly be mediated by an improved depressive mood and sleep quality. However, studies that examine such mechanisms amongst people with mild cognitive impairment are lacking.

This study aims to investigate the effects of a moderate-intensity aerobic exercise programme on the cognitive function and health-related quality of life of Chinese elderly people with mild cognitive impairment. Moreover, this study aims to examine whether or not depressive symptoms and sleep quality mediates the effect of exercise training on cognition. Fig. 1 outlines the hypothesised mediating model. The following research hypotheses are tested amongst the elderly with mild cognitive impairment.

1 A 16-week moderate-intensity aerobic exercise training has greater effect than an attention placebo (i.e. a general health education programme) in improving cognitive function and health-related quality of life.
2 The effects of the 16-week moderate-intensity aerobic exercise training on cognitive function are mediated by improved depressive symptoms and sleep quality.

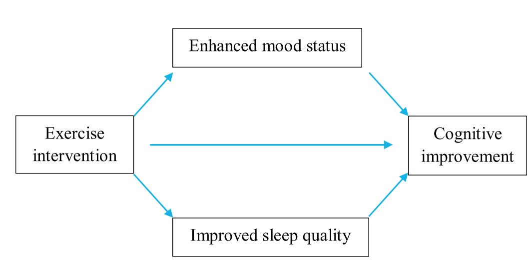

Fig. 1. The hypothesised mediating model.

2. Methods

2.1. Study design and setting

This study was a single-blinded, randomised controlled trial (registration number: CUHK_CCRB00531), conducted at two community healthcare centres in Hangzhou, Southeast China from October 2017 to July 2018. Eligible participants were randomly allocated to receive either moderate-intensity aerobic exercise training or a general education programme with a block size of 20. The random sequence was generated using a computer-generated random list. Random numbers with the group allocation code were kept in opaque and sealed envelopes, which were prepared by a person who was not involved in data collection. The outcome and mediating variables were measured at baseline before randomisation and within 1 week upon the completion of the study interventions via face-to-face interviews. Single blinding was maintained because research assistants who were involved in the collection of post-test data did not have any information of group assignment.

2.2. Participants

Participants for this study were recruited via: 1) study posters attached with the contact information of the researchers; 2) health talks held at the community healthcare centres; 3) and word of mouth by the researchers. Individuals who showed interest were invited for an in-person interview to screen for study eligibility. Those individuals who met all the inclusion criteria were invited to participate in this study. Eligible participants were community-dwelling elderly people aged 60 or above and were identified with mild cognitive impairment by the Montreal Cognitive Assessment (Chinese version, MoCA-C), which is a validated cognitive screening tool specifically developed to detect mild cognitive impairment. A cut-off point of between 19 and 26 was used as the range of scores' optimal sensitivity (92.4% and 93.2%) and specificity (88.4% and 71.7%) to differentiate patients with mild cognitive impairment from those with normal cognition and dementia (Yu et al., 2012). The influence of education on cognitive performance was adjusted by adding one point for those having less than 6 years of education. Exclusion criteria included participants with (1) conditions which were contraindicated for exercise training according to the American College of Sports Medicine (ACSM) (American College of Sports Medicine, 2017); (2) prescription of antidepressant agents, which may confound the outcome measurement; (3) severe neurological disorders (e.g. brain injury, stroke, Parkinson's disease) which greatly impairs cognitive function; (4) regular engagement in moderate or vigorous-intensity aerobic exercises of >150 min per week.

2.3. Sample size estimation

Power analysis was used to estimate the sample size. Referring to an randomised controlled trial of good methodological quality performed by Lautenschlager et al. (2008) which identified moderate effects of a moderate-intensity aerobic walking programme on cognitive function (Cohen's $d = 0.58$), a sample of 60 participants per group was required to detect a difference between groups at a 5% significant level with 80% power, allowing for a 20% attrition rate.

