University of Porto

Faculty of Sport

Research Center of Physical Activity and Leisure

Multicomponent Exercise mitigates Dementia burdens

Relevance for Physical Fitness, Cognition, Functional Capacity, Neurophsychiatric Symptoms and Quality of Life.

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KEYWORDS: AGING, ALZHEIMER´S DISEASE, COGNITIVE FUNCTION, PHYSICAL ACTIVITY, MULTICOMPONENT EXERCISE, ACTIVITIES OF DAILY LIFE

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General Table of Contents

List of tables

List of Figures

Study 3

List of Abbreviations

ACSM - American College of Medicine;

AD - Alzheimer disease;

ADL - Activities of Daily Life;

BDNF- Brain-derived Neurotrophic Factor;

BMI - Body Mass Index;

BPSD - Behavioural and Psychological Symptoms of Dementia;

DSM - Diagnostic and Statistical Manual;

IGF-1 - Insulin-Like Growth Factor 1;

MMSE – Mini-Mental State Examination;

MND - Major Neurocognitive Disorder;

ME - Multicomponent Exercise;

NpI - Neuropsychiatric Inventory;

PwD - Person with Dementia;

QoL - Quality of Life;

SFT - Senior Fitness Test;

WHO - World Health Organization.

Abstract

In an attempt to counteract dementia-related diseases, the efficiency of numerous adjunct therapies has been investigated, including physical exercise. Physical fitness seriously impacts the ability to perform activities of daily life and the quality of life (QoL) of older people with dementia. Moreover, cognitive beneficial effects resulting from increased physical activity also might occur. The relevance of this research topic relies on the need to integrate the current knowledge about the protective effect of exercise, as a feasible therapeutic intervention to counteract dementia. The present thesis, comprises a general introduction and three experimental studies conducted with institutionalized older adults with dementia. The first intended to analyze the association between physical fitness components and functional capacity, cognition and QoL. The further two experimental studies were performed focusing on the effects of a 6 months' multicomponent exercise (ME) intervention on: a) physical fitness and cognition of older adults with Alzheimer disease; b) physical fitness, cognition and the caregiver's perspective of the functional capacity, QoL and Behavioral and Psychological Symptoms of Dementia (BPSD). Generally, physical fitness was associated with the cognition, functional capacity and QoL. The ME intervention improved the physical fitness and delayed the decreased in functional capacity in institutionalized older adults with dementia. Based on the caregiver's perspective, a ME intervention helped to contain the BPSD and to preserve patients' functional capacity and QoL. The data support the notion that chronic exercise mitigates dementia burdens. Alterations in physical fitness seem to positively impact the cognition, functional capacity, QoL and BPSD in institutionalized older adults with dementia.

KEYWORDS: AGING, ALZHEIMER´S DISEASE, COGNITIVE FUNCTION, PHYSICAL ACTIVITY, MULTICOMPONENT EXERCISE, ACTIVITIES OF DAILY LIFE

Resumo

Na tentativa de minimizar os efeitos das doenças relacionadas com a demência, têm sido investigadas numerosas terapias complementares, incluindo o exercício físico. A aptidão física parece ter um forte impacto na capacidade de realizar as atividades de vida diária e na qualidade de vida (QV) de idosos com demência. Além disso, o aumento da atividade física pode ter efeitos benéficos sobre a cognição. A relevância deste tópico de investigação resulta da integração do conhecimento atual sobre os efeitos protetores do exercício, como uma possível terapêutica capaz de minimizar os efeitos da demência. A presente tese compila três estudos experimentais realizados com idosos institucionalizados com demência. O 1º estudo analisou a associação entre as diferentes componentes da aptidão física e a capacidade funcional, cognição e QV. Os seguintes tiveram como objetivo compreender os efeitos de 6 meses de um programa de exercício físico multicomponente na: 2º estudo - aptidão física e cognição de idosos com a doença de Alzheimer; 3º estudo - percepção do cuidador sobre a capacidade funcional, QV e sintomas comportamentais e psicológicos da demência (SCPD) em idosos com demência. No geral, a aptidão física esteve associada com a cognição, capacidade funcional e QV. O programa de exercício físico multicomponente permitiu a melhoria da aptidão física e o atenuamento do declínio na capacidade funcional do idoso com demência. Na perspectiva do cuidador o programa de exercício físico multicomponente contribuiu para diminuir os SCPD e ajudou a preservar a capacidade funcional e QV dos pacientes. Os resultados apoiam a ideia de que o exercício crónico ajuda a atenuar o “peso” da demência. Alterações na aptidão física parecem ter impacto positivo sobre a cognição, capacidade funcional, QV e sobre os SCPD em idosos com demência.

PALAVRAS CHAVE: ENVELHECIMENTO; DOENÇA DE ALZHEIMER; FUNÇÃO COGNITIVA; ATIVIDADE FÍSICA; EXERCÍCIO MULTICOMPONENTE; ATIVIDADES DE VIDA DIÁRIA

GENERAL INTRODUCTION/THEORITICAL BACKGROUND

Dementia: A brief introduction

The global demographic structure has been changing with the world population ageing. In 2015, the number of older adults has reached 901 million worldwide, projections show that the numbers will increase 56% till 2030 and will duplicate till 2050 (United Nations, 2015). Inherent into the accelerated progression of the world ageing it is the increase of age-related health problems, including dementia.

According to the fifth edition of the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM-V), the previously called dementia (DSM-IV) is a Major Neurocognitive Disorder (MND) (through this thesis we will address it as dementia) and is caused by a variety of neurodegenerative diseases, including Alzheimer Disease (AD), Vascular Dementia, Dementia with Lewy bodies and Parkinson Disease (American Psychiatric Association, 2013). According with DSM-V the criteria for MND (previously dementia) includes: a) evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains: Learning and memory; Language; Executive function; Complex attention; Perceptual-motor; Social cognition. b) The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications. c) The cognitive deficits do not occur exclusively in the context of a delirium. d) The cognitive deficits are not better explained by another mental disorder (eg, major depressive disorder, schizophrenia).

Currently, the World Health Organization (WHO) estimates that 47.5 million people worldwide are living with Dementia, a figure that might increase to 75.6 million by 2030, and to 135.5 million by 2050 (WHO, 2015). In Europe, 8.7 million people lived with Dementia in 2012, including 182.5 thousand Portuguese citizens (Alzheimer Europe, 2013). Due to the magnitude of these numbers, and the social and economic burden, in 2012 the WHO recognized dementia as a public health priority (WHO, 2012).

Although dementia is not a natural consequence of aging, advanced age is the major risk factor for develop dementia, doubling every 5 years from age 65 (van der Flier & Scheltens, 2005). It is still controversial, whether increased rates of dementia with age are simply caused by the brain becoming older or whether they are trigger by other diseases or events that become more prevalent in later life (Alzheimer's Disease International, 2015). The etiology of dementia-related disorders is complex and multifactorial, involving genetic predisposition, environmental and endogenous factors (Skoog et al., 1999). Thus, although the exact causes of dementia are still not fully understood, several epidemiological studies demonstrate that history of stroke or transient ischemic attack, hypertension, hypocholesteremia, obesity, diabetes and insulin resistance, congestive heart failure and chronic inflammation, among others, can significantly influence the onset and the progression of cognitive impairment and dementia (Kern et al., 2001). The aggregation of vascular and metabolic risk factors has been suggested to have a greater impact on the development of dementia than each factor independently (Morris et al., 2014). In this context, dementia preventative measures largely focus on reducing risk factors, particularly those associated with vascular a metabolic disruption, including unhealthy dietary habits and physical inactivity (National Collaborating Centre for Mental Health, 2013).

The symptoms of dementia might appear several years after the disease initiation and are generally characterized by a progressive impairment of multiple higher cortical functions, mostly related with memory and thinking, language impairment, confusion and disorientation and difficulty with spatial awareness and skilled movement (Castro-Caldas & Mendonça, 2005). Additionally, behavioral and psychological symptoms in dementia (BPSD) are also frequently present and include apathy, depression, agitation, anxiety and alterations in emotional control (Castro-Caldas & Mendonça, 2005). Together, these progressive symptoms contribute to gradual motor and physical deficits and have an important impact on the ability to perform activities of daily life (ADL) and quality of life (QoL) of patients and their caregivers (Forbes et al., 2015). Clearly, this syndrome is associated with systemic manifestations that extend beyond the cognitive and behavioral impairment, contributing to physical and social disabilities, being considered a major health concern in nowadays society.

AD is the most common cause of dementia, representing 70% of all cases of dementia (Prince et al., 2011), and is characterized by neuritic plaques from abnormally aggregated Amyloid-Beta (Aβ) peptide and intracellular neurofibrillary tangles from paired helical filaments of hyperphosphorylated microtubule-associated tau protein in the brain (Castro-Caldas & Mendonça, 2005). Physiological consequences of Aβ include oxidative stress leading to accumulation of cell damaged, which can be an important factor in the progression of neuronal death (Mestel, 1996), a loss of cholinergic function that compromises memory and learning processes, degradation of synapses and a reduction in metabolic and immunologic functions (Mattson, 2002). Neurofibrillary tangles induce cytoskeleton alterations, causing neural function degradation (Mattson, 2002). Moreover, important neurochemicals for brain health, such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1), decline in patients with AD, promoting the degeneration of neurons and the cholinergic system in the brain (Eriksson et al., 2009). There is also evidence that alterations on synaptic plasticity, resulting from the decrease of BDNF and IGF-1, contribute to cognitive impairment in AD.

Dementia is a heavy burden for those living with the disease and their families (Alzheimer's Disease International, 2015). Dementia is tightly associated with a functional dependency that can culminate in institutionalization, exacerbating the social and economic impact of dementia in healthcare in coming years (Alzheimer's Disease International, 2015). Truly important is to highlight that dementia-related diseases steal from “their” patients some of the most essential features that make long lives worth living as thinking, feeling, remembering, deciding, and moving (Ransohoff, 2016).

Physical exercise has been recommended as a preventive and therapeutic non-pharmacological strategy in the management of patients with dementia and neurodegenerative disorders, including AD (Ahlskog et al, 2011). The present thesis discusses the potentiality of physical exercise as a non-pharmacological therapeutic tool in the management of dementia-related disorders. It is our belief that the understanding of the potential interaction between physical exercise engagement and possible adaptive responses in cognitive, physical and functional domains are essential to fully ascertain the safety and efficiency of exercise as an active lifestyle and supportive intervention to delay and antagonize dementia side effects.

Boosting cognitive, physical and functional capacity with exercise

In addition to improving general health status, QoL and physical fatigue, chronic exercise also mediates multisystemic adaptations associated with health benefits against several chronic pathologies including metabolic disorders, pulmonary and cardiovascular diseases, ageing-related systemic organ and/or tissue impairments and cancer (Ascensao et al., 2011; Deslandes et al., 2009; Pedersen & Saltin, 2015).

Chronic physical exercise allows the maintenance of higher levels of aerobic fitness that in turn maintains functionality, brain blood supply and reduces brain atrophy and promotes better cognition in those with early-stage of dementia (Cotman et al., 2007). Exercise seems to have a neuroprotective effect, regulating chemicals such as BDNF and IGF-1, allowing to increase dentric spines, enhance the glutamatergic system and reduce cell death (Cotman et al., 2007). As reported by Cotman and collaborators (2007) exercise may facilitate learning, elevate mood, delay age-related memory loss, speed information processing, increase brain volume, and hippocampal neurogenesis. Other studies have found that exercise has a positive effect on cognitive function in older adults without dementia (Rovio et al., 2005), as well as those presenting with mild cognitive impairment (Heisz et al.,2015) and individuals with dementia (Heyn et al., 2004). Due to its potential to increase and regulate BDNF and IGF-1, physical exercise can be used as a neuroprotective strategy to prevent and manage AD (Cotman et al., 2007). Moreover, exercise seems to prevent some of dementia modifiable risk factors, improving BPSD and delaying both cognitive and functional decline (McAuley et al., 2004). A growing challenge is to maintain elderly people with dementia independent, i.e. able to carry out ADL "with vigor and alertness, without undue fatigue and with ample energy to enjoy [leisure] pursuits and to meet unforeseen emergencies" (Garber et al., 2011). Among the physiological changes associated with aging, those affecting the cardiorespiratory and vascular system, and skeletal muscles are the ones most affecting physical fitness. However, exercise can attenuate these entire multisystem age-related decline.

Therefore, identifying the modifiable factors that can be stimulated with exercise and contribute to functional independence seems of unquestionable importance.

Literature points out that besides cognition, functional autonomy is directly dependent on physical fitness (Garber et al., 2011). Physical fitness is determined by several measurable health-related phenotypes (Garatachea & Lucia, 2013), including cardiorespiratory endurance, muscular endurance, muscular strength, body composition, and flexibility. These components are constantly required for carrying out ADL, such as getting up from a sitting or lying position, taking a shower, avoiding obstacles and walking (Gonçalves et al., 2010). Better fitness also was associated with a lower risk of mortality from dementia in a large cohort of men and women surveyed over a course of 17 years (Liu et al., 2012). Forbes and collaborators (2015) identified several recent trials and systematic reviews that have reported promising findings on the impact of exercise on people with dementia, particularly regarding its effect on cognitive functioning and on their ability to perform ADL.

QoL is a multidimensional concept, and physical fitness has been considered as one of its key components due to its importance to perform ADL independently (Ferrucci et al., 2004). In fact, among older adults with dementia, a negative QoL is associated with a diminished physical and cognitive function (Idler & Benyamini, 1997). As a factor that can be modified by increasing physical activity, physical fitness is essential for maintaining the motor skills that are critical for performing ADL and consequently for enhancing QoL in people with dementia (Forbes et al., 2015). Taken together, all older adults, and particularly those with dementia should remain physically active for as long as possible. Hence, a physically active lifestyle is also recommended as a non-pharmacological preventive and/or therapeutic strategy against numerous signs of cognitive impairment and neurologic diseases, as well as to counteract behaviour potentially risk factors associated with the onset and development of dementia-related diseases.

Evidence-based exercise interventions for older adults with Dementia

Although clinical trials have suggested that exercise is a feasible and safe supportive intervention, which increases the cognitive, physical and functional capacity with repercussions on the QoL in elderly with dementia-related disorders (Forbes et al., 2015) the consistence of all these major outcomes are low. The wide variety of methodologies applied regarding duration (e.g. 2 weeks;18 months), frequency (e.g. 2 times per week; daily) and exercise type (e.g. aerobic, strength, balance), different dementia population (e.g. stages of dementia; types of dementia) and different settings (e.g. institutionalized; community; home-based programs) may contribute to inconsistent or even contradictory outcomes (Forbes et al. 2015), as it can be depicted in table 1.

