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Effects of functional tasks exercise on older adults with cognitive impairment at risk of Alzheimer’s disease: a randomised controlled trial

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Abstract

Objective: the aim of this study was to compare the effects of a functional tasks exercise programme to a cognitive training programme in older adults with mild cognitive impairment.

Design: a single-blind randomised control trial with the intervention group compared with an active control group.

Setting: out-patient clinic.
Participants: older adults with mild cognitive impairment (n = 83) aged 60 and older living in the community.

Methods: participants were randomised to either a functional task exercise group (n = 43) or an active cognitive training group (n = 40) for 10 weeks. All outcome measures were undertaken at baseline, post-intervention and 6-month follow-up using Neurobehavioral Cognitive Status Examination, Trail Making Test, Chinese Version Verbal Learning Test, Category Verbal Learning Test, Lawton Instrumental Activities of Daily Living Scale and Problems in Everyday Living Test.

Results: the functional task exercise group showed significant between-group differences in general cognitive functions, memory, executive function, functional status and everyday problem solving ability. The improvements were sustained over time at 6-month follow-up.

Conclusion: a functional tasks exercise programme is feasible for improving cognitive functions and functional status of older adults with mild cognitive impairment. This may serve as a cost-effective adjunct to the existing interventions for populations with mild cognitive impairment.

Trial registration number: ACTRN12610001025022.

Keywords: mild cognitive impairment, functional tasks exercise, geriatric rehabilitation, randomised controlled trial, older people

Introduction

The rising prevalence of cognitive impairment with age increases the potential impact of dementia upon global health and health care. Individuals with mild cognitive impairment (MCI) are at high risk of progressing to Alzheimer's diseases (AD) and other dementias, with reported conversion rate of 12% in 1 year up to 60–100% in 5–10 years [1, 2]. These projections signify the need to identify effective interventions to delay or even revert the disease progression in population with MCI.

The beneficial effects of physical activity/exercise in improving the cognitive functions of older adults with cognitive impairment or dementia have been reported. However, diverse findings can still be found [3]. Snowden et al. (2011) reported in a systematic review that evidence from the effects of physical activity/exercise on cognition in older adults is still insufficient [4]. Nevertheless, there is increasing evidence, such as the Seattle protocol, suggesting beneficial effects of exercise [5] and that exercise training increases plasticity of the human brain [6]. Surprisingly, studies found that although numerous new neurons can be generated in the adult brain, about half of the newly generated cells in the brain die during the first 1–4 weeks [7]. Research has found that spatial learning or exposure to an enriched environment can rescue the newly generated immature cells and promote their long-term survival and functional connection with other neurons in the adult brain [8]. Animal studies have also shown that a combination of exercise and an enriched environment induces a greater increase in neurogenesis than either exercise or environmental enrichment alone [9].

Daily functional tasks are innately cognitive-demanding and involve components of stretching, strengthening, balance and endurance as seen in traditional exercise programmes. Particularly, visual spatial functional tasks, such as locating a key or finding the way through a familiar or new environment, demand complex cognitive processes and play an important part in everyday living [10].

A structured functional tasks exercise programme was developed [11] to facilitate the cognitive functions of older persons with MCI. Details of the functional tasks exercise (FcTSim) programme have been reported previously [11], whereby simulated (Sim) functional tasks (FcT) incorporated with exercise are used as an intervention. The FcTSim programme involved five levels of functional task movement, including unilateral movement, bimanual movement, task switching and body mid-line crossing. Participants were required to perform simulated functional tasks (object placing and collection) following specific patterns of a movement sequence. A chair-rise movement is performed between each table task movement to intensify the exercise demand as well as acting as an interference to facilitate the training effect [12]. A brief description of the five levels of movement is illustrated in Supplementary data available in Age and Ageing online, Appendix S1.

It is hypothesised that FcTSim can be used as a means of cognitive-exercise intervention to influence different cognitive domains leading to improvements in cognitive functions, whereby the functional tasks act as a cognitively demanding activity to provide an enriched environment to influence cognitive functions, further enhanced by the incorporated exercise component.

The aim of this study was to determine whether a FcTSim programme can improve the cognitive functions of older adults with cognitive impairment at risk of AD.

Methods

Study design

The study was a single-blind randomised controlled trial. All outcome measures were conducted by an assessor masked to the group status of the participants. After baseline assessment, participants were randomised to the intervention group (FcTSim) or the active control (AC) group (existing cognitive training) according to a list of computer-generated random numbers, conducted by a hospital staff, which was
concealed until completion of baseline assessments. Ethics approval for this study was obtained from the James Cook University Human Research Ethics Committee and the Hospital Authority Research Ethics Committee.

