

University of Groningen

Physical exercise and dementia

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Document Version

Publisher's PDF, also known as Version of record

Publication date:

2014

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Bossers, W. (2014). *Physical exercise and dementia: Delaying cognitive and motor decline via exercise*. [Thesis fully internal (DIV), University of Groningen]. [S.n.].

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CHAPTER

1

General introduction

STATUS QUO

The number of people older than sixty is growing faster than any other age group, and with increasing age the number of people with chronic disease will grow, leading to a higher healthcare burden.¹ High age and the genetic apolipoprotein-ε4 allele have been identified as the main risk factors for the onset of dementia, especially of the Alzheimer-type.² It is estimated that with high age the number of patients with dementia worldwide (i.e., 35.6 million in 2010) will grow exponentially, with increments ranging from 84% in 2030 to 224% in 2050.³ Specific estimations for the Netherlands predict a 21% increase in the number of patients with dementia in 2020, resulting in 300,000 patients.⁴

A healthy lifestyle can play a positive role in delaying the onset and progression of dementia.⁵ An aspect of a healthy lifestyle is physical activity, which the World Health Organization defined as: “Any bodily movement produced by skeletal muscles that requires energy expenditure”.¹ Physical activity obviously opposes physical inactivity, and a physically inactive lifestyle has been identified as a major risk factor for many health related pathologies, including cardiovascular (e.g., high blood pressure) and metabolic diseases (e.g., obesity, diabetes mellitus). Inactivity-related pathologies do not only dramatically increase the risk of developing dementia, they also accelerate dementia progression.⁵ Despite the generally known consequences of physical inactivity, it is striking that nine out of ten patients with dementia who live in Dutch nursing homes are physically inactive (i.e., “less than twice a year physically active for a period longer than twenty minutes at a moderate to high intensity”).⁶

With the recent recognition by the American College of Sports Medicine that ‘exercise is medicine’, physical activity in daily life (e.g., household tasks, gardening) and exercise (i.e., planned, structured physical training) in patients with dementia is suggested to be an effective non-pharmacological treatment that potentially can slow down disease progression with fewer side effects than current pharmacological treatments.

PHYSICAL EXERCISE IN PATIENTS WITH DEMENTIA

A model that can help us to understand the dynamic social and medical pathway from disease to functional decline in daily life is the Disablement Process Model.⁷ This model is a socio-medical model that comprehends the pathological processes leading towards disability. According to this model, the presence of a disease (pathology) leads to anatomical and structural abnormalities (impairments), which in turn leads to restrictions in basic and mental actions (functional limitations) that will eventually lead to difficulties in carrying out activities of daily living (ADL) (disability). Previously, the Disablement Process Model has been used to describe the disablement process in patients with dementia.⁸ Figure 1.1 illustrates the pathway, risk factors, extra-individual factors, and intra-individual factors, which are assumed to slow down or speed up the process towards disability.

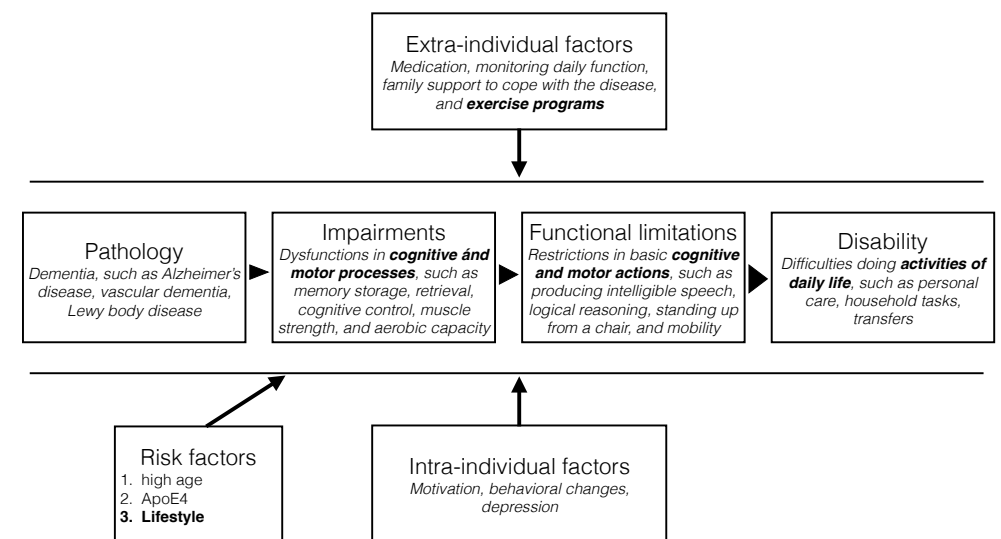


Figure 1.1. The Disablement Process Model to illustrate exercise / physical activity in context of patients with dementia. Factors that will be studied in the current thesis are printed in **bold font**.

The pathology of dementia is mainly expressed in behavioral changes (e.g., a disturbed circadian rhythm) and cognitive decline (e.g., a loss of memory and executive function). To date, treatment has focused mainly on those symptoms and their management. However, the motor symptoms of the dementia pathology

have been neglected, including impairments in walking endurance, muscle strength, mobility, and balance.⁹ These impairments are augmenting risk factors, which in turn are determinant characteristics for the origin of dementia and its progression (pathology). Inactivity as a result of these impairments can speed up the disease process along the model-pathway. Altogether, the impairments result in functional limitations that lead to problems in ADL, which is an important factor for admission to a care facility and a strong predictor for the overall care burden.^{10, 11} Finally, the rate of decline along the pathway from pathology to disability can also be influenced by extra-individual factors and intra-individual factors (Figure 1.1).