Table 1. Effects of exercise programs in old individuals with cognitive impairment or Dementia-related disease (adapted from Marques-Aleixo et al., 2012).

Population	Intervention/groups	Major Outcomes*	Reference
16 patients with slightly to moderately PD	14 wk, 2 days/wk intensive exercise	Intensive exercise improved motor disability, mood and subjective well-being in early to medium stage PD patients	Reuter et al. (1999)
153 patients with AD 55 to 93 years	3 months, 30 min/day -Moderate intensity exercise - Control group	Exercise training combined with teaching caregivers behavioral management techniques improved physical health and depression in AD patients	Teri et al. (2003)
25 old patients with Dementia	3 months, 30min/day - Physical exercises supported by music - Control group	Beneficial effect of a music-based exercise program on cognition in patients with moderate to severe Dementia	Van De Winckel et al. (2004)
75 old patients with mild cognitive impairment	10wk, 3days/wk, 30min/day - Frail aged appropriate, exercise program - Social visit - Control	Exercise may slow the rate progression of cognitive symptoms related to Dementia, slowed/reversed the disability in daily living activities	Stevens and Killeen (2006)
134 patients with mild to severe AD 62 to 103 years	12mon, 2days/wk, 1h/day, - walking, strength, balance, and flexibility - control group	Exercise slowed disability in performance activities of daily living in AD patients, although no observed effect on behavioral disturbance or depression	Rolland et al. (2007)

Population	Intervention/groups	Major Outcomes*	Reference
90 patients with moderate and severe AD	16wks, 5days/wk, up to 30min/day - walking - walking, strength, balance, and flexibility - social conversation	Long-term exercise resulted in better outcomes in mood and affect	Williams and Tappen (2007)
36 patients with moderate to severe Dementia, 85 years	12wk, 3 days/wk, 30min/day - moderate-intensity exercise - before and after measurements	Moderate-intensity exercise reduced symptoms of depression	Edwards et al. (2008)
50 years or older individuals who reported memory problems but did not meet criteria for Dementia	24-week PA intervention	PA program provided a modest improvement in cognition over a 18-month follow-up period in adults with subjective memory impairment	Lautenschlager et al. (2008)
45 patients with moderate to severe AD, 71 to 101 years	16wk, 5days/ wk, 30 min/day - strength, balance and flexibility + walking - walking - social conversation.	Depression was reduced in all three groups with some evidence of higher benefit in exercise groups	Williams and Tappen (2008)
27 patients with AD mean 75 years	12wk - exercise program: Aerobic 3.6 days/wk Strength 2.9 days/wk Balance 2.7 days/wk - control group	No significant differences between groups were noted in any of the cognitive outcome measures	Steinberg et al. (2009)
20 patients with mild to moderate PD, 65.4 years	6 months, 3days/wk, 60min/day - Aerobic exercise - control group	Exercise improved executive functions in PD patients.	Tanaka et al. (2009)
230 patients with AD	24wk, 150 min/wk - moderate PA - control group	PA in combination with usual care alleviated AD symptoms and improved their management and quality of life	Cyarto et al. (2010)
9 patients with PD, 65.8 years	6wk, 3days/wk, 50min/day - treadmill walking with additional body load - control group	Exercise had positive effects on cognition	Filippin et al. (2010)
28 patients with PD	12wk, 2days/wk, 60min/day - aerobic and strength exercise - control group	Exercise exerted a selective benefit for frontal lobe-based executive function	Cruise et al. (2011)
132 patients with AD 81 years	6 months, 7days/wk - 30min/day walking, -1 h/day light exercise - combination walking+light - control group	Walking, light exposure, and their combination improved sleep	Mccurry et al. (2011)
24 patients with advanced AD, older than 65 years	6 months, 4days/wk, 30min/day - aerobic walking - control group	Walking program stabilized progressive cognitive dysfunctions and improve performance of activities of daily living	Venturelli et al. (2011)

Population	Intervention/groups	Major Outcomes*	Reference
27 patients with AD 70.5 and 75.7	6 wks, 2h/wk - non-aerobic exercise - control group	Short course of non-aerobic exercise was effective at least in some aspects of cognitive functioning	Yaguez et al. (2011)

AD - Alzheimer disease, PA - physical activity, PD - Parkinson disease, *Adjusted for confounders, if applicable.

Research on the role of exercise and physical activity against dementia-related diseases has been a topic of considerable interest over the last years, but the diversity of methodologies used weaken the consistency of the outcomes (Heyn et al., 2004).

Despite the current recommendations recognize that a combination of aerobic activity, strength training, balance and flexibility exercises is important for maintaining physical and cognitive function in older adults with dementia, the existing body of evidence is mainly based on cross-sectional studies or based on experimental setups using isolated endurance training protocolos (Forbes et al., 2015). Thus, studies examining the effects of multicomponent exercise (ME) intervention on cognitive function are less frequent.

Some studies support that ME, generally defined as a combination of strength training, aerobic endurance, coordination, balance and flexibility (Carvalho et al., 2009), may have a larger effect on cognition than aerobic or resistance training alone (Smith et al., 2010). Although ME has been less investigated, studies have shown promising results as an effective approach to improve functional fitness in healthy older adults (Carvalho et al., 2010; Justine et al., 2011), and is also beneficial for cognitive function in older adults with cognitive impairment (Suzuki et al., 2013). Thus, rising attention should focus on the exercise type, intensity and volume, following the diagnosis of the disease, that is needed to optimize cognitive and physical fitness required to perform autonomously the ADL.

As referred before, together with cognition, physical fitness and the ability to perform ADL decline, another domain extremely relevant for the QoL of this population and their caregivers is BPSD, which develops over time and tends to persist throughout the course of the disease (Kaymaz & Ozdemir, 2016). BPSD that can manifest as hitting, pushing, self-harm, swearing, wandering, apathy, depression or continuously and repetitively asking questions are seen in 92% of patients with dementia (Cummings et al., 2007). These symptoms have devastating consequences for both the diagnosed individual and the entire family, who are no longer able to cope with these demands. Usually is due to BPSD that older adults often require institutionalization (Brodaty et al., 2014).

Frequently, institutional settings lack physical activity (Egerton & Brauer, 2009) and independent ADL opportunities, a situation that further emphasizes the decline of physical fitness contributing, in turn, to a faster progression of dementia.

Conversely, despite the strong evidence indicating potential benefits of exercise, there is currently no mandatory inclusion of simple, pleasant and feasible exercise program in institutional settings. However, developing safe and effective non-pharmacological programs, such as exercise interventions could contribute positively as a public health strategy to manage this worldwide problem that is dementia.

Aim of the present dissertation

The overall aim of this PhD thesis was to understand the effectiveness of a ME program, as a non-pharmacological intervention, intending to delay the progression physical fitness, cognitive and functional capacity declines due to dementia, the management of BPSD and correspondent distress in formal caregivers and QoL among institutionalized older adults with dementia. The general objective of this thesis supported the specific goals of the original articles presented in the experimental work of this thesis. Therefore, three experimental studies were conducted:

The cross-sectional study 1, aimed to understand of the association between the different components of physical fitness with cognition, functional capacity and QoL in older institutionalized population with dementia. It is our belief that a ME may be one of the most effective strategies to improve functional capacity and QoL. To test this hypothesis, two other experimental studies were performed. The study 2 was developed to better comprehend the effects of ME intervention on cognitive function, functional capacity and anthropometric variables in a particular institutionalized population with AD; Finally, the caregiver's perspective of the alterations of the BPSD, functional capacity and QoL following a ME intervention in institutionalized population with dementia, was the focus of the 3rd study.

EXPERIMENTAL STUDIES

The studies of this thesis were conducted in 15 nursing homes from different locations, including Lavra, Viana do Castelo, Viseu and Ovar. Figure 1 illustrates the main methodological features of the experimental work, detailing, for each paper, the sample size, participants' mean age, outcome variables, measurement techniques and the data analysis procedures. The complete description for each study is presented in the corresponding methods section. All participants provided a voluntary written consent and the ethical approval was granted by the Ethics Committee of the Faculty of Sport - University of Porto (CEFADE 02.2014 - see appendix).

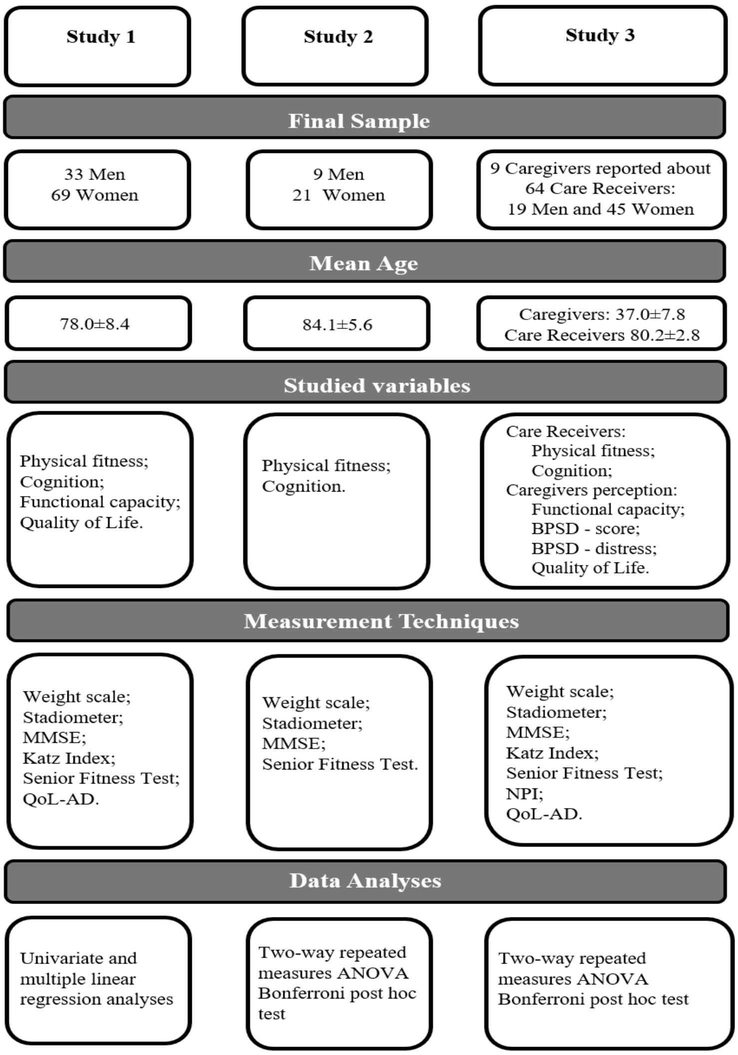

Figure 1. Outline of the experimental work

[Study 1]

Physical fitness in institutionalized older adults with dementia: Association with cognition, functional capacity and quality of life

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Study submitted to publication

ABSTRACT

This cross-sectional study investigated the association of physical fitness with cognitive function, functional capacity and quality of life among institutionalized older adults with dementia. One hundred and two older adults aged 78.0±8.4 years, predominately female (67.6%), with neurocognitive disorder due to Alzheimer's Disease (AD) (49.2%), vascular dementia (14.7%), Parkinson's disease (2%), dementia with Lewy bodies (2%) or unspecified dementia (32.1%) participated in the present study. Regression analyses were used to examine associations between physical fitness components (Senior Fitness Test) and cognitive function (Mini-Mental State Examination), functional capacity (Katz Index of Independence in Activities of Daily Living) and Quality of Life (QoL-Alzheimer's Disease scale). Results of univariate regression indicate that strength, flexibility, agility/dynamic balance and aerobic endurance are relevant for cognitive function, physical capacity and perceived QoL in institutionalized older people with dementia. After multiple regression analysis, adjusted for body mass index (BMI), results showed that aerobic endurance had a significant positive association with Total Katz Index. For both, caregiver perception of QoL-AD and global QoL-AD, BMI remained significantly and positively associated. Agility-dynamic balance presented a significant negative relation with global QoL-AD. Overall, our findings suggest that a better physical fitness is important for cognition and autonomous functional capacity, and that it has positive repercussions on the QoL in institutionalized older adults with dementia. Consequently, exercise-based therapeutic strategies aiming to improve physical fitness should be implemented.

Keywords: Alzheimer's disease; Physical Fitness; ADL; Aging; Institutionalization

Introduction

Dementia is a progressive degenerative syndrome that affects memory, thinking, behavior and the ability to perform Activities of Daily Life (ADL, Alzheimer's Disease International, 2014). According to the fifth edition of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-V), dementia is a Major Neurocognitive Disorder (MND) and is caused by a variety of neurodegenerative diseases, including Alzheimer Disease (AD, most common type), Vascular Dementia, Dementia with Lewy bodies and Parkinson Disease. Dementia affects over 48 million people worldwide, and it has been predicted that this number will double every 20 years (Alzheimer's Disease International, 2015). Due to its progressive degenerative nature, this syndrome contributes to physical, cognitive and social disabilities that culminate in functional dependency, usually leading to institutionalization. Therefore, dementia has devastating social consequences, not least on healthcare costs, effectively making it one of the main age-related health problems affecting worldwide (Castro-Caldas & Mendonça, 2005). Major international public health organizations and national governments are calling for policies to solve and/or mitigate the global burden of dementia (Shah et al., 2016). Among the innumerous preventive and therapeutic strategies used counteract dementia-associated diseases, physical exercise has been considered a promising non-pharmacological approach.

Aging is associated with a decrease in all health-related components of physical fitness, including cardiorespiratory endurance, muscular endurance, muscular strength, body composition, and flexibility (Caspersen et al., 1985). Moreover, as during the aging process older adults become less physically active (Sun et al., 2013), their physical fitness is negatively affected (Beherer et al., 2010). The physical fitness components are constantly required for carrying out ADL, such as getting up from a sitting or lying position, taking a shower, avoiding obstacles and walking (Gonçalves et al., 2010). However, functional capacity, in the sense of the ability to perform ADL autonomously (Wang, 2004), is not only associated with physical fitness but also with psychological factors acting together over extended periods of time (Verbrugge & Jette, 1994). Importantly, most older adults with dementia live in nursing homes and other institutional settings which lack opportunities for physical activity (Anderiesen et al. 2014) and thus exacerbates the decline of physical fitness.

