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Research article

A multicomponent program improved cognitive and physical functions of older adults with lower GDS values

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Abstract

Background: MCI is an intermediate stage between cognitive impairment status and persons with MCI are at high risk of developing AD. This study aimed to investigate the effects of a multicomponent program (aerobic, resistance exercises, cognitive training, music, myofascial release exercises, acupoint stimulation, and oral gymnastics) on the cognitive and physical functions of older adults in community dwellers and it is to clarify which measurement factors are predictive to reverse MCI to normal.

Results: In this study, we measured cognitive functions, physical functions, and the diagnosis of MCI. We assessed factors before (pre-test), and after treatment of 12 training sessions (post-test). The participants were divided into two groups (Improve group and the Non-Improve group). The Mann-Whitney test was used to analyze the differences between pre-and post-test and revealed significant differences in the UWS ($p < 0.05$), WM ($p < 0.01$), SDST ($p < 0.01$), and MMSE ($p < 0.01$). Moreover, binomial logistic regression analysis revealed a significant association of the Improved group with the GDS-15 (Odds ratio, 0.587; 95% Confidence Interval [95% CI], 0.309-0.791; $p = 0.003$) and MMSE (Odds ratio, 0.494; 95 % CI, 0.360-0.957, $p = 0.033$).

Conclusion: This study indicated that this program improved physical and cognitive functions in those who were not prone to depression before treatment and suggests that the GDS measurement might be able to predict the intervention effects of a multicomponent program.

Abbreviations

MCI: Mild Cognitive Impairment; AD: Alzheimer's Disease; UWS: Usual Walking Speed; WM: Word list Memory; SDST: Symbol Digit Substitution Test; MMSE: Mini-Mental State Examination; GDS-15: Geriatric Depression Scale-15

Introduction

The rate of global population aging is increasing steadily, contributing to the increased risk of developing cognitive dysfunction and frailty [1]. As well known, Japan, in particular, is aging faster than any other country. As an issue for the elderly, cognitive decline is a crucial issue not only for patients but also for their families and caregivers. Notably, Alzheimer's Disease (AD) is becoming the fifth leading cause of death among the elderly over 65 years old, and 115 million people worldwide will suffer from AD by 2050 [2,3]. Mild Cognitive Impairment (MCI) is an intermediate stage between a state of impaired cognitive function and the persons with MCI are at high risk of developing AD [4,5] and it has been reported that 40% of those diagnosed with MCI will progress to AD after 4 years [6]. Since it has been reported that MCI could reverse a normal cognitive function with effective interventions before the progression of dementia, it is important to perform cognitive tests at an early stage. Unfortunately, pharmacotherapy does not yet exist as a treatment modality for persons with MCI. Peterson, et al. had been conducted an RCT comparing vitamin E and donepezil in patients with MCI [7]. Vitamin E did not postpone progression

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to Alzheimer's disease at any time node and proved ineffective for MCI patients, and donepezil significantly slowed the progression of AD during the first 1 year of the treatment year but did not reduce the rate of progression to AD after 3 years.

Many previous studies have shown that intervention with an excise program could improve the cognitive functions of older adults with MCI [8-10]. In various exercise programs, aerobic exercise is expected to be particularly effective to reduce the risk of AD. Neeper, et al. reported that 2 days of wheel-running increased brain-derived neurotrophic factor (BDNF) in the hippocampus and caudate cortex and promoted neuronal function [11]. Some studies have demonstrated that aerobic exercise reduces the age-related decrease in myelin in the corpus callosum by improving cardiorespiratory fitness and maintaining white matter integrity [12]. It has been shown that regular aerobic exercise acts as a promoter of "brain health", the mediator of neural homeostasis and, through neuroprotective and neurorestorative mechanisms, against brain aging [13]. Moreover, resistance training is another promising approach for cognitive enhancement. For example, Cassilhas, et al. has been reported that when older adult participants underwent moderate- or high-intensity resistance training, levels of insulin-like growth factor 1 (IGF-1), which promotes neuronal growth, were higher than in the control group [14].

