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Walking the line: a randomised trial on the effects of a short term walking programme on cognition in dementia

L H P Eggermont,¹ D F Swaab,² E M Hol,² E J A Scherder^{1,3}

¹ Department of Clinical Neuropsychology, VU University, Amsterdam, The Netherlands;

² Netherlands Institute for Neuroscience, An institute of the KNAW, Amsterdam, The Netherlands; ³ Institute of Human Movement Sciences, University of Groningen, Groningen, The Netherlands

Correspondence to:
Dr L H P Eggermont, Department of Clinical Neuropsychology, VU University, Van der Boechorststraat 1, 1081 BT Amsterdam, The Netherlands; LHP.Eggermont@psy.vu.nl

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ABSTRACT

Background: Walking has proven to be beneficial for cognition in healthy sedentary older people. The aim of this study was to examine the effects of a walking intervention on cognition in older people with dementia.

Methods: 97 older nursing home residents with moderate dementia (mean age 85.4 years; 79 female participants; mean Mini-Mental State Examination 17.7) were randomly allocated to the experimental or control condition. Participants assigned to the experimental condition walked for 30 min, 5 days a week, for 6 weeks. To control for personal communication, another group received social visits in the same frequency.

Neuropsychological tests were assessed at baseline, directly after the 6 week intervention and again 6 weeks later. Apolipoprotein E (ApoE) genotype was determined.

Results: Differences in cognition between both groups at the three assessments were calculated using a linear mixed model. Outcome measures included performance on tests that formed three domains: a memory domain, an executive function domain and a total cognition domain. Results indicate that there were no significant time $\times$ group interaction effects or any time $\times$ group $\times$ ApoE4 interaction effects.

Conclusion: Possible explanations for the lack of a beneficial effect of the walking programme on cognition could be the level of physical activation of the intervention or the high frequency of comorbid cardiovascular disease in the present population of older people with dementia.

Trial registration number: Nederlands Trial Register, TC1230, <http://www.trialregister.nl/trialreg/index.asp>

Physical activity can increase brain volume and benefit cognition in healthy sedentary older people.^{1,2} Based on the results of animal experimental studies, specific neurobiological mechanisms have been proposed through which physical activity may benefit brain function, such as neurogenesis, synaptogenesis and angiogenesis.³

Notably, treadmill running has led to a reduction in the specific neuropathological characteristics of Alzheimer's disease (ie, β -amyloid accumulation in an Alzheimer's disease mouse model).⁴ In view of the burden of dementia on our aging society, it is clinically relevant to determine whether a positive effect of physical activity on cognition is also present in this subgroup of older people. The effects of walking on cognition (ie, communication) in people with dementia have been examined in only two randomised controlled trials involving nursing home residents with advanced Alzheimer's disease, and mixed results were found.^{5,6} In the present study, the focus was on the effects of

physical activity on a broad range of cognitive functions. In view of the fragility of nursing home residents with dementia (ie, high mortality and other adverse events),⁷ a short term walking intervention programme was used to avoid high attrition. Thus this study examined whether a short term walking intervention could benefit cognition in older nursing home residents with dementia.

METHODS AND MATERIALS

For this multicentre (23 homes), randomised, controlled, single blind study, approval was granted by the local medical ethics committee of the VU Medical Centre, Amsterdam, The Netherlands. Medical staff were consulted for possible participants. Criteria for selection were: (1) age >70 years; (2) diagnosis of dementia reported; and (3) being able to walk for short distances with or without a walking aid. Written consent was obtained from participants and their relatives.