Although the association between participation in physical activity programs and cognition in older adults still needs to be further investigated, several studies suggest a link between fitness training and improvements of several components of cognition across a broad range of ages, particularly in healthy subjects (for refs see Hillman et al. 2008). Also, there is some evidence that physical activity/fitness prevents dementia. In a large cohort of men and women surveyed over a course of 17 years, having a better fitness was associated with a lower risk of mortality from dementia (Liu et al. 2012). Based on randomized controlled trials, a recent review concluded that exercise programs might improve the ability to perform ADLs in people with dementia (Forbes et al. 2015). Thus, while there is only modest evidence for an effect of physical activity on cognitive function in people that have already developed dementia, physical training has a positive effect on their physical fitness (for refs see Pedersen and Saltin 2015), contributing to the improvement of their ability to perform ADL.

Quality of Life (QoL) is a multidimensional concept, and physical fitness has been considered one of its key components due to its importance to perform ADL independently (Ferrucci et al., 2004). In fact, among older adults with dementia, a negative QoL is associated with a diminished physical and cognitive function (Idler & Benyamini, 1997). As a factor that can be modified by increasing physical activity, physical fitness is essential for maintaining the motor skills that are critical for performing ADL and consequently for enhancing QoL in people with dementia (Forbes et al., 2015).

Further research is needed to help developing efficient exercise programs, and among others, is necessary to identify which physical fitness components are more relevant for institutionalized older adults with dementia. The present study aims to clarify the association between the different physical fitness components, as modifiable factors throughout life particularly with exercise engagement, with cognitive function, functional capacity and QoL in institutionalized older people with dementia.

Methods

Participants and study design

The participants of this cross-sectional study were recruited in six different Portuguese nursing homes. One hundred and two older adults from both genders, aged 65–93 years and all diagnosed by a physician with an age-related neurocognitive disorder, accepted to participate in the study. The eligible subject pool was restricted to older adults with the following characteristics: age ≥ 65 years, institutionalized for more than 6 months, diagnosis of an age-related neurocognitive disorder at mild or moderate stage according to the Clinical Dementia Rating (CDR, Morris, 1993) and absence of any diagnosed or self-reported musculoskeletal or cardiovascular disorders that contraindicate participation in physical fitness testing. On the initial screening visit, all participants, formal caregivers, and institutions received a complete explanation of the purpose, risks and procedures of the study. A written informed consent was provided and the review boards of the six nursing homes approved all methods and procedures. The investigation was in full compliance with the Helsinki Declaration (World Medical Association, 2009). The sociodemographic and clinical characteristics of participants at baseline are shown in Table 1.

Measurements

The same evaluators, in 6 different nursing homes, performed all measurements. On each nursing home the testing period had 1 week of duration. In the morning the following measurements were collected: weight, height, the Senior Fitness Test battery (SFT), the CDR (at the baseline), the Mini-Mental State Examination (MMSE) and Quality of Life-Alzheimer's Disease scale (QoL-AD). And in the afternoon formal caregivers filled Katz index and QoL-AD questionnaire. Despite de different institutions all assessments were organized in the same way.

Dementia Stage

The CDR test (Morris, 1993) was used to define participant's cognitive stage. CDR is an instrument that assesses the existence and prevalence of the various stages of dementia. It comprises six cognitive-behavioral items covering memory, orientation, judgment and problem solving, community activities, home and hobbies, and personal care. Based on the overall CDR score, participants were classified in one of the two following dementia stages: mild (CDR score =1) or moderate (CDR score =2).

Physical Fitness

Physical fitness was assessed with the SFT (Rikli & Jones, 2013), which is considered a reliable instrument for assessing physical fitness in older adults (≥ 60 years of age), including older people with cognitive impairment (Hesseberg et al., 2015). Participants performed six tests: chair-stand test (to assess lower-body strength); arm curl test (to measure upper-body strength); 2-minute step test (to assess aerobic endurance); chair sit-and-reach test (to assess lower-body flexibility); back scratch test (to assess upper-body flexibility); and 8-foot up-and-go test (to assess agility and dynamic balance); height and weight (to assess BMI).

Cognitive function

The MMSE (Folstein et al., 1975) was used for a global cognitive evaluation. This instrument is clinically used to assess cognitive mental status, as well as to detect and follow the course of a mental illness. It assesses orientation, attention, immediate and short-term recall, language and the ability to follow simple verbal and written instructions. A total score categorizes the individual on a scale of cognitive function ranging from 0 to 30 (Folstein et al., 1975). MMSE normative values consider the subjects' educational level. Operational cut-off values for the Portuguese population (Morgado et al., 2009) are 22 (for 0 to 2 years of literacy), 24 (for 3 to 6 years of literacy) and 27 (for more than 6 years of literacy).

Functional Capacity

The Katz index (Katz et al., 1963) was used for evaluate participant's functioning capacity based on caregiver-report. The index includes six items: bathing, dressing, transferring, feeding, incontinence, toileting and the sum of all items to calculate the Katz total. Independence levels for the ADL questions are recorded on a scale of 0 to 4, where 0 represents dependence and 4 represents complete independence (Sequeira, 2007).

Quality of Life

The QoL-AD (Logsdon et al., 2002) was used to measure participant's QoL. The questionnaire includes 13 items: physical health, energy, mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores, ability to do things for fun, financial situation and QoL as a whole. The QoL-AD uses both self-report and the caregiver's reports of the participant's QoL and is scored on a 4-point Likert scale ranging from 1 (poor) to 4 (excellent), with total scores ranging between 13 and 52 points.

Statistical Analysis

Characteristics of the sample were expressed either as means and standard deviations or proportions. Multiple regression analyses with cognition, functional capacity and QoL as the dependent variables and physical fitness components as independent variables were used. Candidate variables for the multivariable model were screened with univariate methods. At each step, the independent variable not in the model that had the smallest p-value was entered, and variables already in the model were removed if their p-value became larger than the significance level. The model was terminated when no more variables were eligible for inclusion or removal. Significance level in all analyses was set at 0.05. SPSS version 24.0 was used in all analyses.

Results

Characteristics of the Participants

Characteristics of participants are summarized in Table 1. The 102 participants were predominantly female (67.6%) and had neurocognitive disorder (NCD) due to AD. Hypertension, minor heart condition, diabetes mellitus and osteoporosis were the other main diagnoses besides NCD. The CDR showed that the average of the participants was in the moderate stage of dementia.

Table1. Characteristics of the participants

	Participants (n=102)
Age (years)	78.0 ± 8.4
Men, No. (%)	33 (32.4%)
Educational level (years)	3.48 ± 3.3
CDR (Points)	1.09 ± 0.6
Neurocognitive Disorder due to, No. (%)	
Alzheimer´s Disease	50 (49.2%)
Vascular Disease	15 (14.7%)
Parkinson's Disease	2 (2%)
Lewy Bodies Disease	2 (2%)
Unspecified	33 (32.1%)
Diagnosis (Others than NCD)**, No. (%)**	
Hypertension	32 (31.4%)
Heart Disease	20 (19.6%)
Diabetes Mellitus	15 (14.7%)
Osteoporosis	9 (8.8%)
Blood Pressure, (mmHg)	
Systolic	125.8 ± 20.8
Diastolic	73.9 ± 12.3
BMI (kg/m^2)	27.4±4.6
Physical Fitness	
Lower-body strength (Rps)	9.7 ± 4.2
Upper-body strength (Rps)	10.7 ± 5.0
Lower-body flexibility (cm)	19.2 ± 10.8
Agility/dynamic balance (sec)	19.2 ± 10.5
Upper-body flexibility (cm)	40.4 ± 14.2
Aerobic endurance (step)	64.5 ± 31.9
MMSE (Points)	17.9 ± 4.9
Total Katz (Points)	13.5 ± 4.2
	Participants (n=102)
Quality of Life (Points)	
Participant total score	25.8 ± 5.2
Caregiver total scor	24.2 ± 5.6
Global total score	25.3 ± 4.6

Number and proportional distributions are presented for categorical variables: Gender; Neurocognitive disorders and Diagnosis. All other variables are mean ± standar deviation

The association between the cognition (assessed by total MMSE) and physical fitness components are presented in Figure 1. With the exception of the lower-body strength and flexibility (p>0.05), physical fitness components were significantly associated with cognition. Aerobic endurance and upper-body strength were the components with the higher relation with cognition (Figure 1f and 1b), explaining ≈ 7.4% and 7.2% of the variance, respectively.

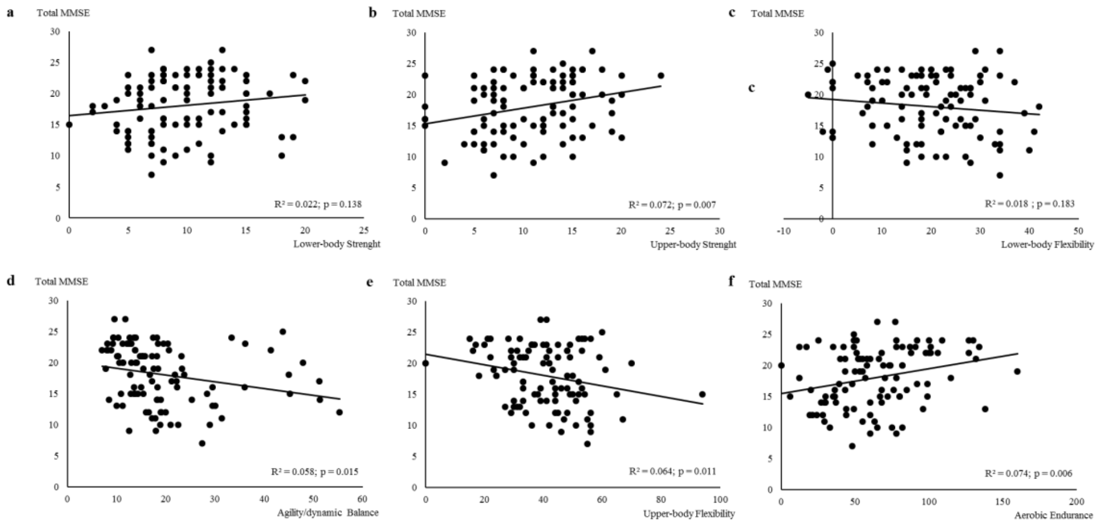

Figure 1. Regression relationships between cognition (Total MMSE score, points) and physical fitness components.

The association between functional capacity (assessed by total Katz) and physical fitness components are presented in Figure 2. Lower-body flexibility and agility and dynamic balance were not associated with cognition (p>0.05). All the other physical fitness components were significantly associated with functional capacity. Aerobic capacity was the component with the higher relation with functional capacity (Figure 2f), explaining ≈12.5% of the variance.

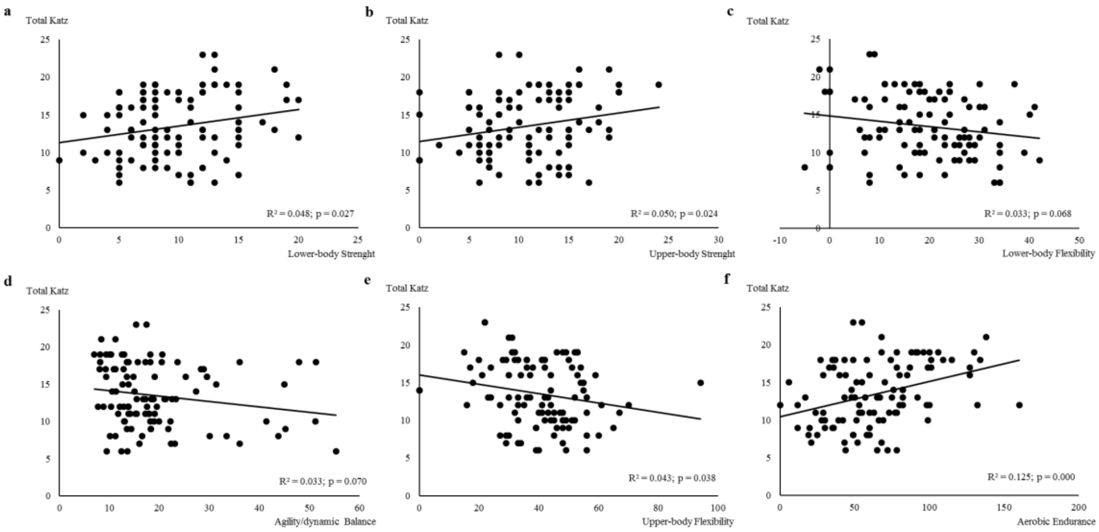

Figure 2. Regression relationships between functional capacity (Total Katz, points) and physical fitness components.

The association between QoL perceived by the participant and physical fitness components are presented in Figure 3. Flexibility (upper and lower body) was not significantly associated with QoL ($p>0.05$). All the other physical fitness components were significantly associated with QoL perceived by the participant. Aerobic endurance and agility/dynamic balance were the components with the higher relation with QoL perceived by the participant (Figure 4f and 4d), explaining ≈ 5.9% and 5.8% of the variance, respectively.

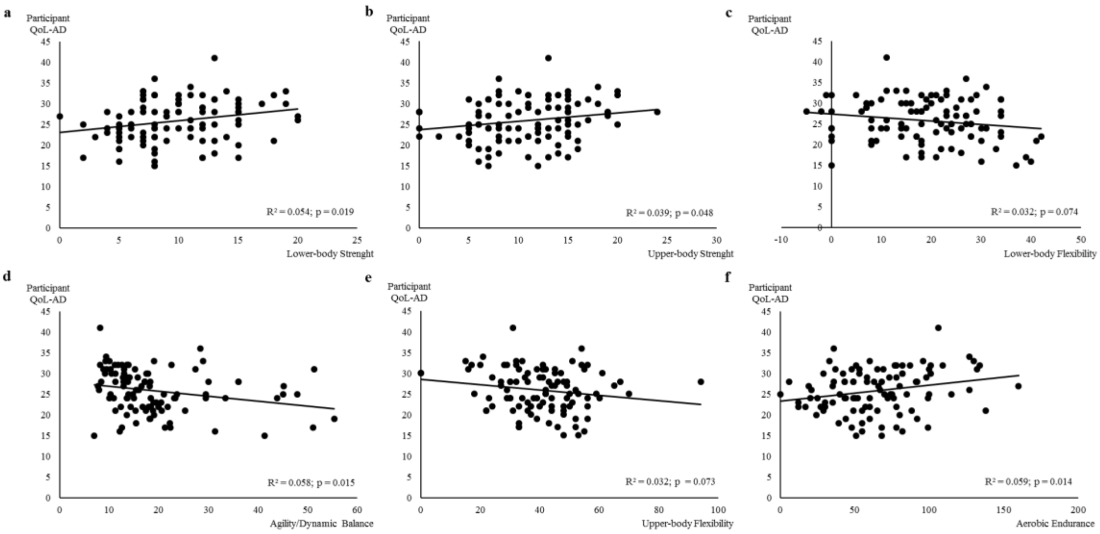

Figure 3. Regression relationships between quality of life perceived by the participant (Participant QoL-AD, points) and physical fitness components.

