Physical exercise as an intervention in women with mild cognitive impairment

Numerous studies have found that people who are physically active seem less likely than sedentary persons to experience cognitive decline and dementia in later life. However, several methodological issues need to be addressed and future research should include more representative samples, longer interventions and evaluate the intervention effect after the treatment. The purpose of the present investigation was to determine whether a physical activity exercise intervention reduces the rate of cognitive decline among older women diagnosed with Mild Cognitive Impairment Clock Drawing Test (CDT). The study was based on a pre and post test design using The Fullerton’s Functional Fitness Test. This battery measures a variety of physiological parameters. Participants were recruited by a randomized sampling method. Fifteen women aged 55-80 years old (70.3±7.03), diagnosed with MCI, volunteered to participate in the study. The participants were randomized into 2 groups and completed a 12-weeks training period. The Experimental group (E) received physical training whereas the Control group (C) did not. Both groups followed the cognitive intervention program. Strong correlations in experimental group were found between CDT and chair sit & reach before (p<0.024, r=0.87), and after the intervention (p<0.023, r=0.87) and between CDT and 8-foot Up&Go (p<0.02, r=-0.88) before and after the intervention (p<0.01, r=-0.89). There were significant negative correlations in the control group before and after the intervention between

**Key Words:** Functional fitness test, Physical activity, Cognition, Physical training.
MMSE and 8-foot Up& Go (p<0.02, r=-0.88 and p<0.004, r=-0.95, respectively). Moreover, a strong correlation between CDT after the intervention and chair sit & reach (p<0.006, r=0.94) and arm curl (p<0.02, r=0.88) was found. In this study of older women with MCI, a 12-weeks physical exercise program combined with a cognitive program provided an improvement in physical status and a cognitive stability. However, due to the limitations of the study, present findings must be interpreted with great caution.

INTRODUCTION

Mild Cognitive Impairment (MCI) is characterized by a slight but noticeable and measurable decline in memory according to the Petersen’s criteria [15]. Older adults with MCI are at higher risk of developing dementia (12% per year) than normal elderly (1-2% per year) [19]. MCI is widely viewed as being an optimal stage at which to intervene with preventative therapies (Physical exercise and Cognitive training). Several prospective studies have shown that physically active people have a lower risk of developing dementia compared with those who are less physically active. There has been growing interest in exercise training as an alternative intervention approach. Positive effects of physical exercise on the cognitive function of older adults have been demonstrated in a number of clinical studies [4, 20]. Recent studies suggest that physical exercise is associated with improvements in cognitive function. Resistance and aerobic training has been found to benefit cognitive functioning and result in functional plasticity in healthy older adults [13]. Furthermore, a walking exercise intervention for older adults in Japan, has revealed improvements in word fluency, social interaction and motor function [11]. Older adults with MCI participated in a 24-weeks home based exercise training program and improvement was reported in Alzheimer Disease Assessment Scale-Cognitive Subscale [10]. Additionally, women with amnestic MCI have demonstrated improvements in selective attention, conflict resolution, processing speed and verbal fluency after a six-month aerobic training intervention [2].

The primary aim of this study is to investigate the effects of a physical exercise intervention in cognitive performance in older women diagnosed with mild cognitive impairment (MCI). Is a well-recognized risk factor for dementia, characterized by cognitive decline which however does not affect everyday functioning. Therefore, identifying and treating older adults with MCI is important to prevent the progression of Alzheimer Disease [3].
METHODS

Study design

This study was based on a pre and post test design. Participants were recruited by a randomized sampling method.

Participants

Fifteen women with MCI aged 55-80 years old (70.3±7.03), volunteered to participate in the study. All of them participated in the non-pharmacological interventions (physical and cognitive training) of the three Day Care Centers of Athens Association of Alzheimer Disease and Related Disorders. Their mini-mental state examination (MMSE) scores ranged from 26 to 30. None of the subjects had previous experience with physical exercise sessions. Exclusion criteria were severe musculoskeletal impairment (inability to participate in the program) and no diagnosis of dementia. The study protocol was approved by the Ethics Committee of Alzheimer Association. Prior to participation, all participants were informed in detail about the study and signed a written informed consent document.

Randomization and Intervention

The participants were randomized into 2 groups and completed a 12-weeks training period. The Experimental group (E, n=9) received physical training and the Control group (C, n=6) did not follow the physical exercise intervention program. Both groups followed the cognitive intervention program of the three Day Care Centers of Athens Association of Alzheimer Disease and Related Disorders.