The study procedures have been published in more detail elsewhere.⁸ Cognitive functioning of the participants was screened using the Mini-Mental State Examination (MMSE). Residents were excluded if they had: (1) an MMSE score <10 or >24 ; (2) visual disturbances; (3) hearing difficulties; (4) history of alcoholism; (5) personality disorders; (6) cerebral trauma; (7) hydrocephalus; (8) neoplasm; or (9) disturbances of consciousness. Participants consisted of a heterogeneous group of older persons with dementia. Information on comorbid disease was extracted from the medical notes. Two questionnaires were administered to determine the level of depression and anxiety, and level of education was determined on a 7 point scale. Buccal swabs were taken to determine the apolipoprotein E4 (ApoE4) genotype (ApoE4 allele present or not). In 13 participants (13.4%), the ApoE genotype could not be determined.

Physical activity intervention

By tossing a coin, study participants were randomly allocated to either an experimental or a control group. Both conditions were applied one-on-one by psychology students. Interventions were offered for 30 min, five times a week, over a period of 6 weeks. In the experimental group, the participants walked at a self-selected speed. Short moments of rest were included, if necessary. Walks were primarily on the wards or in public places in the nursing home. The control group received social visits in the same frequency and during the

Table 1 Means (SD) of the independent variables separately for the two groups

	Experimental group (n = 51)						Control group (n = 46)					
	Pre		Post		Delayed*		Pre		Post		Delayed†	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Digit span fo	4.96	1.73	4.63	1.64	4.96	1.51	5.11	2.03	4.98	1.57	5.00	1.91
Digit span ba	3.88	1.36	3.69	1.28	3.78	1.49	4.13	1.34	3.89	1.25	3.78	1.51
Letter flu	17.04	7.33	16.20	7.95	16.71	7.29	16.56	8.40	15.96	9.36	17.02	9.45
Category flu	13.24	5.19	12.92	5.71	12.12	5.86	13.49	6.63	14.11	7.38	12.58	6.92
Faces	4.92	3.05	5.84	3.21	5.67	3.06	6.00	2.96	5.77	3.69	5.95	3.21
Pictures	11.88	5.45	10.86	6.30	10.86	6.47	12.16	5.91	13.73	5.78	13.27	6.47
Imm recall	16.41	4.61	16.82	5.38	17.65	5.03	18.11	5.30	16.98	6.64	17.93	5.40
Del recall	0.35	0.78	0.24	0.78	0.29	0.71	0.41	0.87	0.20	0.63	0.32	0.83
Recognition	11.04	1.94	11.31	2.03	10.92	2.13	10.98	2.22	11.30	2.15	11.16	2.44

*Values (n = 2) are missing for the delayed assessment.

†Values for one person are missing for the delayed assessment.

ba, backward; del, delayed; fo, forward; flu, fluency; imm, immediate.

same period. Missed interventions were subsequently caught up over the weekend.

Cognitive assessment

Trained psychology students blinded to the intervention assignment evaluated primary outcome measures at baseline (pretreatment: T1), the day after 6 weeks of intervention (post-treatment: T2), and again after 6 weeks without treatment (delayed: T3). The following tests were administered (details are published elsewhere)⁸: *face recognition* from the Rivermead Behavioural Memory Test which measures recognition of faces (maximal score is 10); *picture recognition* from the Rivermead Behavioural Memory Test which measures verbal memory (maximal score 20); *eight words test* (list learning test) consisting of an encoding score (immediate recall score; maximal score 40), delayed recall score (maximal score 8) and a recognition score (maximal score is 16); *digit span* (Wechsler Memory Scale-revised) consisting of digit span forward (maximal score 12) and digit span backward (maximal score 12); and *category fluency* and *letter fluency*. In the latter test, the participant is asked to produce as many words as possible beginning with a given letter of the alphabet (D, A and T).

Statistical analysis

We aimed to detect as significant an effect of a moderate magnitude (0.5), based on the results of other physical activity intervention studies in older people with cognitive impairment.⁹ Setting the level of significance (α) at 0.05, the power (1–beta) at 0.80 and the within subject correlation at 0.75, the required total number of participants was 63.