The association between QoL perceived by the caregiver and physical fitness components are presented in Figure 4. Flexibility (upper and lower body) was not associated with QoL perceived by the caregiver (p>0.05). All the other physical fitness components were significantly associated with QoL perceived by the participant. Lower and upper body body strength were the components with the higher relation with QoL perceived by the participant (Fig. 4a and 4b), explaining ≈ 12% and 14% of the variance, respectively.

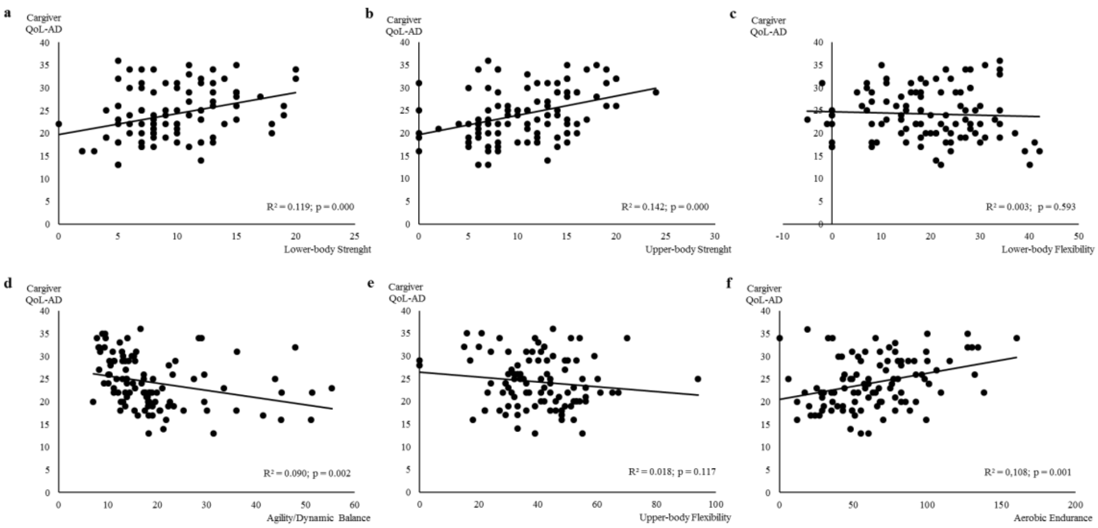

Figure 4. Regression relationships between quality of life of the participant perceived by the caregiver (Caregiver QoL-AD, points) and physical fitness components.

The association between global QoL and physical fitness components are presented in Figure 5. Flexibility (upper and lower body) was not associated with QoL perceived by the caregiver (p>0.05). All the other physical fitness components were significantly associated with QoL perceived by the participant. Lower body strength and aerobic endurance were the components with the higher relation with global QoL (Fig. 5a and 5f), explaining ≈ 9.7% of the variance for both components.

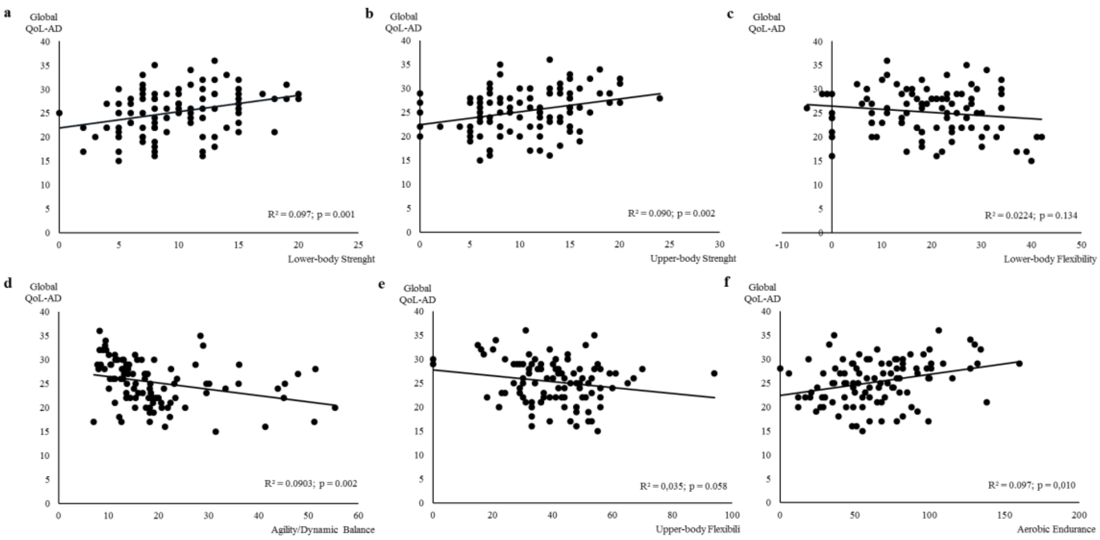

Figure 5. Regression relationships between global quality of life of the participant (Perception of participant + Perception of the caregiver) (Global QoL-AD, points) and physical fitness components.

Adjusted coefficients and 95% CI with cognition, functional capacity and quality of life as the dependent variables in linear multiple regression analyses are presented in Table 2. Age, gender and educational level were not correlated with cognition, functional capacity or QoL (data not shown), thus they were not included as confounding variables in the regression models. As BMI was associated with global QoL and caregiver´s perception of QoL (data not shown), this variable was included as a confounder variable in the multiple regression models for global QoL and caregiver´s perception of QoL. Aerobic endurance had a significant positive association with Total Katz index. For both, caregiver perception of QoL-AD and global QoL-AD, BMI remained significantly and positively associated. Agility-dynamic balance presented a significant negative relation with global QoL-AD. Additionally, lower-body strength had a significant positive effect in caregiver QoL-AD. No component of physical fitness was associated with cognition or with participant perception of QoL, suggesting that for these variables, there was not a physical fitness component that stands above others.

Table 2. Multiple linear regression analyses of associations between the cognition, functional capacity and quality of life and the components of physical fitness.

Multiple Linear Regression	**Adjusted R^2**	**Adjusted β (95% CI)**	**p-value**
Cognition [a]			
Functional Capacity [b]			
Aerobic endurance	**0.097**	**0.04(0.01 to 0.08)**	**0.012**
Participant QoL-AD [c]			
Caregiver QoL-AD [d]			
BMI	**0.346**	**0.42(0.15 to 0.70)**	**0.003**
Lower body strength		**0.51 (0.03 to 0.98)**	**0.038**
Global QoL- AD [d]			
BMI	**0.295**	**0.31(0.09 to 0.54)**	**0.008**
Agility/dynamic balance		**-0.18(-0.30 to -0.06)**	**0.003**

[a] Multiple regression adjusted for: Upper-body strength, Agility/dynamic balance, Upper-body flexibility and Aerobic endurance.
[b] Multiple regression adjusted for: Lower and upper-body strength, Upper-body flexibility and Aerobic endurance.
[c] Multiple regression adjusted for: Lower and upper-body strength, Agility/dynamic balance and Aerobic endurance.
[d] Multiple regression adjusted for: Lower and upper-body strength, Agility/dynamic balance, Aerobic endurance and BMI

Discussion

Although the relationship between higher levels of physical activity and functional capacity has been established previously (Manini & Pahor, 2009), the association between the specific dimensions of the physical fitness and the ability to perform ADL are still unclear, particularly among older adults with dementia. Moreover, studies regarding the impact of physical fitness on cognition mainly investigate aerobic fitness (Forbes et al., 2015) and the association between the different components of physical fitness and cognitive function, needs to be clarified in this frail population. Overall, the present study demonstrates that the different components of physical fitness are relevant for cognitive function and functional capacity in institutionalized older people with dementia. As physical fitness can modulate cognitive function and functional capacity, and as these are important for QoL (Forbes et al., 2015), this study also highlights the association between different physical fitness components and the QoL in this particular population.

Strength

The prevalence of age-related loss of muscle mass and strength (sarcopenia) seems to be more predominant in older adults with dementia than older adults without dementia. Gillette-Guyonne et al. (Gillette-Guyonnet et al., 2000) reported a sarcopenia prevalence of 40.6% in female subjects with AD in comparison to 21.9% in age-matched controls with no AD. Although the mechanisms behind these differences are not completely clear, it is possible that dementia and sarcopenia share certain mechanisms of pathogenesis (Auyeung et al., 2008), such as malnutrition, hormonal changes, oxidative stress, inflammatory process and usually involving a decreased exercise and activity (Roubenoff and Hughes, 2000). Previous reports suggested that the unintended weight lost and decreased BMI (White et al., 1998), observed in older adults with AD was predominately related with the loss of lean mass (for exemple seen in sarcopenia) (Burns et al., 2010). In our study, multivariate linear regression showed that BMI was positively associated with caregivers' perception and with global QoL. However, one of the limitations of the present study is the fact that it was not possible to measure the percentage of body fat mass and thus it is not possible to sustain that the QoL is influenced by the amount of the lean mass in older adults with dementia. Sarcopenia has been suggested to mediate the association between poor cognition and functional decline in cognitively impaired older adults (Auyeung et al., 2008). Nourhashemi (2002) and collaborators found that low cognitive function was associated with muscle loss in a group of over 7,000 community-dwelling older women. Raji (2005) and collaborators showed in a 7 years' cross-sectional study an association between having poor cognition and lower handgrip muscle strength in community-dwelling older adults. In accordance, in our study upper body strength showed to be positively associated with cognitive function (Figure1) in institutionalized older adults with dementia.

Deterioration of the functional capacity in general represents an increased risk of frailty, loss of independence and physical disability (Roubenoff and Hughes, 2000). In agreement with the literature, our data showed that upper and lower body strength was significantly associated with functional capacity and QoL (Figure 2, 3, 4 and 5). Although functional capacity and QoL are generally considered to be directly connected, in the present study, only lower body strength, in the multivariate model, was positively associated with QoL from the caregivers' perspective (Table 2). Since the lower-body strength is crucial to perform daily tasks (e.g. bathing, transferring or dressing) with a higher degree of autonomy, we might speculate that the caregivers related it with a better QoL.

Flexibility

Aging-induced reduced articular mobility is considered one of the main alterations in the neuromuscular system (de Souza Vale et al., 2009) that can compromise the functional capacity, as well as loss of autonomy and independence (Lojudice et al., 2008). This could be an even more problematic in institutionalized older adults with dementia. The range of motion of the upper-limb joints has been considered imperative for the ability to perform ADLs (Gates et al., 2016). Additionally, decreased flexibility of the lower limbs has been associated with the risk of injuries and falls and changes in the gait pattern (American College of

Sports et al., 2009). Although the present study failed to find an association between lower body flexibility and functional capacity a significant association between upper body flexibility with cognition and functional capacity was found in this frail population. This can suggest that some ADL (such as bathing and dressing) performed autonomously require upper body flexibility and may be cognitively challenging for people with dementia. Unexpectedly, no significant results were observed in the present study between flexibility and QoL.

Agility/dynamic balance

Our results showed that better agility/dynamic balance scores were positively associated with general cognition. In fact, older adults that have a better agility/dynamic balance also have more opportunities of physical practice, more autonomy and better environmental interaction, which could be important for maintaining their cognitive function. Evidence shows that cognition plays a key role in the regulation and control of mobility (Montero-Odasso et al., 2015). This motor behavior involves dissociable neural systems that control gait initiation, planning and execution and the adaptation of these movements to meet motivational and environmental demands (Rossignol et al., 2006). Cross-sectional studies have shown that level of cognition is related to mobility, in community-dwelling older adults (Carlson et al., 1999, Ble et al., 2005, Soumaré et al., 2009, Buchman et al., 2011). Moreover, agility/dynamic balance is inversely associated with the risk of falls (Shaw et al., 2003) being one of the main geriatric problems that significantly increase the risk of hospitalization and institutionalization (Davis et al., 2015) decreasing consequently their QoL. In our study, agility/dynamic balance scores were positively associated with participant's perception, caregivers' perception and global QoL. After a multivariate linear regression agility/dynamic balance was still positively associated with global QoL. These results corroborate the literature that had already established the relation between mobility and QoL, in non-demented older adults (Fagerstrom and Borglin, 2010). Furthermore, Davis et al. (2015)

points to agility/dynamic balance as a predictor of health related QoL in community-dwelling older adults (Davis et al., 2015).

Aerobic Endurance

Aerobic endurance is the most frequently studied component in physical fitness in older adults with dementia, being considerate a predictor of cognitive performance, in healthy older adults (Barnes et al., 2003) and the most effective type of exercise to improve cognition in older adults with dementia (Forbes et al., 2015). Our study results showed a positively association between aerobic endurance with cognition, corroborating other studies that have shown that higher levels of aerobic fitness are related to better brain health (Colcombe & Kramer, 2003, Gordon et al., 2008, Johnson et al., 2012) and cognition (Baker et al., 2010), preserving of critical brain areas in cognitively healthy older adults (Colcombe & Kramer, 2003) and persons with AD (Honea et al., 2009), as well as reduced brain atrophy in those with early-stage AD (Burns et al., 2008). Multiple mechanisms may account for associations between aerobic endurance and cognitive function. In fact, higher aerobic fitness is linked with upregulation of neurotrophins (e.g. the brain-derived neurotrophic factor, BDNF), neurovascular plasticity (primarily via angiogenesis) and neurogenesis contributing to better cerebral health (Churchill et al., 2002). BDNF levels (which contribute to growth regulation, maintenance and survival of neurons) can be increased by aerobic endurance training (Rasmussen et al., 2009, Seifert et al., 2010). In our study aerobic endurance is also associated with functional capacity. After a multivariate linear regression aerobic endurance still positively associated with functional capacity. These results are according with Morey et al. (Morey et al., 1998) that showed that aerobic endurance capacity is directly and independently associated with the ability to perform ADL independently.

Conclusions

In summary, we believe that our findings contribute to better understanding the impact of the different physical fitness components on cognition, functional capacity and QoL in institutionalized older adults with dementia. Although aerobic endurance stands out as the key factor of physical fitness in association with cognitive function, functional capacity and QoL, the results of this study suggest that the contribution of every component of physical fitness seems to be singular and irreplaceable. Thus, strategies to attenuate the decline of the different physical fitness components, such as the implementation of multicomponent exercise interventions (combined aerobic exercise, flexibility, strength and agility/balance training) may contribute to preserve cognitive function, functional capacity and to maintain QoL, in this particular population.

