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**Effects of Functional Tasks Exercise on Older Adults with Cognitive Impairment
at Risk of Alzheimer Disease – A randomized controlled trial**

Abstract

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

Design: A single-blind randomized control trial with the intervention group compared to 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 randomized 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-months follow-up.

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

Key words: mild cognitive impairment, functional tasks exercise, geriatric rehabilitation, randomized controlled trial

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 and other dementias, with reported conversion rate of 60%-100% in 5 to 10 years [1]. 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 [2]. 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 [3]. Nevertheless, there is increasing evidence that exercise training in older adults increases cortical volume as well as the plasticity of the human brain [4]. 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 [6]. 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 [6]. Animal studies have also shown that a combination of exercise and an enriched environment induce a greater increase in neurogenesis than either exercise or environmental enrichment alone [7].

Daily functional tasks are innately cognitive-demanding and involve components of stretching, strengthening, balance and endurance as seen in traditional exercise programs. 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 [8].

A structured functional tasks exercise program was developed [9] to facilitate the cognitive functions of older persons with MCI. Details of the “FcTSim” program have been reported previously [9] whereby simulated (Sim) functional tasks (FcT) incorporated with exercise are used as an intervention. The FcTSim program 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 [10]. A brief description of the five levels of movement is illustrated in Appendix 1.

It is hypothesized that functional tasks exercise 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 functional tasks exercise program can improve the cognitive functions of older adults with cognitive impairment at risk of Alzheimer's disease (AD).

METHODS

Study Design

The study was a single-blind randomized controlled trial. All outcome measures were conducted by an assessor masked to the group status of the participants. After baseline assessment, participants were randomized to the intervention group (functional tasks

exercise) or the active control group (existing cognitive training) according to a list of computer-generated random numbers, 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 in Hong Kong. Patients with subjective memory complaint or suspected cognitive impairment were referred by the out-patient clinic of 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 mild cognitive impairment (MCI) [11]: (1) Memory/cognitive complaint as reported by the patients or the carers; (2) Objective cognitive impairment in 1 or more domains as revealed by neuropsychological assessment; but with (3) intact personal selfcare functions; (4) No confirmed diagnosis of dementia. The exclusion criteria were: (1) History of brain lesion/psychoactive substance abuse/co-morbid medical condition associated with cognitive/functional decline; (2) Clinically significant depression; (3) Known psychiatric cause

of cognitive dysfunction; (4) Medical conditions which rendered patients unable to engage in physical activity; (5) Undertaking medications with significant impacts on cognitive function; and (6) Significant impairment of vision, hearing or communication that might affect participation in the assessments or the program. All the participants provided written informed consent.

Measurements

Assessments were undertaken at baseline, post-intervention at 11-12 weeks and during 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) [12], Chinese Version Verbal Learning Test (CVVLT) [13], Category Verbal Fluency Test (CVFT) [14], Trail Making Test A (TMT-A) and Chinese version Trail Making Test A (TMT-B) [15]. Secondary outcomes were the Chinese versions of Lawton Instrumental Activities of Daily Living Scale (Lawton IADL) [16] and Problems in Everyday Living Test (C-PEDL) [17]. 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 [18].

Interventions

Functional Tasks Exercise (FcTSim) Group

The functional tasks exercise (FcTSim) program involved a total of 13 sessions in 10 weeks, facilitated by an occupational therapist. All sessions began with a 5-10 minutes warm-up of light stretching, followed by a 30-minutes core functional tasks exercise and a 5-10 minutes cool-down.

Active Control (AC) Group

This was an existing cognitive training program which involved a total of 6 sessions (group of 3-4 members) over 10 weeks, facilitated by an occupational therapist and an assistant. Each session included 30 minutes of computer-based cognitive training (visual searching, forward-backward digit recall and calculation), and 30 minutes 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). 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-months 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 was analyzed according to the intention-to-treat principle. Missing data for participants who did not complete the program 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 female and 33 male), aged 60 to 88 years (mean = 73.8, SD = 7.1), were randomized into the intervention (FcTSim) group (n = 43) or the active control (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.

[Insert Figure 1 at about here]

[Insert Table 1 at about here]

Compliance

Of the 83 participants who completed the baseline assessment, 75 (90.4%) participants performed the post-intervention evaluation, and 70 (84.3%) 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 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-months 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-months 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-PEDL; $F(1, 77) = 19.55, P < 0.001$). 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; $F(1, 75) = 3.99, P = 0.049$).