Suzuki, et al. devised a treatment program of a dual-task format in which physical exercise and cognitive tasks are performed simultaneously [15]. Dual tasks require executive functions that are particularly important for Activities of Daily Living (ADLs). Doi, et al. have reported that increased prefrontal activation during dual-task tasks correlated with executive function for older adults with MCI [16]. Other previous studies have shown that interventions using dual-task task training could be a promising approach for persons with MCI [17,18]. Oswald, et al. have reported that combining cognitive and physical exercises may be more effective than either alone and raised the point that cognitive decline is multicausal and onefold intervention will possibly remain insufficient [19]. Thus, limited research examined or evaluated the effects of the multicomponent program on health outcomes, and a multi-component program could be more effective than a single type of training for improving cognitive function for older adults with MCI. Regarding this, the aim of this study is to investigate the effects of a multicomponent program (aerobic, resistance exercises, cognitive training, music, myofascial release exercises, acupoint stimulation, and oral gymnastics) on the cognitive and physical functions of older adults in community-dwellers. Furthermore, it is to clarify which measurement factors are predictive to reverse MCI to normal.

Materials and methods

Participants

Participants were recruited from three municipalities: the city of Mitane, the city of Katagami, and the village of Ogata in Akita prefecture, Japan. The target population is 80 people aged 65 and over who are able to walk independently and live at home without assistance. Participants were considered ineligible if they met any of the following criteria: (1) diagnosis of AD or other types of dementia; (2) serious mental disorder (depressive disorder, bipolar disorder, and schizophrenia); (3) history of brain injury; (4) unstable cardiac, renal, lung, liver, or another severe chronic disease. The demographic data comprised age, gender, education, and health variables including body mass index (BMI) [kg/m2] and geriatric depression scale-15 (GDS-15). We divided participants who had MCI on the pre-test Non-MCI on the post-test into the improved group, and the other participants into the Non-Improved group. The study was conducted from May 13, 2021, to March 12, 2022.

Study design and procedures

This proposed study is a before-after study with pre-test and post-test. The present study's proposal was approved by the ethics committee (approval No. 1649). Participants will receive 90 minutes of training once a week for a total of 12 training sessions with a health and fitness instructor. Outcome measures, including cognitive functions, physical functions and determination of MCI, will be evaluated before the treatment (pre-test), and after 12 training sessions (post-test).

Intervention

As previously reported [19], a multicomponent exercise intervention was performed, where cognitive training was incorporated into the sessions combined with resistance and aerobic training. The participants engaged in 90-minute training sessions once a week for three months conducted by health and fitness instructors. The content of the program is to maintain and improve ADLs and lead to preventive care for the elderly. Each session included as follows; First, started with bending exercises such as per and lower limb stretching. After that, physical training was 20 min aerobic exercises with cognitive stimulation, and 20min resistance exercises with cognitive stimulation. The therapist adjusted the level of aerobic exercise according to each participant's ability, and the participant rested when needed. Dumbbells suited the person was used for the upper extremity strength program, and squats were used for the lower extremity strength program. These cognitive exercises included puzzles, addition, subtraction, and grid exercises. The music was a folk song from Akita prefecture, which was sung while exercising. Moreover, myofascial release training focused on the plantar muscles was performed for 10min using a foam roller to stimulate blood circulation. After that, self-acupressure was performed for 10 min on the soles of the feet. Acupressure is one of the major modalities of traditional Chinese medicine. Finally, oral gymnastics were performed for 10 min.

Outcome

The present study applied the National Center for Geriatrics and Gerontology Functional Assessment Tool (NCGG-FAT) [20,21], and Mini-Mental State Examination (MMSE) [22,23] to assess cognitive functions in the participants and to divide the participants into non-MCI and MCI. Participants completed the NCGG-FAT subtests as follows; (1) word list memory (WR), (2)

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Trail Making Test A version, (3) Trail Making Test B version, and (4) Symbol Digit Substitution Test. The WM test consists of immediate recognition and delayed memory performed using a computer. A higher score in WM indicates a better word list memory. In the TMT-A subtest, participants are instructed to choose the target number as quickly as possible. The target numbers 1 to 15 are displayed in pieces on a screen. The TMT-B consists of selecting the target numbers and characters in sequence. The TMT-A & B of lower numbers indicates greater executive functions. In the SDST, participants are asked to choose the number corresponding to the target symbol as quickly as possible. A higher score on the SDST indicates a higher ability for information processing. We also examined motor function in terms of usual walking speed (UWS) and grip strength (GS).