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[Study 2]

Effects of a Multicomponent Exercise Program in Institutionalized Elders with Alzheimer's Disease

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ABSTRACT

This study examined the effect of a Multicomponent Exercise (ME) intervention on cognitive function, functional fitness and anthropometric variables in institutionalized patients with Alzheimer's Disease (AD). Thirty-seven institutionalized elders (84.05 ± 5.58 years) clinically diagnosed with AD (mild and moderate stages), were divided into two groups: Experimental Group (EG, n= 19) and Control Group (CG, n= 18). The EG participated in a 6-month supervised ME intervention (aerobic, muscular resistance, flexibility, coordination and postural exercises) of 45-55 minutes/session, twice/week. Cognitive function (MMSE), physical fitness (Senior Fitness Test) and anthropometric variables (Body Mass Index and Waist Circumference), were assessed before (M1), after 3 months (M2) and 6 months (M3) of the experimental protocol. A two-way ANOVA, with repeated measures, revealed significant group and time interactions on cognitive function, chair stand, arm curl, 2-min step, 8-foot up-and-go (UG), chair sit-and-reach (CSR) and back scratch tests as well as waist circumference. Accordingly, for those variables a different response in each group was evident over the time, supported by a significantly better EG performance in chair stand, arm curl, 2-min step, UG, CSR and back scratch tests from M1 to M3, and a significant increase in MMSE from M1 to M2. The CG's performance decreased over time (M1 to M3) in chair stand, arm curl, 2-min step, UG, CSR, back scratch and MMSE. Results suggest that ME programs may be an important non-pharmacological strategy to improve physical and cognitive functions in institutionalized AD patients.

Keywords: Alzheimer's Disease, Cognitive Function, Functional Fitness, Exercise, Aging.

Introduction

The world's population is ageing at an exponential rate, accompanied by an increase of age-related pathologies (Castro-Caldas & Mendonça, 2005) such as dementia and Alzheimer's Disease (AD). The World Health Organization (WHO) estimates that 47.5 million people worldwide are living with dementia, a figure that might increase to 75.6 million by 2030, and to 135.5 million by 2050 (WHO, 2015). In Europe, 8.7 million people lived with dementia in 2012, including 182.526 Portuguese citizens (Alzheimer Europe, 2013). AD is the most common cause of dementia and may contribute to 60–70% of cases. Starting at age 65, the risk of this neurodegenerative disorder doubles every 5 (Prince et al., 2013).

The benefits of moderate exercise in relation to chronic degenerative diseases are well known (Barnes et al., 2007), contributing towards the prevention and reduction of morbidity and mortality of the elderly (Barnes et al., 2007). Regular exercise reduces vascular risk, obesity, levels of inflammation markers and it improves metabolism (Rovio et al., 2005). Besides improving general health status, strong evidence shows that functional fitness and cognitive function in older adults can be improved by regular physical activity (Heyn et al., 2014).

Functional fitness is universally accepted as an indicator of health status and quality of life in older adults (Justine et al., 2011). It comprises aerobic capacity, muscle strength and static/dynamic balance agility and flexibility (Justine et al., 2011). During the aging process, there is a natural decline of physical functioning that is amplified by the progression of AD, including the loss of ability to perform Activities of Daily Living (ADLs), thus leading to higher levels of dependency (Noro et al., 1996).

Due to cognitive-behavioral functioning impairment and compromised ability to perform ADLs inherent to AD progression (Melrose et al., 2011), older adults with AD tend to lose their autonomy. This has devastating consequences for both the diagnosed individual and the entire family, who are no longer able to cope with these demands. As result, patients often require institutionalization (Brodatz, et al. 2014). Usually, institutional settings lack physical activity opportunities, a situation that further emphasizes the decline of functional fitness contributing in turn to a faster progression of AD.

Although there are a growing number of publications on exercise programs for people with dementia, the studies reveal a wide variety of methodologies applied to different stages of dementia, resulting in inconsistent or even contradictory outcomes (Heyn et al., 2004).

The majority of studies have assessed the effectiveness of aerobic training on cognitive function and brain health. The literature points out that aerobic training can increase blood flow in the brain and regulate neurotrophic factors which, in turn, have been associated which improvements of cognitive functions, neurogenesis, angiogenesis and brain plasticity (Rovio et al., 2005). Aerobic training is also associated with higher cortical tissue on the temporal, parietal and frontal lobes, which are the key areas associated with cognition (Colcombe et al., 2003) and brain activation patterns (Voss et al., 2011). Fewer exercise intervention studies have examined the effects of resistance training on cognitive function. However, there is some evidence that resistance-only training contributes to functional plasticity in brain regions associated with executive function and increased levels of IGF-1, thought to be related to the preservation of cognitive function (Cassilhas et al., 2007).

Thus, multicomponent exercise (ME [1]), including 3 or more physical fitness components, may have a larger effect on cognition than aerobic or resistance training alone (Kirk-Sanchez & McGough, 2014; Smith et al., 2010). Although ME has been less investigated, studies have shown that it is an effective approach to improve functional fitness in healthy older adults (Justine et al., 2011), and is also beneficial for cognitive function in older adults with cognitive impairment (Suzuki et al., 2013).

The present study was designed to determine the effect of ME on cognitive and functional fitness in institutionalized AD patients following 3 and 6 months of training. Due to its wide applicability and feasibility, it is pertinent to assess to

[1] ME is generally defined as a combination of strength training, aerobic endurance, coordination, balance and flexibility, and is recommended by current PA guidelines for older adults (Carvalho et al. 2009).

what extent ME (integrating several important physical abilities to perform the ADLs, and involving playful and social group activities and cognitive stimulation) can contribute to AD therapy as a low cost alternative to mitigate symptoms, alleviate disease progression (thus allowing the preservation of physical and brain health of patients with AD) and offset the lack of physical activity opportunities in institutions.

Methods

Study Design

Nine nursing homes took part in this quasi-experimental non-randomized study. Four nursing homes implemented the ME t intervention for 6 months (EG); while five haven't participated in structured physical activity program and maintained with their normal routine, during the same period (CG) [2].

Participants

Of twelve nursing homes invited, nine nursing homes in suburban areas Viseu, Portugal, accepted to be part of this study. Participants were recruited from these institutions, forty-nine older adults from both genders clinically diagnosed with AD, aged 69–94 years, volunteered to participate in this study.

The eligible subject pool was restricted to older adults with the following characteristics: age ≥ 65 years, not engaged in any regular exercise training in the last year, institutionalized for more than 6 months, diagnosis of AD at mild or moderate stage according to Clinical Dementia Rating (CDR) (Morris 1993) and lack of any diagnosed or self-reported musculoskeletal or cardiovascular disorders that contraindicate participation in moderate exercise and testing. A 70% minimum attendance rate to the exercise sessions was required for

[2] Participants were assigned to the different groups according to the results of the CDR test. After screening the stage of dementia of all participants, the allocation of the institutions was based on the homogeneity of participants in the initial and moderate stage of dementia in the EG and the CG.

participants in the EG.

After initial screening, all participants, formal caregivers, and institutions received a complete explanation of the purpose, risks and procedures of the study. A written informed consent was provided. The investigation was in full compliance with the Helsinki declaration (World Medical Association, 2009) and the nine institutions where the intervention took place approved all methods and procedures. The Ethical Commission of the Faculty of Sports of the University of Porto also approved this study. The participants flow diagram is represented in

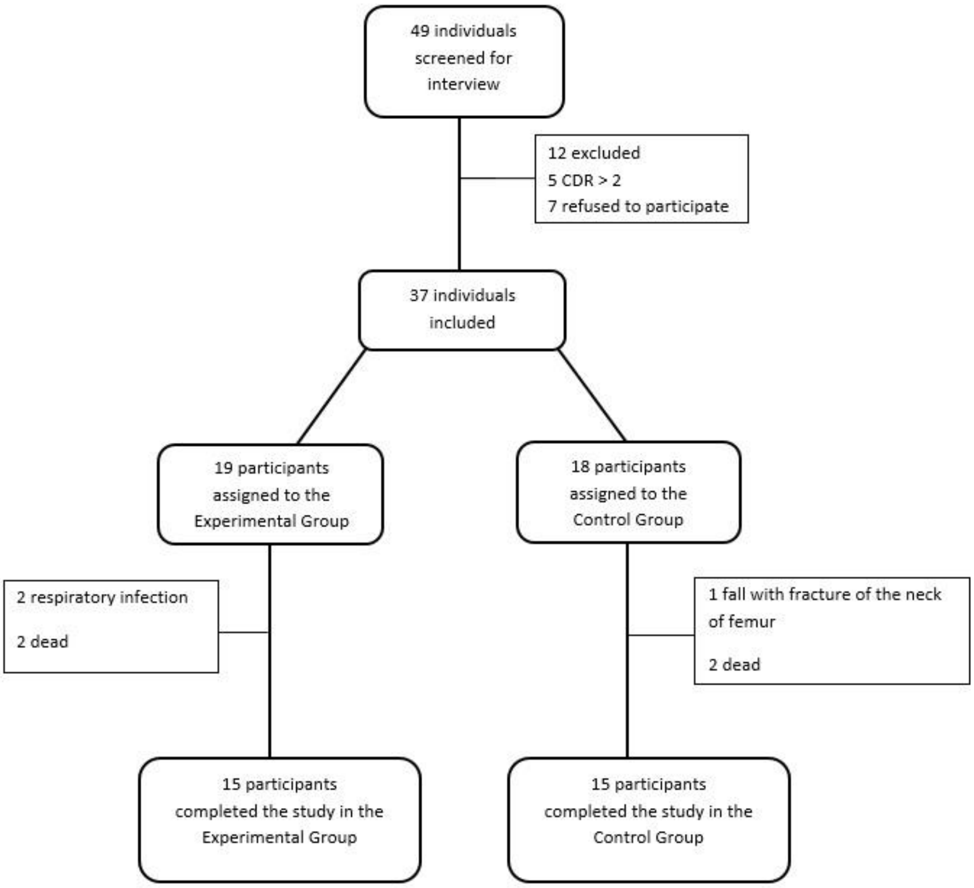

Figure 1. Participants flow diagram from initial screening to the end of the study.

Exercise Intervention

The EG completed a 6 month ME intervention following the recommendations of the American College of Sports Medicine (Nelson et al., 2007), including aerobic, muscle strengthening, flexibility, balance and postural exercises with 2 sessions per week on non-consecutive days. Sessions contained 4-7 participants and took place in specific rooms with peaceful and pleasant music environment. Sessions lasted for 45-55 minutes and were conducted by the same exercise trainer in all settings. The sessions were divided into 3 main parts: Warm-up (5-10´, including postural and stretching exercises for general activation), specific training (30-35´, including 15´ of moderate aerobic exercises + 15-20´ motor and muscular tasks for strength and coordination/balance training) and cool down (5´ with respiratory and flexibility exercises). In order to make the exercise program more efficient and attractive, regular similar routines that prioritized enjoyable and familiar exercises were established (as simulating walking, running, biking, rowing) (Teri, Logsdon et al. 2008). Due to the frailty condition of the participants and for safety reasons, sessions were mainly chair-based and routines of functional exercises with low coordination requirements stressed allowing the participants to achieve the session's goals.

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics of the participants were provided by the nursing homes where they were residing. Their sociodemographic and clinical characteristics are given in Table 1.

Table1 Characteristics of the participants

	Exercise Group (n=19)	Control Group (n=18)	p[a]
Age (years)	77.29±8.60	80.15±2.80	0.179
Men, No. (%)	4 (21.1%)	5 (27.8%)	0.685
Marital Status			0.693
Single/ Widower	16 (84.2%)	14 (77.8%)	
Married	3 (15.8%)	4 (22.2%)	
Educational level (years)	3.89±3.70	2.27±1.54	0.039*
Profession (%)			0.508
Domestic/Agricultural	10 (52.6%)	12 (66.7%)	
Others	9 (47.6%)	6 (33.3%)	
Diagnosis, No. (%) (Others than AD)			
Hypertension	12 (63.2%)	13 (72.2%)	0.728
Heart Disease	5 (26.3%)	8(44.4%)	0.313
Diabetes mellitus	3 (15.8%)	6 (33.3%)	0.269
Depression	7 (36.8%)	4(22.2%)	0.476
Medication, No.	7.79±1.75	8.3±2.11	0.448
Blood Pressure, mmHg			
Systolic	126.72±22.50	128.81±22.10	0.718
Diastolic	76.47±14.64	76.73±17.31	0.950
Clinical Dementia Rating scale Baseline	1.68±0.48	1.13±0.63	0.911

[a]Student´s t-test or Mann Whitney for continuous variables; Chi-squared or Fisher´s exact test (two-tailed) for categorical variables.

Outcome Measures

All following measures were assessed at baseline and after 3 and 6 months of experimental protocol.

Dementia Stage

The CDR test (Morris, 1993) was used only at baseline to distribute the participants according to their cognitive stage. CDR is an instrument that assesses the existence and prevalence of the various stages of dementia. It comprises 6 cognitive-behavioral items covering memory, orientation, judgment and problem solving, community activities, home and hobbies, and personal care. The cut-off points were CDR=1 (mild dementia stage) and CDR=2 (moderate dementia stage).

Anthropometry

Anthropometric variables included Body Mass Index (BMI) and Waist Circumference (WC). BMI was determined using the standard formula: weight divided by height squared (kg/m^2). Body weight was measured to the nearest 0.1 kg with a digital weight scale. Participants were weighed barefoot wearing light clothing. Height was measured to the nearest 1mm with a standard stadiometer. Participants were required to maintain the Frankfurt plane, standing as tall as possible with hands hanging by their sides, and taking a deep breath before the measurement. WC was assessed at the midpoint between iliac crest and the bottom of the ribcage using a spring-loaded measuring tape.

Functional Fitness

The Senior Fitness Test (Rikli & Jones, 2013) battery for older adults was used to assess functional fitness associated with maintaining physical independence into later life. The test items included: chair-stand test- to assess lower-body strength; arm curl test - to measure upper-body strength; 2-min step test - to assess aerobic endurance; chair sit-and-reach test - to assess lower-body flexibility; back scratch test - to assess upper-body flexibility; and 8-foot up-and-go test - to assess agility and dynamic balance.