2.4. Study interventions

2.4.1. Moderate-intensity aerobic stepping exercise programme

The tested intervention was a 16-week aerobic stepping exercise programme with three 60-minute group training sessions (20 participants per group) per week. The overall exercise programme was designed by a team comprising a nurse academician, a physiotherapist and exercise physiologists in accordance with the recommendations of the ACSM position stand on exercise and physical activity for the elderly (Nelson et al., 2007; Yu et al., 2018). The moderate-intensity aerobic exercise training was conducted by two registered nurses, one serving as an instructor and the other as a facilitator, in accordance with a standardised intervention protocol. The two registered nurses attended a four-week training, performed a return demonstration and exhibited good protocol compliance. For the aerobic exercise training, each session started with a 10-minute warm-up, which included walking and stationary stretching exercises for trunk and limb joints at the upper and lower bodies, followed by moderate-intensity stepping exercises. A stepping exercise programme that involved patterns of stepping up and down on a 10-cm-high stable stepping bench was adopted. This exercise mode was selected because it is highly suitable for old people, especially for those who are less physically active or have decreased joint flexibility and bone strength (Mori et al., 2011). Additionally, various sets of simple and entertaining upper limb movements resembling daily activities, such as washing the face, were added to enhance exercise motivation and to facilitate overall body movement (Yu et al., 2018). The participants were supported to achieve the moderate intensity of the workout by using the Borg Scale, which measures the perceived exertion. A rating of 12–14 on this scale, which indicated a feeling of "somewhat hard", was recommended as equivalent to the exertion in moderate-intensity aerobic exercise (Borg, 1998). The interveners explained the Borg scale to the participants and instructed them to speed up or slow down their movements to achieve a feeling of "somewhat hard" at the Borg rating of 12–14. The aerobic exercise programme was introduced in a progressive manner with the duration gradually increasing from 20 min to the targeted 40 min in 4 weeks' time to enhance adherence and avoid injury risks (Nelson et al., 2007). Participants performed the stepping exercise in multiple bouts of at least 10 min each rather than in a single continuous bout to reach the targeted duration, with a maximum of 5 min of rest in between exercise bouts. Each training session ended with a 10-minute cool-down session with the same walking and stationary stretching exercises as those in the warm-up session. The training was in accordance with the ACSM safety guidelines. Blood pressure, heart rate and contradictory symptoms were assessed before training was performed. Motivational strategies, including goal setting, verbal encouragement and emotional incentives based on the self-efficacy theory, were incorporated into this exercise intervention to ensure compliance. The compliance of the participants was monitored using an attendance record. A practice log was also provided to the participants to allow self-monitoring.

2.4.2. Control intervention

The control intervention was a 16-week health education programme that was delivered by a general practitioner in the community healthcare centre and served as an inactive attention placebo to neutralise the effects of extra attention from the interveners on the measured cognitive and health-related outcomes. The health education programme included eight bi-weekly educational classes (45 min/each session). No information relating to brain health and physical exercise was included. For any questions inquired by the control participants, general advice, but not information relating to physical exercise and brain health, was given for ethical consideration.

2.5. Measurement

2.5.1. Socio-demographic profile

At baseline, a self-designed demographic data sheet was used to collect the social–demographic data, including age, gender, marital status, income, education and living condition.

2.5.2. Outcome measures and mediating variables

The primary outcome was cognitive function, and the secondary outcome was health-related quality of life. The mediating variables included depressive mood and sleep quality. All the outcome and mediating variables were measured at baseline and immediately after the 16-week intervention.

2.5.3. Cognitive function

The MoCA-C was used to measure cognitive function using a paper-and-pencil approach. The Montreal Cognitive Assessment contains cognitive tasks for a range of domains, including episodic memory, visuospatial ability, executive function, attention, language and orientation to obtain an overview of one's cognitive function (Nasreddine et al., 2005). The MoCA-C displays good reliability with Cronbach's α of 0.836 (Yu et al., 2012) and is more sensitive than Mini-Mental State Examination in measuring cognitive function in patients with mild cognitive impairment (Dong et al., 2010). Additionally, the relative brevity of Montreal Cognitive Assessment compared with other complex neuropsychological batteries renders it to be more feasible to be administered to elderly people with mild cognitive impairment.

2.5.4. Health-related quality of life

The Quality of Life–Alzheimer's disease (Chinese version, QOL-AD-C) was used in this study to measure the overall well-being of the participants. The 13-item Quality of Life-Alzheimer's disease assesses the quality of life domains, including social relationship, physical conditions, mood and overall assessment of life satisfaction, which are important for persons affected by cognitive impairment (Logsdon et al., 2002). Its Cronbach's alpha in this study was 0.800.