As described above, due to these motor and cognitive impairments that lead to functional limitations, patients with dementia have difficulties in performing ADL.^{12, 13} In addition, in contrast to their cognitively non-impaired peers, patients with dementia can also rely to a lesser extent on cognitive coping strategies to compensate for the loss of these motor and cognitive impairments during ADL tasks. Accumulating to the functional limitations, the additional impairments in cognitive coping strategies may lead to an even further and accelerated disability in ADL. Therefore, a regular aerobic and strength exercise program, for improving motor and cognitive function, may be beneficial to slow down the process towards ADL disability.¹⁴

PHYSICAL EXERCISE TO SLOW DOWN THE DEMENTIA PROCESS

As mentioned earlier, dementia is known for its accelerated deterioration of cognitive and motor function⁹, and one of the proposed strategies in slowing down this deterioration can be the use of an exercise program. Previous studies in healthy elderly agree that the strongest cognitive and motor effects can be reached after following a combination of strength and aerobic exercise training.¹⁵ However, studies in patients with dementia mainly focused on aerobic-only training programs (e.g., walking). The results of these studies are inconsistent and less convincing compared with studies that included healthy older subjects that participated in combined aerobic and strength exercise studies.¹⁶ Therefore, this thesis will focus on the cognitive and motor effects after a combined aerobic and strength exercise program in older patients with dementia.

Figure 1.2 illustrates the potential pathway that may be involved with regular combined aerobic and strength exercise. We expect that leg strength training improves balance and mobility. Improved balance and mobility are important factors for taking part in aerobic (e.g. walking) exercise, which conceptually leads to a higher aerobic training load and higher training intensity, leading to stronger motor responses. Furthermore, based on previous research, we hypothesize that improved motor function mediates improvement in cognitive function.¹⁵ The improvements in motor and cognitive function may then translate into improved ADL.¹⁴

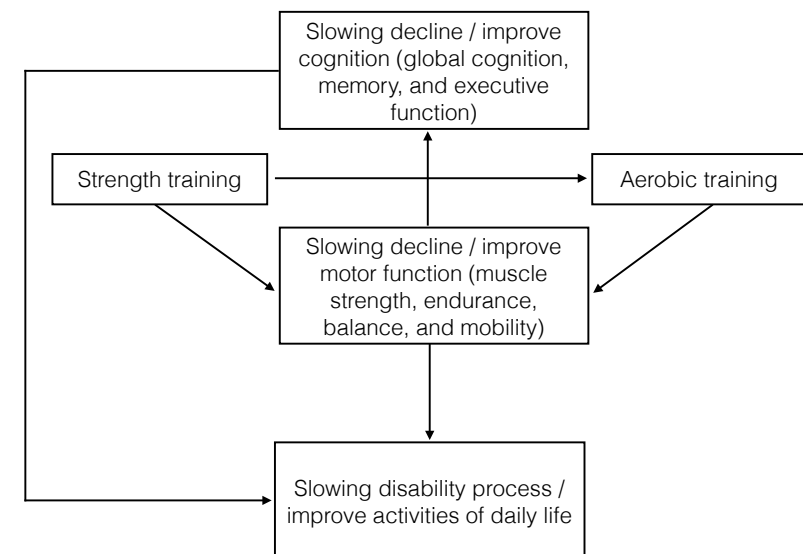


Figure 1.2. Hypothesized complementary motor mechanisms that are involved with regular exercise, consisting of a combination of aerobic and strength training sessions. We hypothesize that combined aerobic and strength exercise improves motor function, which mediates the slowing of deterioration, or the improvement of cognitive function. We expect that both changes in motor and cognitive function then mediate the performance in activities of daily life.

OBJECTIVES

The main objective of this thesis is to study the role of a controlled combined aerobic and strength training program in reducing the rate of cognitive and motor decline in patients with dementia who live in a nursing home. Four subsequent questions address the main objective:

1. What are the most frequently used neuropsychological and physical tests to measure cognitive and motor function effects in randomized controlled trials in patients with dementia?
2. Is a high frequency, moderate-to-high intensity exercise-program, consisting of alternating strength and aerobic (i.e., walking) sessions, feasible in older patients with dementia?
3. Is a combination of aerobic and strength training sessions more effective than aerobic-only training sessions in reducing cognitive and motor function decline in patients with dementia?
4. Is a combination of aerobic and strength training sessions more effective than aerobic-only training sessions in reducing the decline in ADL in patients with dementia?

Studying these four questions will provide more insight into the role of physical activity, disease progression, and ADL in patients with dementia.

OUTLINE OF THE THESIS

Chapter 2 presents a systematic review about the most frequently used neuropsychological and physical tests in randomized controlled trials in dementia patients between the years 2005 and 2011. The knowledge gained from that review was used for the development of a new dynamic walking test; The Groningen Meander Walking Test, specifically tailored to the abilities of patients with dementia, which is described in **chapter 3**. Outcomes of chapter 2 were implemented in the clinical trial development on cognitive and motor effects after a combined aerobic and strength exercise program in older patients with dementia, described in **chapter 4**. In this chapter, the results of a pilot study about the feasibility of a combined aerobic and strength exercise program in patients with dementia are presented, including the exploration of cognitive and motor effects. This preliminary pilot study prompted us to launch a large-scale randomized clinical trial, which is presented in **chapter 5**. This study sheds light on the beneficial effects of a combined aerobic and strength exercise program, when compared to an aerobic-only exercise program. Furthermore, this is the first study that investigated the mediating role of change in motor function on change in cognitive function. **Chapter 6** describes the effects of the developed combined exercise program on activities of daily living, which is of high practical and clinical importance. To conclude, **chapter 7** describes a general discussion of the studies, their limitations, and the potential directions for implementation and future research.

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