Cognitive function

The Mini-Mental State Examination (MMSE) was used for a global cognitive evaluation (Folstein, et al. 1975). It is a widely used method for assessing cognitive mental status. This instrument is clinically used to detect and follow the course of an illness and can also be used as a research tool to screen for cognitive disorders and follow cognitive changes in epidemiological studies. It assesses orientation, attention, immediate and short-term recall, language and the ability to follow simple verbal and written instructions. Furthermore, it provides a total score that categorizes the individual on a scale of cognitive function (Folstein, et al. 1975). Ranging from 0 to 30. MMSE normative values consider the subject educational level. Operational cut-off values for the Portuguese population are 22 (for 0 to 2 years of literacy), 24 (for 3 to 6 years of literacy) and 27 (for more than 6 years of literacy) (Morgado et al., 2009).

Statistical Analysis

All statistical analyses were conducted with the SPSS IBM Statistical Software version 20.0 for Windows with a significance level of 0.05. For the baseline comparisons between EG and CG, data for all participants are presented as absolute (proportions) and relative (percentages) frequencies for categorical values, as means with standard deviation (SD) for interval data. The Chi-square test or Fisher exact tests were used to compare categorical data, and Student's t-test or non-parametric Mann-Whitney were applied for interval data (table1).

A two-way (group and time) factorial ANOVA, with repeated measures on one factor (time) was used to determine differences between and within the EG and the CG for dependent variables. Bonferroni Post-hoc analysis was used to determine differences between the 3 time-points.

Results

Recruitment

The process of recruitment and screening of participants lasted for two months. Of the forty-nine participants who were assessed for eligibility, twelve were excluded. A severe stage of dementia was the reason for the exclusion of five individuals and seven older adults declined to participate in the study after being informed of the details.

The intervention included thirty-seven participants, divided into two groups: EG (n= 19; mean age= 84.8±5.9 years) and CG (n=18; mean age= 83.3±5.3 years). In the EG, two participants dropped out due to respiratory infections and two died. In the CG, three dropouts were registered, one due to a fall and a femoral neck fracture, and two due to death. Thus, the dropout rate from the initial assessment and group's allocation until the end of the study was 18.9%. Resulting in 15 participants for both groups. Figure 1 shows the participant flow from screening to the end of the study.

Attendance rate for the EG was calculated by dividing the number of exercise sessions completed by participants by the full amount of sessions they were expected to perform throughout the study. The attendance levels were 85% or over. The reasons for missing exercise sessions were behavioral disorders (33.3 %), acute diseases (26.7%), unwillingness to participate in a particular exercise session (20%) and other reasons (20%). The dropouts occurred between the 12th and 46th session from a total of 48 ME sessions.

Subject characteristics

The sociodemographic and clinical characteristics of participants at baseline are shown in Table 1. No significant differences at baseline were found between the groups.

The 37 participants in the study were predominately females (75.7%) and single or widowed (81.1%). Apart from AD, in both groups (EG and EC), participants were mainly diagnosed with hypertension, minor heart condition, diabetes mellitus and depression. The CDR (EG = 1.68 ± 0.48: CG = 1.67± 0.49) allowed ensuring that the stage of dementia of all participants ranged between mild (n=12) and moderate (n=25).

The number of participants that did not complete the study was similar in each group (p= 0.737). Dropout participants had no statistically significant differences compared to the other older adults in any descriptive parameters. None of the reasons for dropping out (including deaths) were directly or indirectly related to possible adverse effects of the exercise program.

Changes in body composition, functional fitness and cognitive function in the EG and the CG are reported in Table 2.

Anthropometry

In the baseline values, no significant group differences were found in BMI and WC. For WC a different response in each group was evident over time, supported by a significant decrease of WC in the EG from M1 to M2 ($p<0.05$) and from M2 to M3 ($p<0.05$). During the intervention, the CG presented a subtle, though not statistically significant, increase in the WC test. There was a significant main effect of time on WC ($p= 0.027$) and of group and time interactions on WC ($p<0.001$). No changes – neither significant interactive nor main effects of time and group - were observed for BMI.

Functional Fitness

No significant group differences were found at baseline for all functional fitness variables. Different responses in each group became evident over time. A significantly better performance in the EG in the Chair Stand test from M1 to M2 ($p<0.05$) and from M1 to M3 ($p<0.05$) was found. Also, significant main effects of time ($p<0.001$) and interaction ($p<0.001$) were observed in the chair-stand test. The CG had a worse performance in the chair-stand test over time, although not statistically significant. The EG improved its performance over the time, being statistically significant from M1 to M2 and from M1 to M3 on arm-curl test ($p<0.05$), CSR test ($p<0.05$) back-scratch test ($p<0.05$) and 2-min step test ($p<0.05$). The CG had a statistically significant decrease in their performance, between M1-M3, on arm-curl test ($p=0.047$) and CSR test ($p= 0.020$). Thus, there were significant interactive and main effects of group on arm-curl test ($p=0.045$), CSR test ($p<0.05$) back-scratch test ($p<0.05$) and 2-min step test ($p=0.021$). In the back-scratch test significant interactive ($p=0.022$) and main effects of time (p=0.002) and group (p<0.001) were observed. From M1-M2 (p<0.05) and from M1-M3 (p<0.05), the EG significantly improved their performance in this test. In the UG test, groups responded differently resulting in a significant interaction from M1-M3 (p=0.029).

Cognitive Function

At the baseline, no significant group differences were found in cognitive function. A significant increase in MMSE from M1 to M2 (p=0.016) was observed in the EG, while a significant decrease of performance of the CG was observed over time M1 to M3 (p=0.016). Analysis revealed significant group and time interactions on MMSE (p=0.008) and significant main effects of time for this same variable (p=0.036).

Table 2. Pre-test, 3-month test and post intervention test outcomes for body composition, functional fitness and cognitive variables

Variable	Exercise Group (M ± SD)			Control Group (M ± SD)			p (Group)	p (Time)	p (Interaction)
	Pre-test (M1)	3-month test (M2)	6-month test (M3)	Pre-test (M1)	3-month test (M2)	6-month test (M3)			
BMI (kg/m^2)	27.7±3.2	27.5±3.2	27.3±3.3	27.8±5.8	27.9±6.2	27.9±6.7	0.828	0.766	0.641
WC (cm)	98.5± 6.3	96.9±6.7°	93.5±8.2°°;°°°	99.4±14.8	99.8±15.6	100.7±16.9	0.412	0.027*	<0.001*
Chair Stand	5.7±3.7	8.5±3.9°	9.5±5°°°	6.2±3.1	5.8±3.2	5.2±2.8	0.103	<0.001*	<0.001*
Arm Curl	9.6±4	11.2±4.1°	11.8±4.1°°°	8.9±4	8.0±3.6	7.2±3.7°°°	0.045*	0.672	<0.001*
CSR	-19.7±9.6	-14.4±11.5°	-13.3±9.9°°°	-22.8±8.5	-25.7±9.1	-27,1±8.9°°°	0.008*	0.569	<0.001*
Back Scratch	-42.8±2.2	-32±10.6°	-29.7±1°°°	-41.6±8.7	-43.3±8.4	-43.5±8.7	0.001*	0.002*	0.022*
UG	27.5±32.8	24.6±6.7	23.1±22.5	24.9±10	27.3±12.5	30.1±15.4	0.769	0.658	0.029*
2min Step	59±38	78.6±42.4°	86.4±46.2°°°	51.1±26.7	46.9±27.9	38.3±25.1	0.021*	0.102	<0.001*
MMSE	14.9±6	16.6±6.5°	15.3±6	16.1±4.2	14.9±5	13.3±4°°°	0.822	0.036*	0.008*

Note. °Statistically significant difference from M1 to M2 (p<0.05); °° Statistically significant difference from M2 to M3 (p<0.05); °°° Statistically significant difference between M1 and M3 (p<0.05); * Statistically significant difference

Discussion

The present study tested and confirmed the hypothesis that a 6-month ME intervention can improve cognitive and physical function in institutionalized older adults with mild to moderate AD.

As expected, anthropometric measurements (BMI and WC) showed that, at baseline, participants were generally overweight. Indicators of obesity and overweight have been associated with dementia (Luchsinger et al., 2004; Dahl et al., 2010) and with poor neurocognitive outcomes (Whitmer et al., 2005). Medical conditions frequently related to obesity and overweight (dyslipidemia, hypertension, type 2 diabetes) are also known contributors to cognitive decline and dementia (Skoog et al., 2006; Hayden et al., 2006). However, several clinical settings have also reported associations between lower BMI and dementia at mild severity, increasing with advancing disease severity and duration (White et al., 1998). Although no significant changes were observed for BMI in both groups, the EG's WC significantly decreased after 3 months and again at the end of the intervention, whereas the EG's WC increased during the intervention period. Reducing WC may have relevant health implications, as it has been highly correlated with visceral fat (Molarius et al., 1998). Despite being a frequent and widely accepted measurement of adiposity in young and middle-aged adults (Schreiner, Terry et al. 1996), considering age-related changes in fat and fat-free mass in elderly populations (Harris et al. 2000), the influence of BMI on health risks and dementia has been controversial. The literature points out that WC is as good measure of excess adiposity as BMI among older adults or even better (Leitzmann et al. 2011).

Normal aging is also characterized by the functional fitness decline. With increased physical impairment, the ability to perform ADL decreases (Zhu & Chodzko-Zajko, 2006). In elderly patients with AD functional decline becomes more pronounced and while the disease progresses, physical function becomes increasingly compromised. Limitations in ADLs become more evident, gradually leading to the loss of autonomy. Our data showed that the CG follows this trend, with a decline in all dimensions of functional fitness. In opposition, our ME intervention group seems capable of preventing this tendency.

Age-related loss of muscle mass and strength (sarcopenia) are magnified by the lack of physical activity opportunities in the institutional settings leading to frailty faster (Santana-Sosa, et al., 2008). The CG followed this trend, with their performance declining in both lower and upper limbs strength tests, being significant in the arm-curl test (upper limbs strength test) from M1-M3. A significant improvement in the upper and lower muscle strength tests was observed in the EG from M1-M2 and from M1 to M3. Thus, our results are in accordance with the literature that considers the increment of physical activity as an important therapeutic tool for the attenuation of this loss (Santana-Sosa, et al., 2008). Particularly, frailer older adults with some physiological impairment can improve their levels of strength remarkably (Chandler et al., 1998).

Ageing has a similar effect on flexibility. The decline of this capacity ranges from 20% (hip) to 40% (ankle flexion) by 70 years of age (ACSM, 2009). As a consequence, the risks of injury, falling, and back pain, increases (ACSM, 2009). Our data showed that the EG was able to significantly improve their flexibility after 3 and 6 months, in both upper and lower limbs. Other studies support these results (Toraman & Ayceman, 2005), showing that the decrease of flexibility can be mitigated or even reversed through physical exercise (Batista et al., 2009).

Regarding the UG test, EG improved their performance during the intervention while a significant decrease was observed in the CG, although this difference was not statistically significant. Agility, balance (Toraman & Ayceman, 2005) and lower limb muscular strength (Santana-Sosa, Barriopedro et al. 2008) are capacities that are important to perform the UG test. All these capacities were included in our ME intervention.

According to the literature, an increase in aerobic fitness, as observed in the present study, probably due to the raise in the blood flow and cerebral perfusion preserving critical areas of cognition in older adults (Cotman et al., 2007). Higher levels of aerobic capacity are associated with reduced whole-brain atrophy in persons with AD, thus enhancing the cognitive function (Colcombe & Kramer, 2003). They also reduce the risk of cardiovascular and all-cause mortality (Zhu & Chodzko-Zajko, 2006). The ME intervention was able to improve significantly the participant's aerobic fitness after 3 and 6 months. These results are supported by previous studies that have shown significant improvements in aerobic capacity after ME (Carvalho et al., 2009, Takeshima et al., 2007; Toraman & Ayceman, 2005) in non-demented older adults.

The improvements observed in the present study have significance for functional fitness which has consistently been linked with better health status, the ability to perform ADL and consequently with better QoL (Forbes et al., 2015). Similar results were observed by Santana-Sosa et al. (2008), who conducted a 12 week ME intervention for patients with AD, which succeeded in inducing significant improvements in patients' functional performance.

The Seattle Protocols, a series of evidence-based interventions conducted by Teri et al. (2008), showed that exercise training is beneficial and feasible for community-residing individuals with dementia and cognitive impairment (Teri et al., 2008).

The benefits of chronic exercise on cognitive function have been reported (Kaliman et al., 2011, Stevens & Killeen, 2006), studies found it to be linked to positive changes in brain structures, affecting angiogenesis, neurogenesis and up-regulation of neuroprotective molecules as well as brain volume and functional architecture (Kaliman et al., 2011).

However, others studies have reported that exercise has no effect on cognition (Holliman et al., 2001; Steinberg et al., 2009). In this study, we observed a significant increase in MMSE from M1 to M2 and from the M1 to M3 in the EG. The literature provides evidence that supports the trend from M1 to M2 and from M2 to M3. We believe that, despite the benefits of physical exercise on cognition that could justify better results in the EG from M1 to M2, the neurogenerative nature of AD may justify the decline from M2 to M3. However, between M1 and M3, the results show a slight and not statically significant improvement in the cognitive function, in the EG while the CG had a statistical significant decrease of this function in the same period of time. These data suggest that ME intervention can improve (as in M1 to M2) or at least help preserve cognitive abilities for a longer period of time (as in M1 to M3).

The main limitation of this study was the small sample size, the lack of randomization for group assignment and dietary assessment. Recruiting voluntary AD older adults willing to commit with a 6-month intervention was challenging and several institutions were therefore involved. Although the same exercise trainer supervised all classes, working with different settings with different conditions may have disturbed the homogeneity between exercise sessions.

It is important to highlight the low drop-out rate of our sample, which not only allowed us to maintain a consistent number of participants to conduct the full 6 months' exercise intervention, but also reinforces the idea that mild to moderate AD older adults can and should be engaged in ME intervention in order to improve or maintain functional and cognitive performance.

Besides the proliferation of different types of intervention for AD older adults, the key strength of our study is that our ME intervention attempted to adapt the physical exercise recommendations of ACSM for older adults (Nelson et al., 2007) to a population with highly specific characteristics (elderly with AD, in institutional settings). We believe that the positive results are also linked with extremely low level of physical activity and physical fitness at the baseline. According with the literature, exercise can produce short-term, highly improvements even frailer older adults (Fiatarone et al., 1994). Thus, we believe that our results underline that the adaptation of these recommendations is viable and allows this population to enjoy the benefits of improved levels of physical and cognitive functioning associated to physical exercise.