2.5.5. Sleep quality

Sleep quality was measured by the Pittsburgh Sleep Quality Index (Chinese version, Pittsburgh Sleep Quality Assessment), which provides a global sleep quality score based on seven components including sleep quality, latency, duration, efficiency, disturbance, use of sleep medication and daytime dysfunction due to poor sleep quality (Buysse et al., 1989). Pittsburgh Sleep Quality Assessment has been widely used to measure subjective sleep quality in individuals with cognitive impairment (An et al., 2014; Guarnieri et al., 2012). A global score $\geq$ 6 yields a diagnostic sensitivity of 89.6% and specificity of 86.5% in differentiating good and poor sleepers in Chinese (Tsai et al., 2005). The Cronbach's alpha of Pittsburgh Sleep Quality Assessment in this study was 0.736.

2.5.6. Depressive mood

Depressive mood was assessed by the 30-item Geriatric Depression Scale (Chinese version, Genomics of Drug Sensitivity in Cancer). The scale uses dichotomous questions and presents a total score ranging from 0 to 30, with high scores representing severe depressive symptoms (Yesavage et al., 1983). GDS is easy to administer and is a valid tool for assessing depressive symptoms in individuals with mild cognitive impairment (Debruyne et al., 2009). A cut-off score $\geq$10 gives a sensitivity of 0.94 and a specificity of 0.80 for screening the clinical level of depression amongst elderly people (Smarr and Keefer, 2011). The Cronbach's alpha of Genomics of Drug Sensitivity in Cancer in this study was 0.784.

2.6. Procedure and ethical considerations

The ethical approval for this trial was obtained from the Joint Chinese University of Hong Kong- New Territories East Cluster Clinical Research Ethics Committee (No. 2016.287). The purpose and process of this study were explained to potential participants. Written informed consent was obtained from each participant; each participant was assured of confidentiality and the option to decline participation or to withdraw from the trial at any time without penalty. After obtaining the written informed consent, baseline data collection was conducted by two trained research assistants in the community healthcare centre. After the pre-test data collection, the participants were randomly allocated to receive the aerobic exercise programme or the health education programme. The post-test data were collected within 1 week upon the completion of the 16-week study interventions. The participants were invited to the community healthcare centre for the post-test data collection by the research assistants who had no information about the participants' group status. All the questionnaires were read out to the participants in face-to-face interviews.

2.7. Statistical analysis

Statistical analysis was performed SPSS, version 22 (SPSS Inc., USA). Appropriate descriptive statistics was used to summarise the characteristics of the participants. The normality of all the continuous variables was screened by skewness and kurtosis statistics. The Chi-square and *t*-test were used for checking for any significant group difference in demographic and outcome variables between the two study groups at baseline. The generalised estimated equation (Generalised Estimating equations) model was used to assess for any differential changes in the outcome variables between the two study groups across the pre-test and post-test study periods (i.e. group*time interaction effect). GEE was used, because this method accounts for within-subject correlation of longitudinal data and allows for missing data and time-varying covariate (Hanley et al., 2003). Data analysis followed intention-to-treat (intention-to-treat) principle. Effect size estimates were calculated for all mean differences using Cohen's *d*, relating the mean score differences to the pooled standard deviation (Cohen, 1998).

The PROCESS macro developed by Preacher and Hayes (2004) was employed to examine the mediating effects of depressive mood and sleep quality on the relationship between attending the exercise intervention and cognitive changes. Bias-corrected bootstrapping with 10,000 resamples was used to generate 95% confidence intervals for direct and indirect effects. The nonparametric bootstrapping procedures are superior to traditional regression methods for testing the mediating effects, because the former does not make assumptions regarding the shape of the distribution of the variables or the sampling distribution (Preacher and Hayes, 2004). Confidence intervals not including zero indicated significant mediation.

3. Results

3.1. Recruitment, attrition and adherence

As shown in the CONSORT flow diagram (Fig. 2), 512 elderly people were approached for eligibility screening. Amongst the 158 participants who met the selection criteria, 120 consented to participate. During the study period, 25 of them discontinued (attrition rate: 20.8%) mainly because of illness (n = 8) or unanticipated family duties (n = 11). Post-test data were also collected from the majority of these participants (n = 116) with their consent in accordance with the intention-to-treat principle. The average adherence rate of the exercise intervention group was 73.1%. Approximately 3/4 of the participants (73.3%) attended over 75% of the total sessions. Adherence was considered as desirable for exercise programme of a duration that lasts for 16 weeks (Ette, 2017). No adverse events, such as falling, occurred.