Statistical analysis

The Wilcoxon signed-rank test was applied to compare the results of UWS, GS, WM, TMT-A & B, SDST, and MMSE between the pre-test and post-test of this program for participants. Next, we compared the improved group and Non-Improved group regarding cognitive functions for age, gender, BMI, BI, medication, education, and GDS-15 by using the Mann-Whitney test. Moreover, The Wilcoxon signed-rank test was applied to compare the results of UWS, GS, WM, TMT-A & B, SDST, and MMSE between the pre-test and post-test for each group. Finally, to confirm which factors predict the effect on the improvement of MCI by this program, we applied the binomial logistic regression analysis as a dependent variable for the improved group and the Non-Improved group. As independent variables for the regression modeling, age, gender, BMI, medication, education, GDS-15, UWS, GS and MMSE. SPSS Version 27.0 for Windows (SPSS INC., Chicago, IL) was used for the analysis, and the level of significance was set at $p = 0.05$.

Results

Of the 80 participants, 59 were able to complete the 12 training sessions. The basic characteristics of participants and results of the comparison of the pre-test and post-test of this multi-component program were shown in Table 1. The Mann-Whitney test was used to analyze the differences between the pre-test and post-test and revealed significant differences in the UWS ($p < 0.05$), WM ($p < 0.01$), SDST ($p < 0.01$), and MMSE ($p < 0.01$). Thus, walking speed, memory, information processing speed, and cognitive functions were improved by this multi-component program.

Next, we divided participants who had MCI changed to Non-MCI by this program as "Improved group", and the other participants as "Non-Improved group" to clarify which factors this program was effective for (Table 2). According to MCI determination by NCGG-FAT and MMSE, 59 participants were divided into the Improved group (n=16), and the Non-Improved group ($n = 43$). Analysis of differences in participant characteristics by the Mann-Whitney test showed that there was a significant difference in gender ($p < 0.05$) and GDS-15 ($p < 0.01$) between the Improved and Non-Improved groups. Next,

Table 1: Characteristics of participants, and results of pre-test and post-test of multi-component program.

	Median	IQR			
age (years)	80.0	12.0			
Gender (n)	male: 15, female: 44				
BMI (kg/m2)	24.9	4.5			
Medication (n)	3.0	5.0			
Education (years)	12.0	3.0			
GDS-15 (score)	2.0	4.5			
	Pre-test		Post-test		
	Median	IQR	Median	IQR	*p* value
UWS (m/s)	1.16	0.30	1.23	0.31	0.012*
GS (kg)	22.7	6.1	22.9	7.0	0.514
WM (score)	10.0	4.8	11.7	4.0	0000**
TMT-A (sec)	22.0	11.0	23.0	13.0	0.615
TMT-B (sec)	44.0	41.0	45.0	28.0	0.874
SDST (score)	34.0	14.0	37.0	18.0	0.000**
MMSE (secore)	28.0	4.0	29.0	3.0	0.000**

*$p < 0.05$; **$p < 0.01$, Wilcoxon signed rank test

GDS-15: Geriatric Depression Scale-15; GS: Grip Strength; UWS: Usual Walking Speed; WM: Word List memory; TMT-A: Trail Making Test A version; TMT-B: Trail Making Test B version; SDST: Symbol Digit Substitution Test; MMSE: Mini-Mental State Examination.

we compared the pre-test and post-test in the participants within groups. As a result of the Wilcoxon signed-rank test, there were significant differences in the SDST ($p < 0.05$) and MMSE ($p < 0.012$) in the Improved group, and UWS ($p < 0.05$), WM ($p < 0.01$), and SDST ($p < 0.01$) in Non-Improved group at the post-test.

