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Research paper

Feasibility and baseline findings of a Finnish cognitive training (FINCOG) intervention in a randomised controlled trial among community-dwelling persons with dementia

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ABSTRACT

Introduction: Evidence is unclear whether cognitive training (CT) has efficacy in patients with dementia. We present the recruitment and baseline findings of a carefully designed Finnish cognitive training (FINCOG) trial exploring the effectiveness of CT among community-dwelling older persons with mild-to-moderate dementia.

Methods: Participants were recruited from adult day care centres in Helsinki, Finland, and randomised into two groups: (1) day care with systematic CT twice a week for 12 weeks (n = 76) and (2) day care as usual (n = 71). Demographics, diagnoses and drug use were retrieved from medical records, and baseline cognition, functioning, health-related quality of life (HRQoL) and psychological well-being were assessed. A subgroup of participants was planned to undergo functional magnetic resonance imaging (fMRI) to measure changes in brain activity. Feedback from those attending CT was collected. Primary trial outcomes will be participants' cognition and HRQoL.

Results: The mean (SD) age of the randomised participants was 83.1 (5.4) years, 72% were female and 37% at a moderate stage of dementia. The intervention and control groups were comparable at baseline. Compliance with CT was good, with a mean attendance of 22/24 sessions. General subjective gain was achieved by three-fourths of the feedback respondents. However, the fMRI was not feasible in this patient group.

Conclusions: We successfully randomised 147 persons with mild-to-moderate dementia in the FINCOG trial. The feedback from participants in cognitive intervention was favourable. The trial will provide important information on the effects of CT in patients with dementia.

Trial registration: ACTRN12614000976684.

1. Introduction

The standard treatment for Alzheimer's disease (AD) consists of pharmacotherapies, although there have been no major breakthroughs in drug treatments [1]. Non-pharmacological interventions as a complementary treatment may have a role in delaying the progression of cognitive symptoms, improving quality of life and postponing institutional care [1–3].

Cognitive training (CT) is an intervention specifically designed to address difficulties with various aspects of cognition. CT refers to repetitive practice on a set of standard tasks with different levels of difficulty [4]. Restorative CT aims to enhance specific cognitive abilities, potentially through neuroplasticity [5] or modification of cognitive reserve [6]. One explanation for the effects of CT might be enhancement of impaired attention and executive functions [7,8]. New insights have been gained into CT for healthy older people [9,10] and also for persons with declining cognition [11,12], but evidence for the efficacy of CT in patients with dementia is unclear [13,14]. In a recent systematic review with 31 randomised controlled trials (RCTs), many trials were hampered by design

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limitations, and the pattern of effects on specific cognitive domains was inconsistent across studies [14]. However, more intensive CT seemed to be associated with more frequent positive outcomes [14].

We designed a RCT with a 24 month follow-up to investigate the effectiveness of a systematic CT programme focusing on subskills of executive functions among community-dwelling older persons with mild-to-moderate dementia. Our main goal is to clarify the effects of CT on participants' cognitive functioning, health-related quality of life (HRQoL) and use of health services. We report here the study recruitment, participants' baseline characteristics and feedback regarding the intervention.

2. Methods

The Finnish cognitive training (FINCOG) trial was approved by the Ethics Committee of Helsinki University Central Hospital, and the procedures were planned in accordance with the declaration of Helsinki.

2.1. Study design and participants

The FINCOG study is a single-blinded RCT with two arms (intervention and control groups). The participants in the intervention group receive CT in addition to routine treatment at adult day care centres. The participants in the control group receive only the routine treatment at day care centres.

A total of 302 patients with an established dementia diagnosis and visiting a day care centre twice a week in Helsinki, Finland, were invited to take part in the study. They received a letter containing information on the research, voluntary participation and how to get involved. The voluntary patient-caregiver dyads were interviewed via telephone to confirm patients' interest and inclusion criteria. The diagnoses, medications and demographic data were confirmed via a structured questionnaire and medical records.