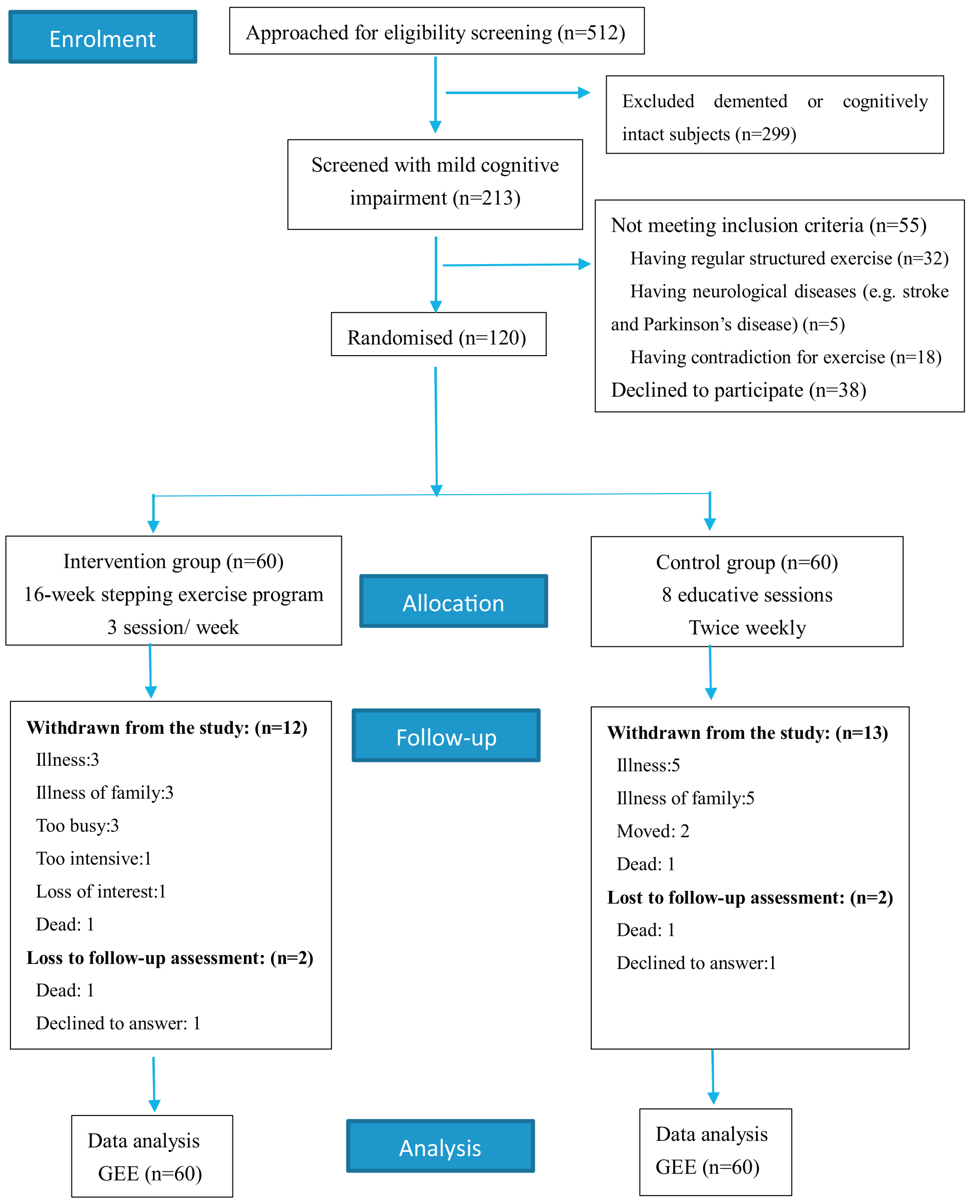

Fig. 2. The Consolidated Standards of Reporting Trials diagram.

3.2. Participant characteristics

The participants were of advanced age (mean = 75.78 years, SD = 6.28), and most of them were female (n = 90, 75%), married (n = 81, 67.5%) and living with their spouses or children (n = 88, 73.3%). Less than 20% of the participants (n = 19) were illiterate, and more than 60% of them (n = 76) had a monthly income less than the average value in the local city (i.e. 4000 Chinese Yuan Renminbi) according to public data. Among the patients, 34 (28.3%) had a clinical level of depressive symptoms, and 89 (74.2%) were poor sleepers. The baseline characteristics of the participants stratified by groups are shown in Table 1. No considerable differences were observed between the intervention and control groups in terms of demographic characteristics, baseline outcome and mediating variables.