Sustainability of Effects

During 6-months 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.

[Insert Table 2 at about here]

DISCUSSION

The aim of this study was to determine whether a functional tasks exercise program can improve the cognitive functions of older adults with cognitive impairment at risk of AD compared to an active training group. The FcTSim group had significantly higher improvements in general cognitive functions, , functional status and problem solving ability, ~~comparing-compared~~ to 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-months follow-up.

The promising findings of this study support previous studies that exposure to an enriched environment/demanding tasks and exercise enhances cognitive functions and leads to effects than having either exercise or environmental enrichment alone. [7,19]. Although the functional tasks involved in the FcTSim program 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 [8]. 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 [20]. Indeed, misplacing objects are commonly reported in MCI and AD [21]. Simple daily tasks can be cognitively challenging to persons with cognitive impairment.

Importantly, the FcTSim group showed significant between-group improvement in ~~the~~ a number of normal cognitive domains. This further supports previous findings that training may induce brain plasticity even in older adults with MCI [22].

Furthermore, the present study found that the greatest effect was observed on everyday problem solving ability ~~and-with~~ the improvement sustained at 6-months 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 to cognitively normal elderly [23, 24]. In line with the improvement in problem solving ability, the FcTSim group also demonstrated significant improvements 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 visuo-spatial training [25]. The significant improvement in everyday problem solving performance ~~might-may~~ be associated with the working memory gained through practice of the visual sequential patterns in the FcTSim program. Further studies with assessments of working memory ~~will-are~~ still ~~be~~-needed to verify this potential effects and correlation.

In addition, functional imaging studies have found that the brain is activated from the

frontal to the parietal lobe during visuo-motor sequence learning and retrieval [26].

These regions have been identified as responsible for attention/ executive functions as well as episodic memory encoding and retrieval [27]. This may explain the intervention effects of the FcTSim program on memory and executive functions.

~~At last~~Lastly, the generalization effects on everyday problem solving ability and functional status ~~that~~ found in the present study supports results from previous studies ~~that whereby the~~ training effects through visuospatial tasks practice can be generalized to non-trained tasks [25, 28]. It has been proposed that the transfer effect to a non-trained task ~~is resulted~~ results from the involvement of attentional control, which is essential for most cognitive functions [29]. Activation over the cerebral cortex during training may then work as a common platform with increased cognitive resources for non-trained tasks performance [30].

This study differs to previous similar studies 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 program that uses cognitively challenging functional tasks with exercise components, as a means of intervention for MCI. The FcTSim program does not require any sophisticated equipment or tools for implementation and has demonstrated the potential for cost-effectiveness and

acceptability of cognitive-exercise programs for this group.

Limitations

While the results of this study are promising, ~~T~~here are limitations ~~in this study~~ that warrant mention. First, the ~~study~~-samples population in the ~~studies~~ were Chinese older adults in Hong Kong and this limits the generalization of the results in other populations. More studies in different countries are needed to further validate the efficacy of using this newly developed program. Second, the small sample size did not allow stratification of patients into more precise MCI sub-groups to examine and compare the potential intervention effects across the clinical subtypes which may demonstrate different responses to the same training exposure. Furthermore, the post-intervention follow-up period of the present study was relatively short in view of the long preclinical period of Alzheimer's disease. Further larger scale studies with extended follow-up period are needed to validate the sustainability of the training gains, as well as to establish possible strategies to maintain or even promote additional training gains. Another limitation was the absence of a no-treatment control group to compare and understand fully the impact of the program.

CONCLUSION

In conclusion, findings from this randomized controlled trial showed that a functional tasks exercise program 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 mild cognitive impairment at risk of Alzheimer's disease. The improvements can be sustained over time after completion of training. The newly developed functional tasks exercise program may serve as a cost-effective adjunct in the existing interventions for population with mild cognitive impairment.

Key Points

- Individuals with mild cognitive impairment (MCI) are at high risk of progressing to Alzheimer's diseases and other dementias
- A combination of exercise and an enriched environment induce a greater increase in neurogenesis
- Daily functional tasks are innately cognitive-demanding and involve components as seen in traditional exercise program.
- Functional tasks exercise may serve as a cost-effective adjunct in the existing

interventions for population with MCI.

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Conflicts of Interest

None declared.

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