Altogether, 155 persons (112 women, 43 men) and their main caregivers agreed to participate (Fig. 1). Inclusion criteria for the trial were: (1) AD or other dementia at a mild or moderate stage (Clinical Dementia Rating scale, CDR [15], 0.5 to 2), (2) age $\geq$ 65 years, (3) Finnish speaking, (4) able to see, hear, read and write, (5) living at home and (6) attending an adult day care centre at least twice a week. Exclusion criteria were any terminal disease; severe dementia (CDR $>$ 2) or no dementia (CDR = 0); age under 65; severe loss of vision, hearing or communicative ability; not speaking Finnish; not living at home or waiting to be institutionalised; and unavailable proxy.

Of the 155 patients assessed at baseline with detailed cognitive measures three persons suffered from severe dementia, four refused to continue in the trial, and one deceased (Fig. 1). This left us with 147 eligible participants, who had AD as the primary clinical diagnosis of dementia in 122 (83%) cases (NINCS-ADRDA criteria [16]). Other primary diagnoses were evaluated by the study team as vascular dementia (n = 11), Parkinson or Lewy body dementia (n = 4) and other/unknown dementia (n = 10).

Informed consent was obtained from each participant and their caregiver before any study procedures. In case of a patient's reduced judgment capacity (Mini-Mental State Examination [17], MMSE score $<$ 20), the closest proxy (spouse or relative) provided informed consent.

2.2. Measurements and follow-up

The dementia severity and cognitive status of participants were assessed at baseline using CDR [15] and MMSE [17], respectively. Charlson comorbidity index [18] was calculated to measure the

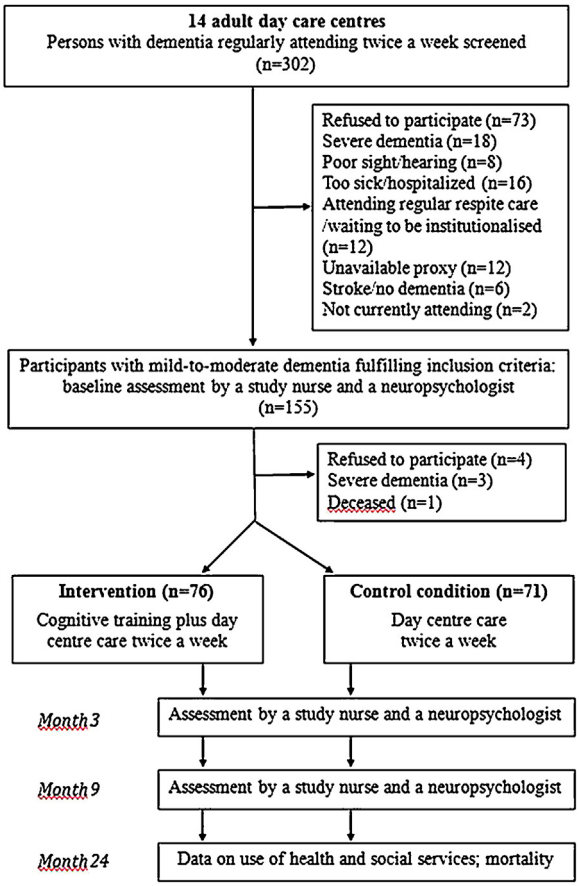

Fig. 1. Flow chart of the study.

severity of disease burden. Self-rated health was evaluated by using a single question "In general, how would you rate your health today" with four answer choices (very good, good, poor or very poor).

The primary outcome measures of the trial are the Alzheimer's Disease Assessment Scale–Cognitive subscale (ADAS-Cog) to assess general cognitive functioning [19], and the 15-dimensional instrument (15D) to assess HRQoL [20]. 15D is a standardized generic questionnaire, which may be administered in an interview with the subject or his/her proxy. It includes 15 multiple-choice items to measure e.g. mobility, sleeping, eating, mental function, discomfort, depression and vitality [20]. 15D may be used as a profile measure, or a single index varying between 0 (poor HRQoL) and 1 (excellent HRQoL) [20]. 15D shows good discriminant validity among various aged populations, and also prognostic validity [21]. Additionally, 15D correlates well with other HRQoL measures, such as SF-20 or EQ-5D [20].