Finally, to confirm which factors predict the effect on the improvement of MCI by this program, we performed a binomial logistic regression analysis (Table 3). As a result, GDS-15 (Odds ratio, 0.587; 95% Confidence Interval [95% CI], 0.309-0.791; $p = 0.003$) and MMSE (Odds ratio, 0.494; 95 % CI, 0.360-0.957, $p = 0.033$) were significantly associated with Improved group (Table 3). The goodness of fit for the regression model was also well observed in the results of the model $\chi 2$ test ($p < 0.01$), and the Hosmer–Lemeshow test ($p = 0.704$), with a higher percentage of correct classifications of 71.2%.

Discussion

Given the limited effectiveness of pharmacological treatments against cognitive decline in the elderly, it is a critical issue for developing effective non-pharmacological intervention programs to address the cognitive decline of MCI. Recent studies have indicated that combining cognitive training with other interventions could have more cognitive benefits than just one intervention approach [24]. In this study, we performed a multi-component program (aerobic, resistance exercises, cognitive training, music, myofascial release exercises, acupoint stimulation, and oral gymnastics) and showed the program had positive effects on the UWS, WM, SDST, and MMSE ($p < 0.01$) compared to pre-intervention (Table 1). Consistent with growing evidence demonstrating

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Table 2: Characteristics and results of pre-test and post-test in each group.

	Improve group (*n* = 16)					Non-Improve group (*n* = 43)				
	Median		IQR			Median			IQR	*p* value
age (years)	81.0		7.0			79			12	0.966
Gender (n)	male: 7, female: 9					male: 8, female: 35				0.049†
BMI (kg/m²)	25.6		5.9			24.7			4.2	0.434
Medication (n)	1.2		3.0			4.0			5.0	0.872
Education (years)	12.0		0.0			12.0			4.0	0.615
GDS-15 (score)	1.0		2.0			3.0			5.0	0.016†
	Pre-test		Post-test			Pre-test		Post-test		
	Median	IQR	Median	IQR	*p* value	Median	IQR	Median	IQR	*p* value
UWS (m/s)	1.10	0.44	1.23	0.42	0.093	1.16	0.30	1.25	0.31	0.046*
GS (kg)	23.3	11.7	22.7	15.3	0.865	22.1	5.7	22.9	6.8	0.371
WM (score)	10.2	4.9	11.8	3.2	0.079	9.7	5.7	11.7	4.8	0.001**
TMT-A (sec)	22.7	15.3	21.5	15.0	0.575	22.9	6.8	23.0	12.0	0.821
TMT-B (sec)	48.5	43.0	50.0	28.0	0.221	44.0	44.0	45.0	48.0	0.408
SDST (score)	35.0	9.0	38.5	11.0	0.029*	33.0	17.0	36.0	19.0	0.003**
MMSE (secore)	26.5	3.0	29.5	1.0	0.001**	28.0	4.0	29.0	9.0	0.110

†p<0.05; Mann-Whitney test, *p<0.05; **p<0.01, Wilcoxon signed-rank test

GDS-15, Geriatric Depression Scale-15; GS, Grip Strength; UWS, Usual Walking Speed; WM, word list memory; TMT-A, Trail Making Test A version; TMT-B, Trail Making Test B version; SDST, Symbol Digit Substitution Test; MMSE, Mini-Mental State Examination.

Table 3: Models according to binomial logistic regression analysis.

	coefficient(β)	odds ratio	95% CI	*p* value
GDS-15	-0.533	0.587	0.309, 0.791	0.003**
MMSE	-0.705	0.494	0.360, 0.957	0.033*
age	-0.005	0.995	0.873, 1.134	0.941
Gender	-1.625	0.197	0.034, 1.149	0.071
BMI	0.016	0.160	0.967, 1.068	0.524
Medication	-0.038	0.963	0.770, 1.203	0.738
Education	-0.102	0.903	0.482, 1.694	0.751