**Participants**

The study was conducted from December 2011 to April 2013 at the out-patient clinic of Occupational Therapy Department in Hong Kong. Participants with subjective memory complaint or suspected cognitive impairment were referred by the Department of Medicine and Geriatric. Older adults (age 60+) with mild cognitive decline living in the community were eligible for the study if they met the inclusion criteria for MCI [13]: (i) memory/cognitive complaint as reported by the patients or the carers; (ii) objective cognitive impairment in 1 or more domains as revealed by neuropsychological assessment; but with (iii) intact personal self-care functions; (iv) no confirmed diagnosis of dementia. The exclusion criteria were: (i) history of brain lesion/psychoactive substance abuse/co-morbid medical conditions associated with cognitive/functional decline; (ii) clinically significant depression; (iii) known psychiatric cause of cognitive dysfunction; (iv) medical conditions which rendered patients unable to engage in physical activity; (v) taking medications with significant impacts on cognitive function and (vi) significant impairment of vision, hearing or communication that might affect participation in the assessments or the programme. All the participants provided written informed consent. Supplementary data available in *Age and Ageing* online, Appendix S2.

**Measurements**

Assessments were undertaken at baseline, post-intervention at 11–12 weeks and during the follow-up at 6 months from the start of the intervention by an independent assessor. Primary outcomes were the Chinese version of Neurobehavioral Cognitive Status Examination (NCSE) [14], Chinese Version Verbal Learning Test (CVVLT) [15], Category Verbal Fluency Test (CVFT) [16], Trail Making Test A (TMT-A) and Chinese version Trail Making Test B (TMT-B) [17]. Secondary outcomes were the Chinese versions of Lawton Instrumental Activities of Daily Living Scale (Lawton IADL) [18] and Problems in Everyday Living Test (C-PEDL) [19]. To summarize the performance of general cognitive functions, a NCSE composite score was calculated by adding all subtest scores (maximum 82) and a NCSE normal domains score (0–10) was calculated by adding up the number of domains scored normal [20].

**Interventions**

**Functional tasks exercise group**

The FcTSim programme involved a total of 13 sessions in 10 weeks, facilitated by an occupational therapist. All sessions began with a 5–10 min warm-up of light stretching, followed by a 30-min core FcTSim and a 5–10 min cool-down.

**AC group**

This was an existing cognitive training programme which involved a total of six sessions (group of —three to four members) over 10 weeks, facilitated by an occupational therapist and an assistant. Each session included 30 min of computer-based cognitive training (visual searching, forward-backward digit recall and calculation), and 30 min of cognitive strategy training. Each session was supplemented with paper and pencil home assignments. All the participants continued with their usual routine medical care.

**Statistical analysis**

All analyses were performed using SPSS 19 (SPSS, Inc., Chicago, IL, USA). Group differences in demographics and all outcome measures at baseline were compared using independent samples t-test and Fisher’s exact test when appropriate. Repeated-measures of analysis of variance (ANOVA) were performed to evaluate the intervention effect by time from baseline to post-training and from baseline to 6-month follow-up. Analysis of covariance (ANCOVA) was performed to evaluate the between-group differences at post-intervention and 6-month follow-up, with baseline score, age, education and exercise pattern as covariates. Post hoc Bonferroni analyses were performed for all measures when significant between-group differences were revealed. Cohen’s $d$ was calculated to estimate the between-group effect sizes at post-intervention and at follow-up. Data were analysed according to the intention-to-treat principle. Missing data for participants who did not complete the programme were replaced by the last available data (last observation carried forward). The statistical significant level was set at $P < 0.05$ (two-tailed).

**Results**

**Participant characteristics**

A total of 211 potential participants were screened for eligibility. Figure 1 shows the flow of participants. Eighty-three participants (50 females and 33 males), aged 60–88 years (mean = 73.8, SD = 7.1), were randomised into the intervention (FcTSim) group ($n = 43$) or the AC group ($n = 40$). Baseline characteristics are tabulated in Table 1. No significant baseline differences were found for demographic characteristics (range $P = 0.659–0.873$) or neuropsychological assessment results (range $P = 0.203–0.910$) between the two groups. Supplementary data available in *Age and Ageing* online, Appendix S3.