In sum, this study confirms that 6 months of ME intervention can positively affect physical and cognitive functions in institutionalized older adults with AD. Due to the frailty of the participants, higher physical fitness contributes for a better performance of ADL and delay the deterioration inherent to AD. Additionally, due its wide application and feasibility, the implementation and dissemination of such exercise program, as a low-cost alternative therapy, could be an important instrument for relevant health promotion policies such as national dementia plans.

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[Study 3]

Caregivers Perception of the importance of an exercise intervention on institutionalized older adults with dementia: functional capacity, quality of life and behavioral and psychological symptoms of dementia

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ABSTRACT

Due to the increasing social and economic costs of dementia, there are urgent calls to develop accessible and sustainable care for people with dementia (PwD) and their caregivers. The aim of this study was to analyse the caregivers' perception of the importance of an exercise intervention on functional capacity and quality of life (QoL) and neuropsychiatry symptoms of institutionalized older adults with mild to moderate dementia. Nine caregivers (female, aged 28-47 yrs old) from nine different nursing homes participated in the present study. These caregivers were responsible for sixty-four institutionalized older adults (from both genders, aged 65–93 yrs. old), clinically diagnosed with dementia, that were divided into two groups: control group (CG, n= 26) and exercise group (EG, 6-month supervised multicomponent exercise intervention n= 38). The caregivers reported about care receiver's functional capacity (Katz index), quality of life (QoL-AD) and behavioural and psychological symptoms in dementia (Npi) before and after 6 months of an exercise intervention (aerobic, muscular resistance, flexibility and postural exercises). Care receivers cognitive function (MMSE) and physical fitness (Senior Fitness Test) were also evaluated. The caregivers perceived that the EG decreased NPi total scores, meaning an improvement in these domains after exercise intervention. Moreover, total Katz decreased in CG, whereas the caregivers reported that the exercise intervention maintained the functional capacity. Generally, the caregivers considered that a multicomponent exercise intervention can be beneficial to institutionalized older adults with dementia.

Keywords: Neurocognitive disorders; Carers, Activities of daily life; Aging; Institutionalization; BPSD; Neuropsychiatric Symptoms.

Introduction

Presently is estimated that 47 million people live with dementia worldwide, and projections show that this number may increase to more than 131 million by 2050, as populations age (Prince et al., 2016). Due to this significant prevalence, the huge social and economic impact makes Dementia one of the main age-related health problems affecting society (WHO, 2012). Dementia is a progressive degenerative syndrome that compromises cognitive and functional capacity essential to perform activities of daily life (ADL) autonomously (Prince et al., 2015). Additionally, Behavioral and Psychological Symptoms of Dementia (BPSD), commonly are developed over time and tends to persist throughout the course of the disease (Kaymaz & Ozdemir, 2016), having a negative impact on the health of patients and caregivers (Barreto et al., 2015). Cognitive impairment, physical and functional dependence, and mainly BPSD contributes to family caregivers burden and predicts the institutionalization of the Person with Dementia (PwD) (Brodaty & Arasaratnam, 2012).

Alzheimer's Disease International (Prince et al., 2015), reported that 33% to 50% of people with dementia (PwD), in high income countries, lives in nursing homes and more than two-thirds of care home residents have dementia. The high proportions of PwD, lack of appropriate education and training on BPSD management are physically and psychologically challenging (Wilde-Larsson et al., 2015) and can result in high levels of emotional exhaustion and distress of the formal caregivers (Miyamoto et al., 2010). Moreover, after institutionalization, formal caregivers are the individuals with whom PwD have the closest relationship, being the ones who have a better knowledge of their cognitive, physical impairments, usual BPSD, Quality of Life (QoL) and are aware of the progress of the disease. This, sets not only the PwD, but also the formal caregiver in a central position of this worldwide health problem.

Although dementia cannot be reversed, evidence suggests that poorer performance in ADL can be delayed (Forbes et al., 2015). Among others, physical exercise, ie, planned, structured, repetitive, and purposeful physical activity, constitutes a promising intervention for PwD and has received increased attention in the last years (Forbes et al., 2015). Indeed, exercise interventions have positive impact on several health outcomes in PwD, including the delay in cognitive impairment and enhancement of functional capacity (Forbes et al., 2015 2016, Sampaio et al., 2016). However, little information has been gathered on the impact of exercise on BPSD (Barreto et al., 2015) incidence and the stress that those symptoms can cause to the caregivers.

Developing safe and effective exercise interventions focus on management of BPSD, aiming at delaying the progression of declines in functional ability, and improving their QoL are urgent for PwD in nursing homes, to enhance the quality of long term care and reduce formal caregiver burden. Despite caregiver's close relationship with the PwD and the unique observational role in institutional settings, their perception of exercise intervention outcomes is not highlighted, from the authors' knowledge. Therefore, it seems relevant to determine the hypothetical positive effect of an exercise intervention in caregivers' perception concerning functional capacity, QoL and BPSD in institutionalized older adults with mild to moderate dementia.

Methods

Study Design

Nine nursing homes took part in this quasi-experimental non-randomized study. Four nursing homes implemented an exercise intervention for 6 months (Exercise Group- EG); while five have not participated in structured physical activity program and maintained with their normal routine, during the same period (Control Group - CG).

Participants

Nine caregivers supervisors, aged 28-47 years, from nine different nursing homes, accepted to participate in the study, reporting about the effects of an exercise intervention performed by their care receivers.

Sixty-four care receivers from both genders, aged 65–93 years clinically diagnosed with dementia, were included in the study. The eligible subject pool was restricted to older adults with the following characteristics: age ≥ 65 years, not engaged in any regular exercise training in the last year, institutionalized for more than 6 months, all diagnosed by a physician with an age-related neurocognitive disorder (dementia) at mild or moderate stage according to Clinical Dementia Rating (CDR) (Morris, 1993) and lack of any diagnosed or self-reported musculoskeletal or cardiovascular disorders that contraindicate participation in moderate exercise and testing.

After initial screening, formal caregivers, care receivers and institutions received a complete explanation of the purpose, risks and procedures of the study. A written informed consent was provided. The investigation was in full compliance with the Helsinki declaration (World Medical Association, 2009) and the nine institutions where the intervention took place approved all methods and procedures. The Ethical Commission of the Faculty of Sports of the University of Porto also approved this study.

A 70% minimum attendance rate to the exercise sessions was required for participants in the EG. Attendance rate for the EG was calculated by dividing the number of exercise sessions completed by participants by the full amount of sessions they were expected to perform throughout the study. The attendance levels were 78.3% or over. The reasons for missing exercise sessions were acute diseases, behavioral disorders, unwillingness to participate in a particular exercise session and other reasons.

The participants flow diagram is represented in Figure 1.

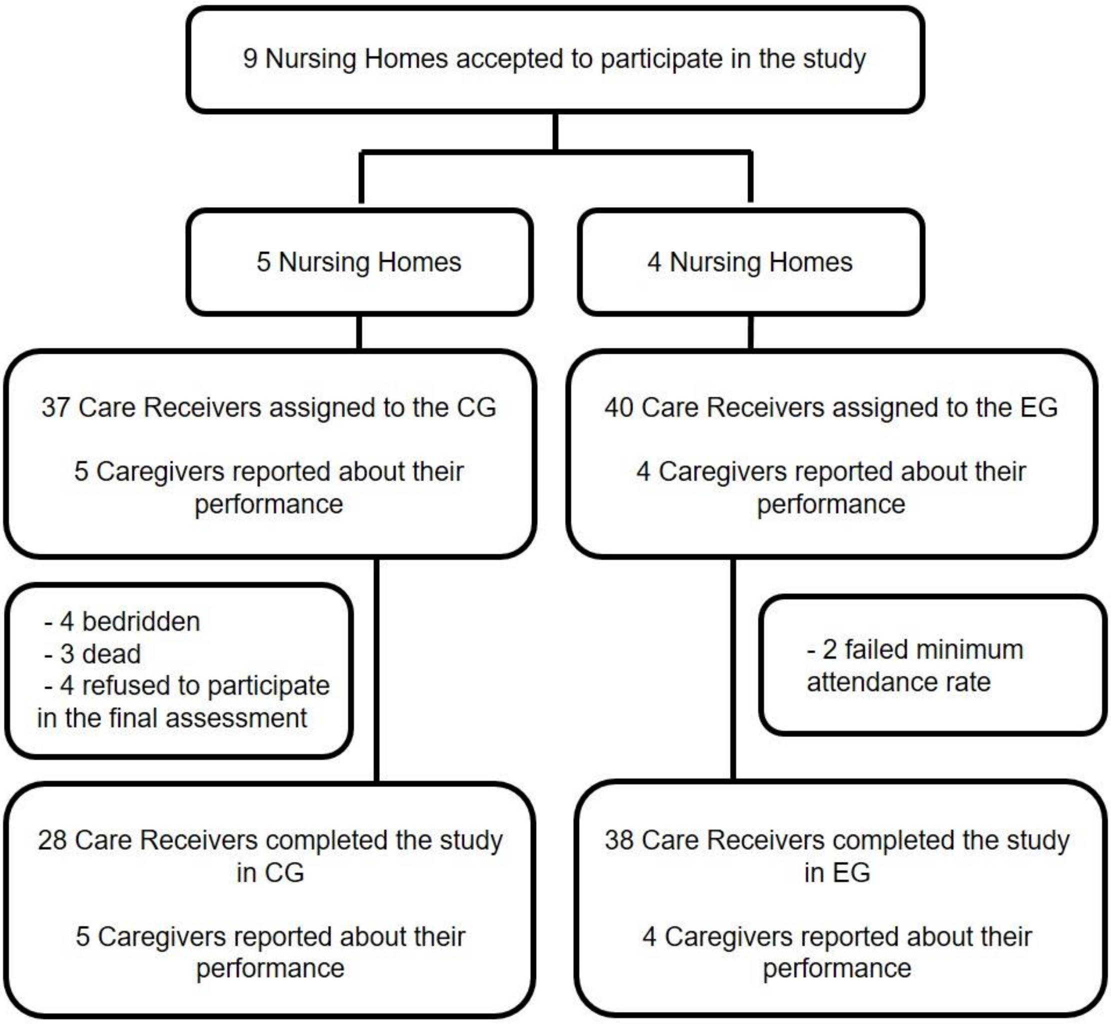


Figure 1. Subjects flow diagram from initial screening to the end of the study. CG, control group; EG, exercise group

Exercise Intervention

The EG completed a 6-month exercise program following the recommendations of the American College of Sports Medicine (Nelson et al., 2007, Chodzko-Zajko et al., 2009), including aerobic, muscle strengthening, flexibility, balance and postural exercises with 2 sessions per week on non-consecutive days. Sessions contained 5-15 care receivers and took place in specific rooms with peaceful and pleasant music environment. Sessions lasted for 45-55 minutes and were conducted by the same exercise trainer in all settings. The sessions were divided into 3 main parts: Warm-up (5-10´, including postural and stretching exercises for general activation), specific training (30-35´, including 15´ of moderate aerobic exercises + 15-20´ motor and muscular tasks for strength and coordination/balance training) and cool down (5´ with respiratory and flexibility exercises). In order to make the exercise program more efficient and attractive, we established regular similar routines that prioritized enjoyable and familiar exercises (as simulating walking, running, biking, rowing). Due to the frailty condition of the participants and for safety reasons, sessions were mainly chair-based and routines of functional exercises with low coordination requirements were emphasized so care receivers could achieve the session's goals.

Sociodemographic and clinical characteristics

Formal caregivers supervisors and care receivers characteristics are given in Table 1.

Outcome Measures

All following measures were assessed at baseline and 6 months of exercise intervention. CDR test, Senior Fitness Test (SFT) and Mini-Mental State Examination (MMSE) were performed by the care receivers. The care receivers Katz index, quality of life - Alzheimer disease scale (QoL-AD) and Neuropsychiatric Inventory (NPI) were reported by the caregivers.

Dementia Stage

The CDR test (Morris, 1993) was used only at baseline to allocate the care receivers according to their cognitive stage. CDR is an instrument that assesses the existence and prevalence of the various stages of dementia. It comprises 6 cognitive-behavioral items covering memory, orientation, judgment and problem solving, community activities, home and hobbies, and personal care. The cut-off points were CDR=1 (mild dementia stage) and CDR=2 (moderate dementia stage).

Physical Fitness

The SFT (Rikli & Jones, 2013) battery is considered a reliable instrument for assessing physical fitness in older adults (≥ 60 years old) including older people with cognitive impairment (Hesseberg et al., 2015). The test items included: chair-stand test - to assess lower-body strength; arm curl test - to measure upper-body strength; 2-min step test - to assess aerobic endurance; chair sit-and-reach test - to assess lower-body flexibility; back scratch test - to assess upper-body flexibility; and 8-foot up-and-go test - to assess agility and dynamic balance.

Cognitive function

The MMSE (Folstein et al., 1975) was used for a global cognitive evaluation. This instrument is clinically used to assess cognitive mental status, detect and follow the course of a mental illness and can also be used as a research tool to screen for cognitive disorders and follow cognitive changes in epidemiological studies. It assesses orientation, attention, immediate and short-term recall, language and the ability to follow simple verbal and written instructions. Furthermore, it provides a total score that categorizes the individual on a scale of cognitive function ranging from 0 to 30 (Folstein et al., 1975). MMSE normative values consider the subject educational level. Operational cut-off values for the Portuguese population are 22 (for 0 to 2 years of literacy), 24 (for 3 to 6 years of literacy) and 27 (for more than 6 years of literacy) (Morgado et al., 2009).

Functional Capacity

Katz index (Katz et al.,1963), one of the most used instruments for measuring the ability to perform ADL, was used for measure caregiver reports of the physical functioning of the care receivers. Katz index includes 6 items: bathing, dressing, transferring, feeding, incontinence, toileting and the sum of all items to calculate the Katz total. Independence levels for the ADL questions are recorded on a scale of 0 to 4, where 0 represents dependence and 5 represents complete independence (Sequeira, 2007).

Quality of Life

The QoL-AD (Logsdon et al., 2002) was used to measure the care receivers QoL. The questionnaire included 13 items: physical health, energy, mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores, ability to do things for fun, financial situation, and QoL as a whole. The QoL-AD provides the participant and caregiver reports of the participant's QoL and is scored on a 4-point Likert scale ranging from 1(poor) to 4 (excellent), with total scores ranging between 13 and 52 points.