Exercise Intervention

The mean duration of the physical exercise program for all participants was 12 weeks. There was an average of 3 sessions per week, each lasting approximately 45 minutes. The exercises were performed under the supervision of an experienced instructor. All sessions were performed in the morning. The exercise intervention consisted of 10 minutes of warm-up exercise, 30 minutes of core content and 5 minutes of cool-down and stretching exercises. Free weights, elastic bands and medicine balls were used for the resistance training exercises. Particularly, strength training exercises included biceps curls, seated row, minisquats, minilunges, calf raises, triceps extensions, abdominal crunches, and exercises for
shoulders and the back. The intensity of the training stimulus was at a work range of 8 to 12 repetitions (two sets) up to 15 repetitions increase when the repetitions were completed without discomfort. The weights ranged from 1 to 1.5 Kg. The aerobic training was conducted in stationary cycling and the intensity was at approximately 40% of one’s age specific target heart rate and was increased up to 60%- 65%. Practice session was followed by a 5-minute cool-down program consisting of stretching exercises and range of motion exercises.

Cognitive Intervention

The intervention program was tailored to the needs of people with MCI. All interventions were performed on a group basis by one specialized clinician. No individual intervention was performed. The intervention program consisted of multi-domain cognitive training. The cognitive component was designed to cover all cognitive functions: attention, memory, language and executive functions. The program lasted 2 hours (1 hour of language activities and 1 hour of other cognitive exercises) and was administered twice a week for a period of 3 months. Cognitive training consisted of both restorative and compensatory exercises such as categorizing information, asking questions and paraphrasing during learning, focusing in a single task, memory tasks with the use of different memory strategies, dual tasks, exercises of executive functions (organizing information, problem solving, decision making and other thinking tasks). Language exercises included word definitions, semantic associations, analogies, synonyms-antonyms, categorization, similarities-differences, anagrams, sentence completion, comprehension of complex sentences and paragraphs, reasoning, creative writing, etc. The selected tasks were of increasing complexity and difficulty.

Anthropometry

Body height was measured to the nearest 0.5 cm using a wall mounted stadiometer (Holtain, UK). Subjects were in standing position wearing no shoes. Participants were weighed to the nearest 0.1Kg on an electronic scale (Tanita TBF 401 A, Japan). No special preparation was required except that participants wore lightweight clothing for these measures. Body Mass Index (BMI) was calculated as body weight in Kilograms divided by the squared height in meters. Anthropometric measures were firstly obtained (same day, before physical testing).

Physical Testing

The Fullerton’s Functional Fitness Test was administered [16] by one trained
research assistant, assisted by a recorder. This battery measures a variety of physiological parameters and functional activities and is especially useful for tracking a person over time. The test items were: 1) arm curl for upper body strength. The score is the total number of hand-weight curls performed in 30sec, 2) 30-Second Chair Stand to assess lower body strength and the score is the total number of stands executed within 30 sec, 3) 2-Minute Step Test (aerobic endurance). The score is the number of times right knee reaches the required height, 4) Chair Sit-and-Reach (Lower body flexibility) and the score is the distance achieved between extended fingers and tip of toe, 5), Back Scratch measures the upper body flexibility and the score is the distance between extended middle fingers, and 6) 8-foot Up-and-Go to measure agility and dynamic balance and the score is the best time achieved to get up from a seated position, walk 2.44 m, turn, and return to seated position. Subjects were familiarized to the Fullerton’s test one week before the actual exercise testing. Firstly anthropometric measures were obtained. After 5 minutes warm up in stationary cycling and stretching exercises, the Functional Fitness test was performed by each participant. The order in which the items were performed was the following: arm curl, back scratch, 30s chair stand, chair sit and reach, 8ft up and go (2.44 m) and 2 minute Step Test. The test battery was performed before and after the 12-week intervention under the same conditions.

Cognitive Testing

Mini-Mental State Examination (MMSE) was performed before and after the intervention by a trained Psychologist. Dementia is characterized by multiple cognitive deficits, which are evaluated through a neuropsychological assessment. Brief cognitive tools are used as screening tools in order to obtain a score of global index of cognitive functioning [8]. Mini Mental State Examination, a screening tool developed for the assessment of cognitive performance of older adults is an instrument widely used in clinical practice and research. MMSE evaluates the performance in five areas of cognitive functioning: orientation, registration, attention and calculation, recall and language, with a maximum score of 30. A cut-off score of 24/30 is concerned to be an indicator of cognitive impairment [5]. Additionally, Montreal Cognitive Assessment (MOCA) was used. Visuospatial abilities and organizational skills were monitored via the Clock Drawing Test (CDT). Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MOCA) and Clock Drawing Test (CDT) for each participant took place a day before physical testing.