3.3. Effects on cognitive function

The baseline and post-test Montreal Cognitive Assessment scores of both groups are presented in Table 2. Participants in the intervention group had significantly greater improvement in their Montreal Cognitive Assessment score compared with the control group across the pre-test and post-test periods (β = 1.895; 95% CI = 1.421, 2.368; $p < 0.001$). Amongst all the subscales of Montreal Cognitive Assessment, the GEE results were significant for memory (β: 0.913; 95% CI: 0.615, 0.211; $p < 0.001$), executive function (β= 0.405; 95% CI= 0.206, 604; $p < 0.001$), attention (β: 0.252; 95% CI: 0.0844, 0.086; $p < 0.003$), language (β= 0.155; 95% CI= 0.047, 0.263; $p < 0.005$) and visual–spatial ability (β= 0.177; 95% CI=0.059, 0.296; $p = 0.003$) (Supplementary Table 1). Effect size estimates fell in the medium and large ranges (Cohen's $d = 0.44–1.16$).

3.4. Effects on health-related quality of life

The baseline and post-test Quality of Life-Alzheimer's disease scores of both groups are presented in Table 2. Participants in the intervention group were found to have a significantly greater improvement in Quality of Life-Alzheimer's disease scores compared with the control group across the pre-test and post-test periods (β = 0.605; 95% CI = 0.295, 0.914; $p < 0.001$). Amongst

Table 1
Baseline data of demographic characteristics, outcome variables, and mediating variables.

Demographic Characteristics	Overall (n = 120)	Intervention (n = 60)	Control (n = 60)	P
Age #	75.78 ± 6.28	76.22 ± 5.76	75.33 ± 6.78	0.44
Gender##				0.21
Female	90	48(80.0%)	42 (70.0%)	
Male	30	12 (20.0%)	18 (30.0%)	
Marital status##				0.56
Married	81	39 (65.0%)	42 (70.0%)	
Single	39	21 (35.0%)	18 (30.0%)	
Education level##				0.49
Below middle school	51	28 (46.7%)	23 (38.3%)	
Middle school	42	21 (35.0%)	21 (35.0%)	
Above middle school	27	11 (18.3%)	16 (26.7%)	
Residence ##				0.26
Living alone	32	20 (33.3%)	12 (20.0%)	
Living with spouse	68	31 (51.7%)	37 (61.7%)	
Living with children only	20	9 (15.0%)	11 (18.3%)	
Monthly income (Chinese Yuan Renminbi) ##				0.45
Less than 4000	76	40 (66.7%)	36 (60%)	
4000 and above	44	20 (33.3%)	24 (40%)	
Outcome variables				
Cognitive function (Montreal Cognitive Assessment score) #	22.07 ± 1.94	22.03 ± 1.97	22.10 ± 1.92	0.85
HRQoL (Quality of Life-Alzheimer's disease score) #	29.49 ± 3.04	29.80 ± 3.32	29.18 ± 2.70	0.27
Mediating variables				
Depressive symptoms (GDS score) #	5.48 ± 3.10	5.33 ± 3.48	5.67 ± 3.70	0.61
Presence of depressive symptoms##	34 (28.3%)	16 (26.7%)	18 (30.0%)	0.69
Sleep quality (PSQI score) #	9.23 (3.79)	9.47 (3.66)	8.98 (3.94)	0.49
poor sleepers (PSQI >/ = 5) ##	89 (74.2%)	45 (75.0%)	44 (73.3%)	0.84

Note: # *t*-test for between-group comparison, ## chi-square for between group comparison, MoCA = Montreal Cognitive Assessment; QoL-AD = Quality of Life-Alzheimer's disease; GDS = Geriatric Depression Scale; PSQI = Pittsburgh Sleep Quality Index.
a: CNY = Chinese Yuan Renminbi; 1 US dollar = 6.9 CNY.

Table 2
GEE results for the comparison of outcome variables between the intervention and control groups.