**Compliance**

Of the 83 participants who completed the baseline assessment, 75 (90.4%) participants performed the post-intervention
evaluation and 71 (85.5%) participants attended the 6-month follow-up. Dropout rates did not vary significantly between the groups at post-intervention ($\chi^2 (1) = 2.54, P = 0.147$) and during the follow-up at 6 months ($\chi^2 (1) = 2.73, P = 0.134$). No adverse events were reported from either group.

**Effects of interventions**

Performance of the two groups for all outcome measures and the between-group effect sizes are illustrated in Table 2. The results of repeated-measures ANOVA revealed that the FcTSim group showed significant within-group improvements in all outcomes at post-intervention and at 6-month follow-up. The AC group also showed significant improvements in different outcomes except functional status or everyday problem solving ability at post-intervention and at 6-month follow-up.

At post-intervention, results of ANCOVA showed the FcTSim group demonstrated significant between-group differences for general cognitive functions (NCSE composite score; $F_{1,77} = 11.02, P = 0.001$ and NCSE normal domains; $F_{1,77} = 14.64, P < 0.001$), memory (CVVLT immediate recall; $F_{1,76} = 5.05, P = 0.028$ and delayed recall; $F_{1,75} = 5.49, P = 0.022$), executive function (TMT-B; $F_{1,77} = 4.13, P = 0.045$ and CVFT; $F_{1,77} = 4.92, P = 0.029$) and everyday problem solving ability (C-PEDI; $F_{1,77} = 19.55, P < 0.001$). When gender and ambulatory level were included as covariates to control for confounding effects, a significant between-group difference was also found for functional status (Lawton IADL; $F_{1,75} = 3.99, P = 0.049$). Supplementary data available in *Age and Ageing* online, Appendix S4.
**Sustainability of effects**

During 6-month follow-up, significant between-group differences were still evident in the FcTSim group for general cognitive functions (NCSE composite score; $F_{1,77} = 5.19, P = 0.025$ and NCSE normal domains; $F_{1,77} = 4.64, P = 0.034$), memory (CVVLT delayed recall; $F_{1,75} = 4.24, P = 0.043$), executive function (TMT-A; $F_{1,77} = 6.82, P = 0.011$) and everyday problem solving ability (C-PEDL; $F_{1,77} = 7.45, P = 0.008$). The between-group effect size (range $d = 0.31–0.98$) is shown in Table 2.

**Discussion**

The aim of this study was to determine whether a FcTSim programme can improve the cognitive functions of older adults with cognitive impairment at risk of AD compared with an active training group. The FcTSim group had significantly higher improvements in general cognitive functions, functional status and problem solving ability, compared with the AC group, at post-intervention and with small to very large effect sizes. The significant group effects on cognitive functions and everyday problem solving ability were also sustained at 6-month follow-up.

The promising findings of this study support previous studies that have exposure to an enriched environment/demanding tasks, and exercise enhances cognitive functions and leads to greater effects than having either exercise or environmental enrichment alone [9, 21]. Although the functional tasks involved in the FcTSim programme are simple placing/collection tasks that most people may do in their everyday life, complex cognitive interplays are required to enable us to see, reach and place the objects to the target positions [10]. These goal-directed actions require integration of information (e.g. object identity and spatial orientation) and simultaneous manipulation of the integrated information that demands intensive loads on the attentional and executive resources to achieve the ongoing tasks [22]. Indeed, misplacing objects are commonly reported in MCI and AD [23]. Simple daily tasks can be cognitively challenging to persons with cognitive impairment.

Novelty can be created to existing task by adding unfamiliar features [24]. The novelty of the FcTSim programme is maintained with the changing visuospatial patterns, sequences and the combinations in different levels, therefore performance of the task will remain challenging and not become subject to automation.

Importantly, the FcTSim group showed significant between-group improvement in a number of normal cognitive domains. This further supports previous findings that training may induce brain plasticity even in older adults with MCI [25].