Secondary outcomes include (1) a set of standard neuropsychological tests to measure different cognitive domains and executive functioning: clock drawing and verbal fluency of the Consortium to Establish a Registry for Alzheimer's Disease [22], Frontal Assessment Battery [23], Trail Making Test-condition A [24], Victoria Stroop Test [25], and Block Design, Similarities, Digit Span and Digit Symbol-Coding of Wechsler Adult Intelligence Scale -IV [26]; (2) Alzheimer's Disease Cooperative Study–Activities of Daily Living (ADCS-ADL) questionnaire to evaluate activities of daily living [27]; and (3) mood and well-being according to Psychological Well-being (PWB) scale, which includes six questions about: life satisfaction, feeling needed, having plans for the future, zest for life, feeling depressed and suffering from loneliness [28]. These simple questions have been used among people with

dementia, and found easy to understand and respond [28,29]. In our trial, answers to PWB come from a structured interview with a participant. PWB index score, which may vary between 0 (poor well-being) and 1 (excellent well-being) [28], shows good concurrent validity with RAND-36 [30].

Participants will be assessed three times during the trial: at baseline, at 3 and 9 months. An experienced neuropsychologist blinded to group assignment carries out all of the cognitive assessments, except MMSE. Two blinded study nurses assess other outcome measures, including MMSE. Additionally, data on use of health and social services will be gathered from hospital and social service documents and medical records, and death dates from the central registers until 24 months from baseline. The 2 year follow-up will be completed by the end of 2018.

2.3. Functional MRI

We aimed to follow a subgroup of participants with functional magnetic resonance imaging (fMRI) to validate whether changes in brain activity were associated with our training programme, especially in the frontal areas of the brain. We designed a visual working memory task suitable for our study population. Out of the first 15 eligible participants prepared for fMRI, only one scanning was completed successfully. Despite pre-screening, participants had various contraindications for fMRI: a possibility of metal implants ($n = 5$), cognition- and hearing-based difficulties in following the task protocol ($n = 4$), and other reasons for low compliance (anxiety, fracture of an arm, refusal). We therefore decided to discontinue fMRI explorations.

2.4. Randomisation

All baseline information was collected before randomisation. Participants were randomised into the intervention group ($n = 76$) or control group ($n = 71$) using computer-generated randomly allocated numbers received by telephone from a randomisation centre. Participants were not actively informed of the study group, which they were assigned to. To enable training in small groups, participants attending a day care centre on the same days were randomised in pairs. Eighteen participants were randomised individually, because no participants attended a centre on the same weekdays. To maintain a regular and manageable weekly programme, we used the participants' original attendance days throughout the trial.

2.5. Intervention

A 12 week systematic CT programme based on paper-and-pencil tasks with cognition as a primary target was designed for the FINCOG trial. The main objective was to stimulate subskills of executive functioning (attention, working memory, planning and cognitive flexibility). The CT programme was a relevant modification of the cognitive remediation therapy (CRT), which is a training-based intervention aimed at improving executive functioning of chronic psychiatric patients [31,32]. We adjusted this cognition-focused treatment for our participants by decreasing the difficulty level of the tasks, reducing the number of sessions (from 44 to 24) and increasing the font size of the tasks. Techniques of repeated practice, errorless learning (reducing the opportunity to make errors), immediate feedback, scaffolding (providing strategies when needed, and gradually increasing task complexity), and facilitating planning and self-monitoring were used during the training [31].

Training was tailored according to participants' cognitive abilities, and therefore, implemented either in small groups of 2–4 participants or individually when needed (due to difficulties in concentration or lack of a training pair). The intervention took place twice a week for 45 minutes during the day care. Each session included cognitive exercises from four different categories: visuomotor (e.g. cancellation tasks), perceptual (e.g. searching overlapping objects, following short instructions), conceptual (e.g. categorising words or play cards, basic arithmetic operations) and interactive tasks to encourage overt conversation (e.g. word finding, simple card games). Trained psychology students administered CT, with the guidance and supervision of an experienced neuropsychologist.

Both the intervention and control groups received routine treatment at a day care centre twice a week, for 6 hours each day. Routine treatment included non-specific social (discussions, musical activities, lunch), physical (light exercise, walking outdoors) and cognitive (orientation, word and number games, reminiscence) activities in groups of 12–16 persons.