	Intervention group	Control group	Group effect		Time effect		Group* time effect		Effect size (*d*)
			β (95%CI)	*p*	β (95%CI)	*p*	β (95%CI)	*p*	
Montreal Cognitive Assessment									
Baseline	22.03 ± 1.81	22.10 ± 1.92	−.171	0.621	−0.301	0.044	1.895	<0.001	1.16
Post-test	23.66 ± 1.92	21.40 ± 2.27	(−0.593, 0.009)		(−0.847, −0.506)		(1.421, 2.368)		
Quality of Life-Alzheimer's disease									
Baseline	29.80 ± 3.23	29.18 ± 2.70	0.224	0.653	−0.139	0.077	0.605	<0.001	0.66
Post-test	30.29 ± 3.41	28.97 ± 2.72	(−0.753,1.201)		(−.294, .015)		(0.297, 0.914)		
GDS									
Baseline	5.33 ± 3.48	5.67 ± 3.70	.333	.609	.069	.477	−.517	<0.001	0.68
Post-test	4.87 ± 3.22	5.70 ± 3.60	(−1.609, 0.942)		(−.121, .259)		(−.770, −.264)		
PSQI									
Baseline	9.47 ± 3.66	8.98 ± 3.94	0.483	0.483	0.240	0.012	−1.257	<0.001	0.89
Post-test	8.33 ± 3.43	6.76 ± 2.94	(−0.866, 1.833)		(0.053, 0.427)		(−1.609, −0.825)		

Note: MoCA = Montreal Cognitive Assessment; QoL-AD = Quality of Life-Alzheimer's disease; group effect = the group differences at the baseline between groups; time effect = the within-subject changes over the evaluative endpoint in the control group; Group* time effect = additional score changes of intervention group compared with control group at post-test; β= regression coefficient; CI = confidential interval.

the Quality of Life-Alzheimer's disease items, the GEE results were significant for energy (β = 0.241; 95% CI = 0.109, 0.374; $p < 0.001$), memory (β= 0.155; 95% CI= 0.037, 0.273; p = 0.010), self-identity (β= 0.158; 95% CI: 0.064, 0.251; p = 0.001), engagement in fun (β= 0.017; 95% CI= 0.015, 0.199; p = 0.023) and life as a whole (β= 0.086; 95% CI= 0.014, 0.159; p = 0.019) (Supplementary Table 2). Effect size was estimated to be moderate for the change in the overall Quality of Life-Alzheimer's disease score with Cohen's d = 0.66.

3.5. Results of the mediating analysis

The GEE results indicated that the exercise group had significantly greater improvement in depressive symptoms (β = −0.517; 95% CI=−0.770, 0.264; $p < 0.001$) and sleep quality (β = −1.257; 95% CI = −1.609, −0.825; $p < 0.001$) compared with the health education control group across the pre-test and post-test periods. The significant differential changes in the two mediators between the two groups supported the further exploration of their mediating roles. Fig. 3 depicts the mediating model. The exercise intervention elicited a significant indirect effect on the enhancement of cognitive function through the improvement of depressive

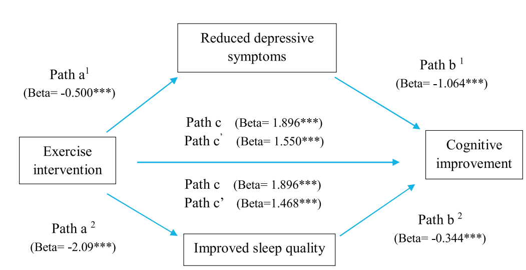

Fig. 3. Mediating roles of depressive symptoms and sleep quality in the relationship between attending the exercise intervention and the cognitive changes.

symptoms (indirect effect: β = 0.346; 95% CI = 0.146 to 0.614) and sleep quality (indirect effect: β = 0.428; 95% CI = 0.112 to 0.824).

4. Discussion

The aims of this study is to investigate the effects of a 16-week moderate-intensity aerobic stepping exercise programme on cognitive function and health-related quality of life of Chinese elderly people with mild cognitive impairment, and the mechanisms underlying the exercise-cognition relationship. This study echoes the cognitive-enhancing benefits of moderate-intensity aerobic exercise amongst a Chinese clinical cohort. This study even finds that the control group showed deteriorated cognitive function over time, the participants who were engaged in regular physical exercise had significant improvement in the same health parameter. This finding implies that moderate-intensity aerobic exercise training can meet the treatment goal of preventing disease deterioration among elderly people with mild cognitive impairment. By incorporating a mediating analysis, this study adds further evidence to indicate that cognitive benefits of physical exercise are manifested through its positive effects on two cognitive risk factors, including depressive mood and poor sleep quality. This exercise intervention also effectively reduces the effect of cognitive decline on the overall well-being of elderly people with mild cognitive impairment.