Baseline characteristics were compared between groups using independent sample t tests, χ^2 tests or Mann–Whitney U tests. Scores on neuropsychological tests were converted into z scores and, according to a factor analysis, summed up to form specific domains. Subsequently, the three domains were analysed over the three assessments using a linear mixed model (LMM). Except for three people who missed the final assessment (T3), all participants underwent all assessments, but by using an LMM, these three persons could also be included. To investigate a potential moderating effect of the ApoE genotype, separate LMM analyses were performed to determine time×group×ApoE4 interaction effects.

RESULTS

Of all the nursing home residents with dementia (n = 103) enrolled in the study, six did not complete the study protocol.

From the remaining 97 participants, seven in the experimental group did not want to continue the experimental condition but were included in the modified intention-to-treat analysis. Mean age and MMSE score of the participants were 85.4 years and 17.7, respectively. Participants were predominantly female (81%). There were no significant between group differences in age ($t(95) = -0.92$, $p = 0.360$), mean MMSE score ($t(95) = -1.64$, $p = 0.103$), level of depression ($t(94) = -0.68$, $p = 0.500$) and anxiety ($t(93) = 1.85$, $p = 0.067$). The distribution of men did not differ significantly between the groups ($\chi^2(1) = 0.08$, $p = 0.779$) nor did the level of education ($z = -0.09$, $p = 0.926$) or presence of the ApoE4 allele ($\chi^2(1) = 0.92$, $p = 0.337$). The most prevalent type of comorbidities included hypertension (n = 30), cataract (n = 23), obstructive pulmonary disease (n = 19), arthritis (n = 16), peripheral vascular disease (n = 16), tumours (n = 16), atrial fibrillation (n = 15), diabetes mellitus (n = 14) and myocardial ischaemia (n = 14). The total number of illnesses did not differ significantly between the groups ($z = -1.66$, $p = 0.097$).

Mean (SD) values for all three cognitive measurements in both groups are shown in table 1. The memory domain (face recognition, picture recognition and delayed recall of the eight words test; Cronbach's $\alpha = 0.63$) did not reveal a significant time×group interaction effect in the LMM analysis ($F(2,93.6) = 0.15$, $p = 0.862$). The EF domain (digit span backwards, category fluency and letter fluency: Cronbach's $\alpha = 0.62$) did not show a significant time×group interaction effect ($F(2,95.2) = 0.37$, $p = 0.692$). LMM analysis did not reveal a significant time×group interaction effect ($F(2,93.3) = 0.12$, $p = 0.887$) of the cognition domain (Cronbach's $\alpha = 0.52$). LMM analyses revealed no significant time×group×ApoE4 interaction effect on the memory domain ($F(2,82.7) = 0.79$, $p = 0.460$), the EF domain ($F(2,83.5) = 0.61$, $p = 0.547$) or the total cognition domain ($F(2,82.7) = 1.15$, $p = 0.291$).

DISCUSSION

This is the first randomised controlled trial to examine the effects of a walking intervention on a broad range of cognitive functions in older nursing home residents with dementia, applying a modified intention-to-treat design. No positive effects on cognition were found, and treatment outcome was not influenced by ApoE genotype. Several issues should be addressed. Firstly, it can be argued that the present walking activity may not have been an activity intense enough to benefit cognition, in view of an earlier finding that aerobic activity led to improved cognition in older healthy persons

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while an anaerobic activity did not.² However, even walking with a rollator is an aerobic activity¹⁰ comparable with that offered to older people without dementia which led to improved cognition.¹ Nonetheless, it may have been the case that participants compensated for their extra activity over the rest of the day.¹¹ In future research, it is recommended that blood pressure and heart rate are measured to acquire a general idea of the level of physical activity. Secondly, most of the participants (89%) had concomitant cardiovascular disease (eg, hypertension). Cardiovascular disease, such as hypertension, may result in a reduced cardiac output,¹² which may lead to decreased cerebral perfusion during exercise.¹³ It can be argued that the presence of vascular disease may have limited the potentially positive effects of walking on cognition as the increase in cerebral perfusion that is normally seen after exercise¹⁴ may have been reduced. Thirdly, although the duration of the walking programme was chosen to reduce attrition, one may argue that the duration of the treatment period was too short to increase cognition. In view of the high cardiovascular comorbidity, perhaps long term walking may benefit cognition in this group of people through a beneficial effect on the cardiovascular system.¹⁵ An important limitation of the study is the lack of information on the specific subtype of dementia diagnosis. More insight into the specific brain pathology of each participant (eg, cerebrovascular problems) could have shed more light on the present findings.