Statistical Analysis

All data were analyzed using IBM SPSS STATISTICS (version 20). Descriptive
statistics (mean, standard deviation) were calculated for all variables. Shapiro-Wilk test of normality was used for all variables because of the small sample size. Spearman’s Rank correlation coefficient ($\rho$) was used to examine possible relationships between MMSE, CDT, MOCA and physical fitness variables. The Wilcoxon signed Rank was used to examine the pre and post difference of each variable and the Mann-Whitney U test to examine the differences between the experimental and control group. Two- mixed Anova repeated measures were used to examine the difference between and within subjects. The statistical significance was set at $p< 0.05$.

RESULTS

Physical Performance outcomes

The groups (E vs C) did not differ significantly at baseline by age (yrs) and height (m). The groups differed significantly on weight before the intervention ($t=-3.16$, $p<0.008$) and BMI ($t=-3.19$, $p<0.007$) and after the intervention ($t=-3.17$, $p<0.007$ and $-3.11$, $p<0.008$), respectively. Table 1 presents the mean values of each variable and the differences between experimental and control group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experimental Group (n=9)</th>
<th>Control Group(n=6)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>68.8±8.31</td>
<td>72.5±4.27</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>58.9±6.89</td>
<td>74.5±12.36</td>
<td>0.007</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.1±3.43</td>
<td>30.9±4.9</td>
<td>0.008</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.56±0.82</td>
<td>1.55±0.73</td>
<td>NS</td>
</tr>
<tr>
<td>30-s Chair Stand (repet.)</td>
<td>15.56±4.55</td>
<td>13.6±4.3</td>
<td>NS</td>
</tr>
<tr>
<td>Arm curl (repet.)</td>
<td>20.3±4.09</td>
<td>22.8±3.9</td>
<td>NS</td>
</tr>
<tr>
<td>Chair Sit &amp; Reach (cm)</td>
<td>-2.5±4.78</td>
<td>0.5±9.3</td>
<td>NS</td>
</tr>
<tr>
<td>Back Scratch (cm)</td>
<td>-10.77±13.75</td>
<td>-4.6±13.6</td>
<td>NS</td>
</tr>
<tr>
<td>Foot Up &amp; Go (sec)</td>
<td>5.71±1.25</td>
<td>6.9±1.23</td>
<td>NS</td>
</tr>
<tr>
<td>2 Minute Step Test (steps)</td>
<td>88.3±20.15</td>
<td>77.0±30.2</td>
<td>NS</td>
</tr>
</tbody>
</table>
Training resulted in a significant difference in performance between the groups in the 30-s chair stand after the training period (Fig.1).

![Graph showing difference in Chair Stand between experimental and control groups.](image)

**Fig.1.** *30-s Chair stand test difference between the two groups (mean, SD) after the intervention*

The comparison between the two groups after the 12-week intervention revealed better time in the experimental group than in control group on foot up & Go test ($p<0.004$) and on 2 Minute step test (Fig.2).

![Graph showing difference in 2 Minute Step Test between experimental and control groups.](image)

**Fig 2.** *Difference between the two groups on the 2 Minute step test (mean,SD) after training period*
The experimental group after the intervention was improved on 30-s chair stand \((t=-2.79, \text{ df}=8, p<0.02)\) and on arm curl \((t=-2.39, \text{ df}=8, p<0.04)\). Additionally, the control group did not present any significant improvement in any item of the functional fitness tests (Table 2).

**Table 2.**

*Mean values at baseline and after the 12 weeks period (mean, SD) of control group.*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before</th>
<th>After</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-s Chair Stand (repet.)</td>
<td>13.6±4.3</td>
<td>13.8±3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Arm curl (repet.)</td>
<td>22.8±3.9</td>
<td>21.3±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Chair Sit &amp; Reach (cm)</td>
<td>0.5±9.3</td>
<td>2.2±2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Back Scratch (cm)</td>
<td>-4.6±13.6</td>
<td>-7.3±8.4</td>
<td>NS</td>
</tr>
<tr>
<td>Foot Up &amp; Go (sec)</td>
<td>6.9±1.23</td>
<td>7.02±1.4</td>
<td>NS</td>
</tr>
<tr>
<td>2 Minute Step Test (steps)</td>
<td>77.0±30.2</td>
<td>66.8±27.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Cognitive Performance outcomes**

The two groups did not differ at baseline and after the intervention on MMSE, CDT and MOCA assessment. The scores on these tests remained almost unchangeable after the intervention program in both groups (Table 3).