Furthermore, the present study found that the greatest effect was observed on everyday problem solving ability with the improvement sustained at 6-month follow-up. Everyday problem solving has been defined as a higher order executive function and an important construct in everyday function that has been found impaired in MCI compared with cognitively normal elders [26, 27]. In line with the improvement in problem solving ability, the FcTSim group also demonstrated significant improvement in functional status at post-intervention, although the training gain decreased slightly to that of approaching significant level. Performance in everyday problem solving is closely related to working memory that can be facilitated through visuospatial training [28]. The significant
Table 2. Outcomes at baseline, post-intervention and 3-month follow-up

<table>
<thead>
<tr>
<th>Measures</th>
<th>Groups</th>
<th>Baseline Mean ± SE</th>
<th>Post-intervention Mean ± SE</th>
<th>Follow-up Mean ± SE</th>
<th>Post-intervention P-value (group)</th>
<th>Post-intervention P-value (time)</th>
<th>Follow-up P-value (group)</th>
<th>Follow-up P-value (time)</th>
<th>Effect size (95% CI)</th>
<th>Effect size (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>FcTSim (n = 43)</td>
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<td></td>
<td>NCSE</td>
<td>50.65 ± 1.79</td>
<td>62.23 ± 0.93</td>
<td>61.91 ± 1.17</td>
<td>0.001*</td>
<td>&lt;0.001</td>
<td>0.025*</td>
<td>0.001*</td>
<td>d = 0.81 (0.36, 1.25)</td>
<td>d = 0.51 (0.07, 0.95)</td>
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<td></td>
<td>AC (n = 40)</td>
<td>53.95 ± 2.12</td>
<td>57.38 ± 0.96</td>
<td>58.03 ± 1.22</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<td>Composite scores</td>
<td>4.77 ± 0.28</td>
<td>6.99 ± 0.20</td>
<td>6.95 ± 0.24</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.034*</td>
<td>0.001*</td>
<td>d = 0.84 (0.39, 1.29)</td>
<td>d = 0.48 (0.04, 0.92)</td>
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<tr>
<td></td>
<td>NCSE</td>
<td>5.35 ± 0.36</td>
<td>5.89 ± 0.21</td>
<td>6.20 ± 0.25</td>
<td>0.01*</td>
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<td></td>
<td>Normal domains</td>
<td>15.49 ± 0.74</td>
<td>19.84 ± 0.59</td>
<td>20.44 ± 0.68</td>
<td>0.028*</td>
<td>&lt;0.001</td>
<td>0.123</td>
<td>&lt;0.001</td>
<td>d = 0.51 (0.07, 0.95)</td>
<td>d = 0.35 (−0.08, 0.78)</td>
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<td></td>
<td>Immediate recall</td>
<td>16.35 ± 0.94</td>
<td>17.90 ± 0.61</td>
<td>18.9 ± 0.70</td>
<td>0.002*</td>
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<td>CVVLT</td>
<td>5.00 ± 0.51</td>
<td>7.24 ± 0.28</td>
<td>7.43 ± 0.32</td>
<td>0.022*</td>
<td>&lt;0.001</td>
<td>0.043*</td>
<td>&lt;0.001</td>
<td>d = 0.52 (0.09, 0.96)</td>
<td>d = 0.47 (0.04, 0.91)</td>
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<tr>
<td></td>
<td>Delayed recall</td>
<td>5.26 ± 0.71</td>
<td>6.29 ± 0.29</td>
<td>6.44 ± 0.34</td>
<td>&lt;0.001</td>
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<td></td>
<td>TMT-A</td>
<td>136.28 ± 10.55</td>
<td>111.51 ± 5.91</td>
<td>93.63 ± 6.19</td>
<td>0.168</td>
<td>&lt;0.001</td>
<td>0.011*</td>
<td>&lt;0.001</td>
<td>d = 0.31 (−0.12, 0.74)</td>
<td>d = 0.58 (0.14, 1.02)</td>
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<td></td>
<td>TMT-B</td>
<td>236.97 ± 13.08</td>
<td>189.90 ± 7.99</td>
<td>202.75 ± 8.28</td>
<td>0.045*</td>
<td>&lt;0.001</td>
<td>0.656</td>
<td>&lt;0.001</td>
<td>d = 0.45 (0.02, 0.89)</td>
<td>d = −0.10 (−0.53, 0.33)</td>
</tr>
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<td></td>
<td>CVFT</td>
<td>9.33 ± 0.56</td>
<td>12.62 ± 0.45</td>
<td>11.87 ± 0.42</td>
<td>0.029*</td>
<td>&lt;0.001</td>
<td>0.19</td>
<td>&lt;0.001</td>
<td>d = 0.49 (0.06, 0.93)</td>
<td>d = 0.30 (−0.14, 0.73)</td>
</tr>
<tr>
<td></td>
<td>Lawton IADL</td>
<td>10.43 ± 0.65</td>
<td>11.19 ± 0.46</td>
<td>11.06 ± 0.44</td>
<td>0.013*</td>
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<td>PEDL</td>
<td>20.67 ± 0.67</td>
<td>21.73 ± 0.52</td>
<td>21.69 ± 0.62</td>
<td>0.049*</td>
<td>&lt;0.001</td>
<td>0.098</td>
<td>&lt;0.001</td>
<td>d = 0.45 (0.01, 0.88)</td>
<td>d = 0.37 (−0.06, 0.81)</td>
</tr>
<tr>
<td></td>
<td>FcTSim (n = 43)</td>
<td>18.12 ± 0.54</td>
<td>22.52 ± 0.63</td>
<td>22.19 ± 0.62</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.008*</td>
<td>&lt;0.001</td>
<td>d = 0.98 (0.53, 1.44)</td>
<td>d = 0.61 (0.17, 1.05)</td>
</tr>
<tr>
<td></td>
<td>AC (n = 40)</td>
<td>18.50 ± 0.71</td>
<td>18.52 ± 0.65</td>
<td>19.75 ± 0.64</td>
<td>0.872</td>
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<td>0.101</td>
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</table>