In conclusion, the current study does not support the notion that physical activity benefits cognition in older nursing home residents with moderate dementia, who suffer from cardiovascular disease. The precise influence of these potential modifiers of treatment outcome after physical activity remains to be elucidated in further studies.

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Competing interests: None.

Ethics approval: The study was approved by the local medical ethics committee of the VU Medical Centre, Amsterdam, The Netherlands.

REFERENCES

1. **Colcombe SJ**, Erickson KI, Scalf PE, *et al.* Aerobic exercise training increases brain volume in aging humans. *J Gerontol A Biol Sci Med Sci* 2006;**61**:1166–70.
2. **Kramer AF**, Hahn S, Cohen NJ, *et al.* Ageing, fitness and neurocognitive function. *Nature* 1999;**400**:418–19.
3. **Churchill JD**, Galvez R, Colcombe S, *et al.* Exercise, experience and the aging brain. *Neurobiol Aging* 2002;**23**:941–55.
4. **Adlard PA**, Perreau VM, Pop V, *et al.* Voluntary exercise decreases amyloid load in a transgenic model of Alzheimer's disease. *J Neurosci* 2005;**25**:4217–21.
5. **Cott CA**, Dawson P, Sidani S, *et al.* The effects of a walking/talking program on communication, ambulation, and functional status in residents with Alzheimer disease. *Alzheimer Dis Assoc Disord* 2002;**16**:81–7.
6. **Friedman R**, Tappen RM. The effect of planned walking on communication in Alzheimer's disease. *J Am Geriatr Soc* 1991;**39**:650–4.
7. **Bernardini B**, Meinecke C, Zaccarini C, *et al.* Adverse clinical events in dependent long-term nursing home residents. *J Am Geriatr Soc* 1993;**41**:105–11.
8. **Eggermont LH**, Knol DL, Hol EM, *et al.* Hand motor activity, cognition, mood, and the rest-activity rhythm in dementia. A clustered RCT. *Behav Brain Res* 2009;**196**:271–8.
9. **Heyn P**, Abreu BC, Ottenbacher KJ. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Arch Phys Med Rehabil* 2004;**85**:1694–704.
10. **Eggermont LH**, van Heuvelen MJ, van Keeken BL, *et al.* Walking with a rollator and the level of physical intensity in adults 75 years of age or older. *Arch Phys Med Rehabil* 2006;**87**:733–6.
11. **Westerterp KR**. Daily physical activity and ageing. *Curr Opin Clin Nutr Metab Care* 2000;**3**:485–8.
12. **Iriarte MM**, Perez Olea J, Sagastagoitia D, *et al.* Congestive heart failure due to hypertensive ventricular diastolic dysfunction. *Am J Cardiol* 1995;**76**:43D–7.
13. **Koike A**, Itoh H, Oohara R, *et al.* Cerebral oxygenation during exercise in cardiac patients. *Chest* 2004;**125**:182–90.
14. **Critchley HD**, Corfield DR, Chandler MP, *et al.* Cerebral correlates of autonomic cardiovascular arousal: a functional neuroimaging investigation in humans. *J Physiol* 2000;**523**:259–70.
15. **Aronow WS**. Exercise therapy for older persons with cardiovascular disease. *Am J Geriatr Cardiol* 2001;**10**:245–9.