**Table 3.**

*Mean (SD) of the scores in cognitive performance tests.*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Experimental Group Before</th>
<th>Experimental Group After</th>
<th>Control Group Before</th>
<th>Control Group After</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>27.5±1.33</td>
<td>27.9±1.45</td>
<td>28.0±1.55</td>
<td>27.6±2.16</td>
</tr>
<tr>
<td>CDT</td>
<td>8.0±2.76</td>
<td>8.17±2.71</td>
<td>8.5±1.76</td>
<td>8.0±1.89</td>
</tr>
<tr>
<td>MOCA</td>
<td>21.3±1.2</td>
<td>23.3±1.51</td>
<td>20.2±2.25</td>
<td>22.0±2.16</td>
</tr>
</tbody>
</table>
Correlations between cognitive and physical performance

Furthermore, strong correlations in experimental group were found between CDT and chair sit & reach before (p<0.024, r=0.87), and after the intervention (p<0.023, r=0.87) and between CDT and 8-foot Up&Go (p<0.02, r=-0.88) before and after the intervention (p<0.01, r=-0.89). There were significant negative correlations in the control group before and after the intervention between MMSE and 8-foot Up&Go (p<0.02, r=-0.88 and p<0.004, r=-0.95, respectively). Moreover, a strong correlation between CDT after the intervention and chair sit & reach (p<0.006, r=0.94) and arm curl (p<0.02, r=0.88) was found.

DISCUSSION

The overall objective of this study was to examine the effect of a three month physical and cognitive intervention on cognitive performance. To begin with, the functional fitness test showed significant improvements after training in the experimental group suggesting that the training program was sufficient to cause an improvement in these participants. More specifically, the experimental group compared to the control group, had better performance to 30-s chair stand, 2 Minute step test and to 8-foot up&go test. Our findings are similar to Alves et al. [1] and Hicks et al. [7] who also verified a muscular improvement after a training period of 12 to 26 weeks.

The experimental group, who followed the physical and the cognitive intervention program, compared to the control group who did not participate in the physical exercise program, did not present higher scores in MMSE, CDT or MOCA test. The cognitive performance of the experimental group showed a positive trend, unlike to the cognitive scores of the control group, who presented a negative trend.

Although, no statistically significant improvement on cognition performance was found in our study, it is important that there was no cognitive decline in the MCI women who participated in the physical exercise program. In contrast to our results, a study by Scherder et al. [18] which involved motor intervention (walking and hand/ face exercises) concluded that physical activity had a selective effect on cognition, specifically on executive functions. Another study by Olarazan et al. [14] examined the effect of physical activity on cognitive functions of older adults with MCI and Alzheimer disease. Their results were positive after the intervention, but the authors did not analyze the findings separately, so it is not clear which group responded better to the intervention. Additionally, a study by Kim et al. [9] found that MCI patients who followed an exercise programme (18-months intervention) showed significant improvements on multiple domains of cognitive function test and balance test when compared to MCI patients who did not participate on ex-
exercise programme. Another recent study by Sadeghi et al. [17] found that inter-
ventional procedures including physical, mental and combined activities led to an improvement in the memory of 50-70 year-old women with mild cognitive impairment. Finally, in the same line with our findings, a meta-analysis of random controlled trials study found that there is very limited evidence that exercise improves cognitive function in individuals with MCI, although published research is of moderate quality and inconclusive due to low statistical power [6].

The link between physical activity and cognitive function is supported by the significant correlation between CDT (executive function test) and foot up&go test in the experimental group. More specifically, slower time on foot up&go test was associated with lower scores on CDT. A strong relationship was also found between CDT and 2 minutes step test. Furthermore, in the control group a lower score in MMSE was associated with slower time in foot up&go test. Our results were similar to those of McGough et al. [12] who found that longer time on Timed up & go test is associated with lower executive function performance.

The study was limited by the small sample size and the fact that included only women. Even though there are numerous published studies that examine the relationship between physical exercise and cognitive function, it is clear that there are several methodological issues to be solved. Therefore, future research should include more representative samples, longer interventions and evaluate the intervention effect after the treatment.

In conclusion, the findings of the present study suggest that participants improved their physical status and remained cognitively stable. A combination of a physical activity and a cognitive program may represent a non pharmacological strategy against cognitive decline. However, due to the limitations of the study, present findings must be interpreted with great caution.

DISCLOSURES

Eleni Dimakopoulou, Maria Karydaki, Xenofon Apostolopoulos, Dimitra Potamianou and Paraskevi Sakka declare that they have no conflicts of interest pertaining the article.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

The submitted paper, the data and results have not been published anywhere before.

Eleni Dimakopoulou: Wrote the paper, Analysed data
Maria Karydaki: performed the research, wrote the paper
Xenofon Apostolopoulos: performed the research
Dimitra Potamianou: performed neuropsychological testing
Paraskevi Sakka: Designed the research

REFERENCES


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