*$p < 0.05$, **$p < 0.001$, model $\chi 2$ test $p < 0.01$, Hosmer Lemeshow test $p = 0.704$, percentage of correct classifications 71.2%

the beneficial effect of other multitask programs [25,26], this program for 3 months also had not only improved motor functions, but also the cognitive functions of those who elderly participated. Since the aging phenomenon impaired physical and cognitive functions, such as muscular strength, power, mobility, and orientation, memory, information processing ability, they seem to be more pronounced in community-dwellers of the declining population like Akita. This multi-component program had no harmful effects and was cost-effective, and our results suggested that the aging process could be delayed by these interventions. Furthermore, Barnes, et al. recruited older adults with cognitive complaints that the participants who received both aerobic exercise and mental activity training showed improvements in cognitive function than those who received a single mode (aerobic exercise only or mental activity only) of training [27].

Representative and effective multicomponent interventions for the prevention of dementia are physical exercise, dietary, cognitive training, and risk management of cardiovascular disorders such as blood pressure and blood glucose levels [28]. Although it is not clear which components were most effective in our improvements, myofascial release training and acupressure, which improve blood circulation, could be also effective for physical and cognitive functions. So far, the effect of myofascial release on the cognitive functions of older adults with MCI has not been reported. Similarly, in terms of acupressure, the evidence is very limited now since there are few studies on the treatment of MCI. Although our acupressure points were different, J Sun, et al recently reported that combined acupressure and cognitive training could improve the cognitive functions of older adults with MCI [29].

Moreover, in order to clarify which measurement factors the intervention of this program is effective, we divided the participants into the MCI improvement group and the non-improved group. Comparing the improved and non-improved groups, the improved group had significantly lower GDS values (Table 2). Furthermore, when comparing the differences in the measured values before and after the intervention within the two groups, both groups showed an improvement trend in physical and cognitive functions, and in particular, WM and SDST were an improvement. Finally, the results of binomial logistic regression analysis also revealed a significant correlation with GDS values (Table 3). These results indicated that this program improved physical and cognitive functions in those who were not prone to depression before the intervention and suggest that the GDS measurement might be able to predict the intervention effects of a multicomponent program. Lorenz BD, et al reported that patients with depression show negatively biased information processing that affects attention and memory as well as their reaction to feedback, and there is an increased motivation to avoid negatively evaluated conditions and at the same time a reduced motivation to approach positive

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goals [30]. Therefore, it may have affected the effectiveness of the intervention because participants with low depressive symptoms were emotionally stable and more self-motivation.

The contents of this program are self-administered, which is important for widespread dissemination. Not only do some older adults have limited opportunities to attend training programs away from their lives, but training programs require the involvement of professional instructors who may not always be available [31]. This program including myofascial release training and acupressure is non-invasive and can be performed by non-professionals. Once acquired, older adults can do it themselves without the limitation of field or equipment at their homes. Thus, widespread dissemination of a training technique of a multicomponent program will require self-administration by older adults.

The present study had several limitations. First, the sample size of this study, a Mann–Whitney test with the number of groups = 2, α = 0.05, power = 80%, and effect size = 0.5 was insufficient to estimate the sample size of the participants (n = 102) to detect a clinically significant effect [32]. In a further study, we plan to increase the sample size. Second, there were significantly fewer male participants in this study. Therefore, it is important to take into account that not only age but also gender, influence the effect of our programs. Third, the participants were not blind to interventions, and this study lacked a control group with no treatment. Case-control comparisons with blinding are needed in addition to before and after the intervention. Finally, the assessment of cognitive function was limited in this study, therefore we need to perform more complete measurement tools and collect brain functional scans such as functional MRI or SPECT. These requirements should be adjusted for further additional research in the future.

Conclusion

This study showed that our multi-component program could improve the cognitive and physical functions of older adults in community dwellers. In addition, comparing the MCI-improved and non-improved groups, the improved group had significantly lower GDS values. These results indicated that this program improved physical and cognitive functions in those who were not prone to depression before the intervention, and we suggest that the GDS measurement might be useful for predicting the intervention effects of a multicomponent program.

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