4.1. Cognitive benefit of exercise training

The cognitive benefits of the 16-week moderate-intensity stepping exercise are consistent with the findings reported in previous studies for elderly people with mild cognitive impairment. However, previous studies have consistently indicated that a longer-term exercise training of at least half a year to up to one year is needed to produce such beneficial effect (Baker et al., 2010; Lautenschlager et al., 2008; Nagamatsu et al.,2012; van Uffelen et al., 2008). The present study has developed an exercise training protocol of a shorter duration (i.e. 16 weeks) to achieve a similar effect. Several design characteristics of the exercise protocol may explain for such difference. Firstly, the 16-week exercise program is developed according to the recommendations of the ACSM, so that participants would have regular exercise practice thrice a week. The regular aerobic exercise as compared with previous studies (i.e. two times per week at most) (Nagamatsu et al., 2012; van Uffelen et al., 2008) would result in cardiovascular and mood-related changes, which favour cognitive functioning. Secondly, the use of stepping exercises rather than a walking programme on a flat surface may be a better exercise modality to help the participants reach moderate-intensity exercise training. By teaching the participants how to use the Borg's scale to pace their activity, the instructor found that they had achieved moderate-intensity exercise output most of the time during the training phase. Exercise intensity monitoring has seldom been mentioned in previous studies (Lautenschlager et al., 2008; van Uffelen et al., 2008). Thirdly, the exercise protocol corresponds to the stepping exercise with upper limb movements, which assimilate daily activities, to prevent boredom and support good body movement. Such arrangement might request the participants to follow the instructions well throughout the exercise session, thereby unintentionally providing a sort of attention and short-term memory training. The stepping exercise training in this study has attained a moderate to large effect size in improving the cognitive function of the elderly with mild cognitive impairment. All the mentioned design characteristics may explain for such a greater effect as compared with the findings reported in a systematic review on exercise training for the same clinical cohort (Song et al., 2018b).

4.2. Effects of exercise training on health-related quality of life

This study also identifies the benefits of the stepping exercise training on reducing the effect of cognitive decline on health-related quality of life of elderly people with mild cognitive impairment. Compared with previous studies that failed to identify similar effects of a 6-month moderate-intensity aerobic walking programme (Lautenschlager et al., 2008; van Uffelen et al., 2007), the unique design characteristics of the current exercise protocol and the use of a disease-specific measure may explain for the different findings. In particular, the participants in the present study had remarkable improvement in vitality, positive outlook on oneself and overall life satisfaction. This improvement in cognitive function would possibly result in such positive changes on one's health perception. Previous studies that examined the life experience of people with mild cognitive impairment have consistently found that the reduced cognitive capacity has disrupted their activity pattern, reduced their social engagement and caused a sense of reduced strength and poor self-concept to the clients (Berg et al., 2013; De Vriendt et al., 2012). The present study suggests that the exercise training may help ameliorate such detrimental disease effects on the clients.

4.3. Depressive symptoms and sleep quality mediated the exercise–cognition relationship

This trial is the first to identify that the cognitive-enhancing effects of exercise are mediated by reduced depressive mood and improved sleep quality. These findings elucidate the therapeutic effects of exercise on cognitive function and suggest the potential psychological and sleep-related mediating pathways in explaining the exercise–cognition relationship. These findings have strong implications, because depressive symptoms and sleep complaints are highly prevalent amongst patients with mild cognitive impairment. For depressive symptoms, we report that the prevalence of depressive symptoms measured by GDS in mild cognitive impairment is 31.8% compared with that in cognitively healthy controls (5.5%) (Song et al., 2018a). For sleep disturbance, McKinnon et al. (2014) reported that the prevalence of sleep disturbance as indicated by the PSQI is 63% in mild cognitive impairment over the 5.5% in the cognitive healthy controls. These two conditions greatly interfere the normal life of elderly people with mild cognitive impairment and considerably predict further cognitive decline as indicated by large-scale longitudinal studies (Diniz et al., 2013; Shi et al., 2018).