2.6. Statistical analysis

Sample size calculations for the FINCOG trial were based on the primary outcome measure ADAS-Cog. Considering previous clinical trials a four-point change on the ADAS-Cog score would indicate a clinically meaningful difference between the treatment and control groups [33]. To ensure 80% power to detect this change with a standard deviation (SD) of eight at two-sided $\alpha = 0.05$ a sample size of 64 participants per group was required. Due to an expected drop-out rate of about 20% we aimed to enrol 150 participants.

In the FINCOG trial, repeated measurements of primary and secondary outcomes over time will be analysed using a mixed-model approach with appropriate distribution and link function. An intention-to-treat (ITT) analysis will be applied; all participants assessed at baseline and at least one of the follow-ups will be included in the data analyses of changes.

Baseline statistical analyses included standard descriptive statistics of the participants: group means with SD, or percentages (%). The differences between the intervention and control groups were analysed using chi square-test, Fisher's exact test, Mann-Whitney U-test or t-test as appropriate. The level of significance was 5% in all analyses. The feedback data regarding the CT programme are presented as percentages.

3. Results

Between September 2014 and March 2016 after screening for inclusion criteria, a total of 302 patients with dementia were invited to participate, and 147 (49% of those invited) were randomised into the trial (Fig. 1). Both the recruitment and baseline assessment were completed during 2016.

3.1. Baseline findings

There were no significant differences in demographic or health status characteristics between the persons randomised into the intervention and control groups (Table 1). The mean (SD) age of the 147 participants was 83.1 (5.4) years, and a high proportion was female (72%). While 71% of the participants were living alone, only 20% were fully capable of personal care. The functional performance on the ADCS-ADL inventory was similar in both groups. The large mean number of prescription drugs and a high Charlson index score indicate a high prevalence of comorbid medical conditions in participants. More than 80% were on AD medication, and almost 50% were using anticholinergic drugs. The use of medication was similar in both groups (Table 1).

The CDR scores and the cognitive status according to MMSE did not differ between the intervention and control groups (Table 1). Furthermore, no statistically significant differences emerged in the

Table 1
Baseline characteristics of participants.

Characteristics	Intervention group ($n=76$)	Control group ($n=71$)	P
Age, mean (SD)	82.6 (5.5)	83.6 (5.4)	0.24
Males, %	34.2	21.1	0.08
Education < 8 years, %	42.1	50.7	0.30
CDR, %			0.75
0.5	11.8	8.5	
1	52.6	52.1	
2	35.5	39.4	
MMSE, mean (SD)	21.0 (4.3)	19.9 (3.9)	0.12
ADAS-Cog, mean (SD)	21.1 (8.1)	21.8 (8.3)	0.64
Dementia diagnosis, %			0.17
AD	76.3	90.1	
Vascular	10.5	4.2	
Parkinson or Lewy body	3.9	1.4	
Other or unknown	9.2	4.2	
Charlson index, mean (SD)	2.7 (1.6)	2.8 (1.9)	0.96
Number of medications, mean (SD)	8.2 (3.2)	7.8 (3.0)	0.34
On AD medication, %	78.9	87.4	0.54
On anticholinergics, %	43.4	52.1	0.29
Self-rated health (Good or Quite good), %	89.5	91.5	0.67
Living alone, %	71.1	70.4	0.93
Daily activities (CDR, Personal care), %			0.67
Full capable (0.5)	19.7	21.1	
Needs prompting (1)	40.8	33.8	
Requires assistance (2–3)	39.5	45.0	
ADCS-ADL, mean (SD)	48.7 (14.8)	47.2 (16.4)	0.63
15D, mean (SD)	0.743 (0.086)	0.745 (0.081)	0.99
PWB, mean (SD)	0.75 (0.16)	0.76 (0.18)	0.32

AD: Alzheimer's disease, ADAS-Cog: Alzheimer's Disease Assessment Scale–Cognitive subscale [19], ADCS-ADL: Alzheimer Disease Cooperative Study Activities of Daily Living [27], Charlson index [18], CDR: Clinical Dementia Rating scale [15], MMSE: Mini Mental State Examination [17], PWB: Psychological Well-being scale [28], SD: standard deviation, 15D: 15-dimension instrument of health-related quality of life [20].

main outcome variables of ADAS-Cog and 15D. On average, also psychological well-being and self-rated health were similar in both groups.