NCSE, Neurobehavioral Cognitive Status Examination; CVVLT, Chinese Version Verbal Learning Test; TMT-A, Trail Making Test-part A; TMT-B, Trail Making Test-part B; CVFT, Category Verbal Fluency Test; Lawton IADL, Lawton Instrumental Activities of Daily Living Scale; PEDL, Problems in Everyday Living Test; FcTSim, intervention group; AC, active control group; SE, standard error; CI, confidence interval.

*Effect size defined as Cohen’s d of the intervention (FcTSim) group (FcTSim) compared with the active control (AC) group.

*P < 0.05; mean = adjusted mean after Bonferroni correction.
improvement in everyday problem solving performance may be associated with the working memory gained through practice of the visual sequential patterns in the FcTSim programme. Further studies with assessments of working memory are still needed to verify this potential effect and correlation.

Lastly, the generalisation effects on everyday problem solving ability and functional status found in the present study supports previous studies, whereby the training effects through visuospatial tasks practice can be generalised to non-trained tasks [28, 29]. It has been proposed that the transfer effect to a non-trained task results from the involvement of attentional control, which is essential for most cognitive functions [30]. Activation over the cerebral cortex during training may then work as a common platform with increased cognitive resources for non-trained tasks performance [31].

This study differs from previous similar studies [32, 33] with cognitively impaired patients in that the intervention group was compared with an active cognitive training group. To the authors’ best knowledge, this is the first programme that uses cognitively challenging functional tasks with exercise components, as a means of cognitive-exercise intervention for MCI. The FcTSim programme does not require any sophisticated equipment or tools for implementation and has demonstrated the potential for cost-effectiveness and acceptability of cognitive-exercise programmes for this group.

Limitations
While the results of this study are promising, there are limitations that warrant mention. First, the populations in the study were Chinese older adults in Hong Kong and this limits the generalisation of the results in other populations. More studies in different countries are needed to further validate the efficacy of using this newly developed programme. Second, the small sample size did not allow stratification of patients into more precise MCI sub-groups or different age groups to examine and compare the potential intervention effects across the clinical subtypes or age groups which may demonstrate different responses to the same training exposure. Another limitation was the absence of a no-treatment or an exercise only control group to compare and understand the mechanism of change and the impact of the programme. Furthermore, hospital policy did not allow for good control over the difference in contact hours between the two groups, therefore, further studies with well-designed comparison groups are still needed.

Conclusion
In conclusion, findings from this randomised controlled trial showed that a FcTSim programme using simulated functional tasks as intervention is feasible for improving general cognitive functions, memory, executive functions, functional status and everyday problem solving ability of older adults with MCI at risk of AD. The improvements can be sustained over time after completion of training. The newly developed FcTSim programme may serve as a cost-effective adjunct in the existing interventions for population with MCI.

Key points
- Individuals with MCI are at high risk of progressing to AD and other dementias.
- Daily functional tasks are innately cognitive-demanding and involve components as seen in traditional exercise programme.
- This study found functional task exercise improved cognitive functions and functional status in MCI population.
- FcTSim may serve as a cost-effective adjunct in the existing interventions for population with MCI.

Acknowledgements
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Conflicts of interest
None declared.

Supplementary data
Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References
Only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on Supplementary data in Age and Ageing online, Appendix S5.


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