The mediating roles of depressive mood and sleep quality in the exercise–cognition relationship can be explained in terms of the ways by which exercise lessens the detrimental effect of these two factors on the cognitive function in terms of functional and physiological perspectives. From the functional perspective, depressive mood and poor sleep are highly debilitating in nature, and both conditions are characterised by mental and physical fatigue and poor motivation. These problems would make concentrating difficult for elderly people with mild cognitive impairment and would make them compromise their cognitive performance (McRay et al., 2016; Walker, 2009). Meanwhile, using exercise to improve depressive mood and sleep quality would reduce their dysfunctional effect on cognitive function. From the physiological perspective, depressive symptoms and poor sleep are associated with neurophysiological alternations. Depression down-regulates the expression of neurotrophic factors in the brain environment, resulting in neuronal atrophy and shrinkage of hippocampus (Molendijk et al., 2014); therefore, relieving depressive symptoms through exercise training could restore the expression of neurotrophic factors and promote hippocampal neurogenesis (Mahar et al., 2014). Meanwhile, poor sleep escalates amyloid-β oligomer production and reduces the metabolic activity in the prefrontal cortex (Kincheski et al., 2017); therefore, improving sleep through exercise would promote the clearance of amyloid-β oligomers and the increase in neural synchrony in the prefrontal cortex (Xie et al., 2013). Through the positive effects of exercise training on depressive mood and sleep quality, exercise may create a favourable functional and physiological condition to increase the cognitive capacity of elderly people with mild cognitive impairment.

5. Limitations

This study has several limitations. Firstly, the sample population might not represent the characteristics of the entire patient group with mild cognitive impairment because that we recruited participants in community healthcare centres through convenient sampling, thereby limiting the generalisability of the findings. Secondly, 20.8% of the participants withdrew from the study, which may compromise the statistical power of this study. Thirdly, only self-reported subjective sleep quality was measured in this study; therefore, the findings did not provide evidence that suggests the role of objective sleep pattern in mediating the exercise–cognition relationship. Fourthly, no evidence indicates the change in the outcome scores to imply clinically significant difference; thus, the result was limited in informing the clinical significance. Finally, the exercise intervention programme in this study was limited to 16 weeks. Hence, conclusions regarding the effectiveness of the exercise programme over longer periods could not be drawn. Further research is needed to explore the above research gaps.

6. Study implications

The current study has implications for practice and research. Firstly, in practice, the successful implementation of this study demonstrated the feasibility of nurse-led, group-based exercise programmes for community-dwelling elderly people with mild cognitive impairment. Nurses in primary care settings could play key roles in educating patients with mild cognitive impairment about the importance of maintaining a physically active lifestyle to protect brain health. The professional training of nurses in implementing exercise interventions should be enhanced to promote the successful application of exercise programmes amongst community-dwelling elderly people with mild cognitive impairment. Secondly, efforts should be devoted to ensuring the compliance of patients with mild cognitive impairment with regular practice as a lifestyle routine. For example, the group-based format enhances the compliance of exercise interventions because of additional social interaction and peer support (Bennett et al., 2018). Involving the patients' family caregivers in exercise training is also beneficial to providing supervision and support (van de Port et al., 2012). Regarding implications for research, considering our findings and the associated limitations, we recommend several refinements in future studies. Firstly, further studies should be performed in other healthcare settings, such as memory clinics and nursing homes, to broaden the clinical application of exercise intervention in the care of patients with mild cognitive impairment. Secondly, future studies should consider long periods of follow-up to evaluate the effectiveness of exercise interventions on delaying or preventing the onset of dementia. Finally, our study identified depressive symptoms and sleep quality as mediators in the relationship between physical exercise and cognitive change. As such, future studies should investigate whether combining exercise interventions with psychological elements and sleep hygiene education have considerable benefits on brain health.

7. Conclusion

This study presented a positive scenario of a 16-week group-based moderate-intensity aerobic exercise programme for improving the cognitive function and health-related quality of life amongst community-dwelling elderly people with mild cognitive impairment. Furthermore, decreasing depressive symptoms and improving sleep quality were firstly identified as part of the possible mechanisms underlying the exercise–cognition relationship. The effectiveness and feasibility of this exercise programme also promoted the need to increase its application against further cognitive decline in elderly people with mild cognitive impairment.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijnurstu.2019.02.019.

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