The available demographic data of the 147 persons who refused to participate or were not eligible during the enrolment (Fig. 1) show their mean age (SD) was 82.8 (6.8) years and they were 71% female.

In general, comparison of the intervention and control groups indicates that randomisation was successful.

3.2. Feasibility of intervention

Altogether 14 adult day care centres participated in the study. Nurses took an active interest in the CT intervention and were helpful in organizing the time and place for training sessions over 12-week periods. Participant compliance with CT was good, with a mean attendance of 22/24 (92%) sessions.

We received favourable feedback from those participating in the training. Of the intervention group, 55 responded to the feedback questionnaire (response rate 72%). More than 80% of the respondents reported that the exercises were variable and sufficiently challenging, and only 5% found the programme too difficult (Table 2). General subjective gain was achieved by three-fourths of the respondents, and more than half of the respondents felt the training was beneficial to their memory.

Table 2
Feedback from participants in the CT intervention. The feedback questionnaire was answered anonymously after participating in the intervention for 12 weeks ($n=55$).

Question	Yes (%)
Were the exercises variable enough? (yes/no)	82
Were the exercises challenging enough? (yes/no)	82
Was the training programme too difficult? (yes/no)	5
Do you feel that the training was useful for you? (yes/no)	76
Did the training improve your memory? (yes/no)	56

4. Discussion

We successfully randomised 147 dementia patients, aged 65 years and older, into two arms to investigate the effects of a 12 week CT intervention performed in adult day care centres in Helsinki, Finland. The baseline data is complete, and the randomisation groups are well balanced. Participants in the intervention and control groups did not differ in the stage of dementia or other health status, functional and demographic characteristics. Furthermore, primary cognitive and HRQoL outcome measures were similar in both groups. Based on session compliance and participant feedback, the FINCOG intervention was well accepted. Half of the respondents reported a subjective benefit on memory, and more than half found the cognitive exercises to be generally useful.

Some positive effects on dementia patients' cognition have been reported in previous CT trials, but the low methodological quality limits the current evidence [13,14]. Small sample sizes, inactive control groups, poorly described randomisation methods and insufficient information regarding the trial drop-outs have been common limitations [14]. Multimodal intervention programmes and heterogeneity in defining cognitive interventions as CT add to the paucity of available evidence [14]. The current trial is designed to overcome such limitations.

We have a large sample of persons with dementia randomised into a CT intervention group and active control group receiving non-specific social, physical and cognitive stimulation. Our sample is larger than in most of the previous trials [14]. The outcome measures are valid, and HRQoL a meaningful outcome for the participants. Experienced study nurses and neuropsychologist ensure the validity of the data collection, and all the assessors are blinded to group assignment. A systematic, theoretically coherent CT intervention was designed to fit our study population. The length of the programme was 12 weeks with 24 sessions to gain sufficient intensity [14]. Trained psychology students were responsible for CT, and compliance was good.

In order to have external validity, the exclusion criteria were kept to a minimum in our trial. We allowed various dementia diagnoses, both mild and moderate stages of dementia, as well as very old persons with comorbid conditions. This heterogeneity of the participants may dilute our outcomes. Randomisation stratified by day care centres and days of attendance was challenging, and some participants had to be randomised individually. However, the randomisation appeared successful. The FINCOG intervention received favourable feedback from the participants, but the response rate was not very high. Many respondents also complained that they did not remember their training sessions. Additionally, two of the 14 days care centres started their own CT programme during the FINCOG trial, which may dilute our trial effects.

The participants in our trial are older and have a higher number of comorbidities and disabilities than those in many previous dementia studies [14,34]. In previous trials participants were typically at a mild stage of dementia [14], whereas our participants have somewhat more advanced disease.

5. Conclusions

This is a large RCT investigating the effects of a systematic CT intervention on dementia patients' cognition, daily activities and HRQoL. Baseline assessments and randomisation were successful, and feedback on the training was favourable. The FINCOG trial will provide important information on the effects of CT among community-dwelling persons with dementia.

5.1. Trial registration

The trial is registered at the Australian and New Zealand Clinical Trials Registry, identifier ACTRN12614000976684.

Disclosure of interest

The authors declare that they have no competing interest.

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