Behavioral and Psychological Symptoms of Dementia

The Neuropsychiatric Inventory (NPI) (Cummings et al.,1994) is an instrument administrated to caregivers of dementia patients to measure changes in BPSD during time. The NPI originally assessed 10 behavioral domains (Delusions, Hallucinations, Agitation, Dysphoria, Anxiety, Apathy, Irritability, Euphoria, Disinhibition, and Aberrant motor behavior). Two more domains have been added since its development: night-time behavioral disturbances and appetite and eating abnormalities (Cummings et al., 1994). For each of the 12 behavioral symptoms on the NPI, caregivers rated the level of distress they experienced on a scale from 1 (low) to 5 (extreme). The NPI Distress score (NPI-D) (Kaufer et al., 1998) is the sum of these 12 ratings (range 0–60). In the present study we used the Portuguese version published in the Book of Scales of the Study Group on Brain Aging and Dementia (GEECD).

Statistical Analysis

Results were expressed as either means (standard deviations) or proportions (Table 1). Differences between groups at baseline were tested using unpaired sample t-tests, Mann-Whitney and chi-square tests. The intervention effects results were expressed as percentage of the baseline values of the CG, and were examined by repeated measures analysis of variance (ANOVA). The Bonferroni test for multiple comparisons was used. Significance level was set at 0.05 throughout the analyses. Statistical analyses were performed using SPSS 24.0.

Results

Characteristics of the Participants

Sociodemographic and clinical characteristics of the participants are summarized in Table 1. The sample included 9 caregivers supervisors, all female and with geriatric nursing assistance certification. The care receivers that participated in the study were 70.3% females and all presented a neurocognitive disorder (NCD). Hypertension, minor heart condition, diabetes mellitus and osteoporosis were the other main diagnoses besides the NCD. The CDR showed that the average of the care receivers was in the moderate stage of dementia for both groups.

Table1. Characteristics of the participants at baseline

CAREGIVERS	Exercise Group (n=4)	Control Group (n=5)	p[a]
Age (years)	37.75±8.14	36.40±7.54	0.806
Geriatric working experience (years)	9.50±3.51	8.60±2.51	0.683

CARE RECEIVERS	Exercise Group (n=38)	Control Group (n=26)	p[a]
Age (years)	77.29±8.60	80.15±2.80	0.179
Men, No. (%)	14 (36.8%)	5 (19.2%)	0.169
CDR (Points)	1.18±0.90	1.13±0.63	0.808
Educational level (years)	2.60±1.72	2.27±1.54	0.381
Neurocognitive Disorder due to, No. (%)			0.259
Alzheimer´s Disease	16 (42.1%)	18 (69.2%)	
Vascular Disease	6 (15.8%)	3 (11.5%)	
Parkinson's Disease	1(2.6%)	0 (0%)	
Lewy Bodies Disease	1(2.6%)	0 (0%)	
Unspecified	14 (36.8%)	5(19.2%)	
Diagnosis, No. (%) (Others than NCD)			
Hypertension	14 (36.8%)	4 (15.4%)	0.045*
Heart Disease	9 (23.7%)	2(7.7%)	0.141
Diabetes mellitus	5 (13.2%)	5 (19.2%)	0.463
Osteoporosis	3 (7.9%)	3(11.5%)	0.650
Blood Pressure (mmHg)			
Systolic	126.72±22.50	128.81±22.10	0.718
Diastolic	76.47±14.64	76.73±17.31	0.950

[a] Student´s t-test or Mann Whitney for continuous variables; Chi-squared or Fisher´s exact.

No significant differences at baseline between groups were observed in physical fitness and cognition variables (Table 2).

Table 2. Physical Fitness and cognition results of the care receivers at baseline.

CARE RECEIVERS	**Exercise Group** (n=38)	**Control Group** (n=26)	p^a
Physical Fitness			
Lower Strength (reps)	8.95±4.31	9.96±4.16	0.352
Upper-Strength (reps)	9.71±5.18	11.77±4.11	0.096
Lower Flexibility (cm)	20.86±10.43	19.69±12.82	0.691
Agility/ Dynamic balance (sec)	19.33±10.86	20.36±12.52	0.726
Upper Flexibility (cm)	43.53±16.44	42.88±10.34	0.861
Aerobic Endurance (steps)	58.61±32.82	69.46±34.72	0.209
Cognition (MMSE)	18.11±4.81	17.77±5.07	0.789

[a] Student´s t-test; * p ≤ 0.05.

The baseline results showed significant differences in mobility and continence (functional capacity components) between EG and CG, reported by caregivers.

Caregivers did not perceive other significant differences between groups at baseline, including BPSD-score, BPSD-distress, functional capacity components and QoL (Table 3).

Table 3 BPSD-score, BPSD-distress, functional capacity and QoL results of the caregivers' perception at baseline.

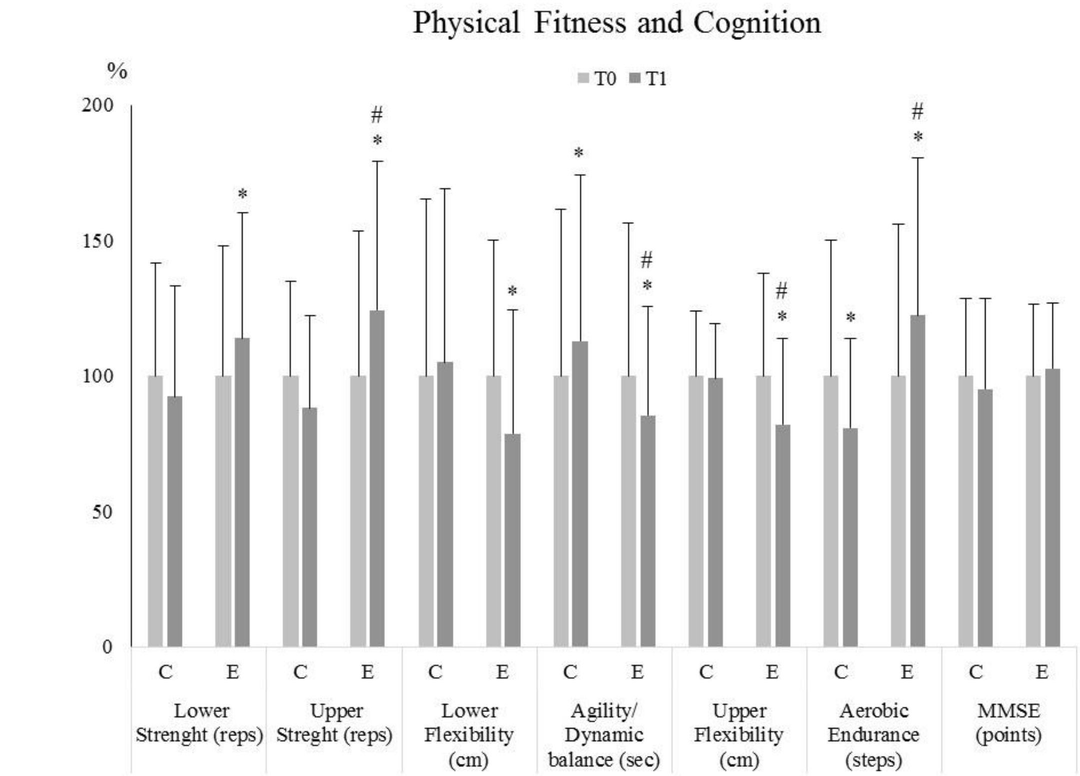
CAREGIVERS	Exercise Group (n=4 about 38 care receivers)	Control Group (n=5 about 40 care receivers)	p[a]
BPSD – Score			
Delusions	0.97±1.92	1.15±2.75	0.759
Hallucinations	0.61±1.48	1.31±3.37	0.259
Agitation	1.79±3.01	2.35±3.07	0.473
Dysphoria	1.11±2.04	1.54±2.67	0.465
Anxiety	1.89±2.72	2.58±3.08	0.354
Euphoria	0.84±2.39	1.81±3.64	0.205
Apathy	1.39±2.33	1.27±2.55	0.839
Disinhibition	1.37±2.73	2.42±4.09	0.220
Irritability	1.82±3.27	2.31±3.67	0.576
Aberrant motor activity	1.45±2.71	1.04±2.46	0.540
Night-time behavioral disturbances	1.13±2.22	1.38±2.77	0.687
Appetite and eating abnormalities	1.55±3.00	2.35±3.81	0.355
NPI Total	15.92±18.42	21.5±26.66	0.325
BPSD – Distress			
Delusions	0.82±1.31	0.77±1.37	0.890
Hallucinations	0.53±1.03	0.73±1.37	0.499
Agitation	1.11±1.71	1.38±1.58	0.510
Dysphoria	0.82±1.41	1.12±1.58	0.430
Anxiety	1.11±1.39	1.5±1.48	0.281
Euphoria	0.47±1.06	0.92±1.44	0.155
Apathy	0.79±1.21	0.96±1.46	0.609
Disinhibition	0.79±1.28	1.04±1.58	0.490
Irritability	0.97±1.46	1.19±1.47	0.560

CAREGIVERS	**Exercise Group** (n=4 about 38 care receivers)	**Control Group** (n=5 about 40 care receivers)	**p**[a]
Aberrant motor activity	0.87±1.19	0.65±1.26	0.492
Night-time behavioral disturbances	0.68±1.30	0.88±1.48	0.568
Appetite and eating abnormalities	0.89±1.52	1.23±1.75	0.417
NPI Total - Distress	8.87±10.01	11.19±14.13	0.444
Functional Capacity			
Bathing	1.74±0.89	1.81±0.75	0.740
Dressing	2.00±1.09	1.88±1.07	0.677
Toileting	2.47±0.80	2.00±1.20	0.062
Transferring	2.53±0.80	2.08±1.13	0.066
Incontinence	2.61±0.82	2.12±0.91	0.029*
Feeding	2.71±0.87	2.19±1.39	0.070
Total Katz	14.11±3.90	12.00±4.95	0.062
Quality of Life (QoL-AD)	24.13±5.07	22.27±5.30	0.162

[a] Student´s t-test; * $p \leq 0.05$.

Physical Fitness and Cognitive Capacity

As seen in Figure 2, for all the physical fitness components, a significant group by time interaction was found. A 6 months of an exercise intervention improved the EG, physical fitness components whereas no alteration were seen in CG (with the exception of agility-balance and aerobic endurance in which a decrease in performance was observed). No significant changes were observed for the total cognitive function score assessed by MMSE after 6 months in both groups.



p Group	0.034	0.105	0.330	0.305	0.179	0.098	0.571
p Time	0.237	0.054	**0.007**	0.324	0.055	0.216	0.853
p Interaction	**0.025**	**<0.001**	**0.001**	**<0.001**	**0.029**	**<0.001**	0.070

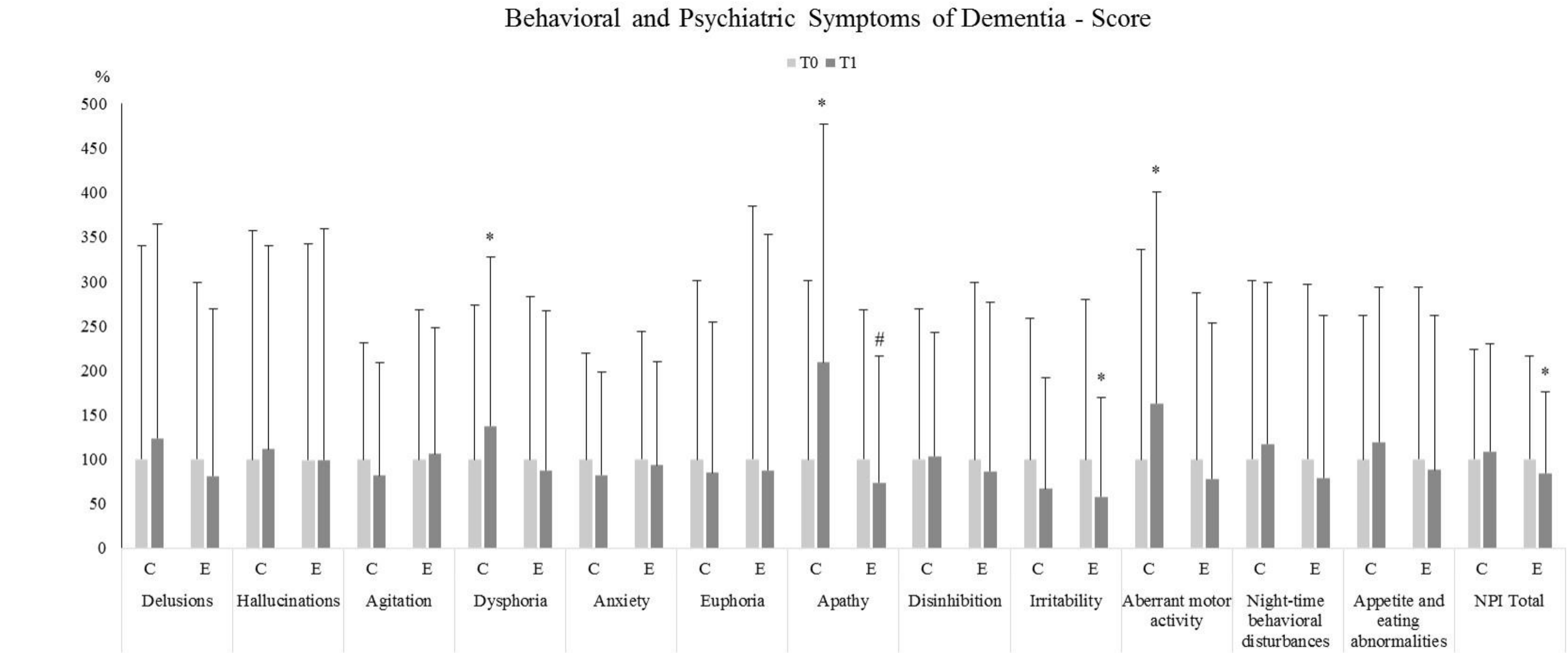
Figure 2. Effects of a multicomponent training intervention on physical fitness components and cognitive capacity total score of institutionalized older adults with dementia; n= 26 in the CG and n= 38 in the EG. Results were expressed as percentage of T0. *vs T0; # vs EG (p ≤ 0.05). Significant (p ≤ 0.05) main effects of Group, Time and/or their interaction are indicated. T0 baseline values, before the exercise intervention; T1 after 6 months of exercise intervention.

Behavioral and Psychological Symptoms of Dementia Score

Alterations in BPSD scores following the exercise intervention (EC) and control period (CG) perceived by the caregivers are shown in Figure 3. The analyses for dysphoria, apathy, aberrant motor activity and NPI total indicated a significant group by time interaction effect. In CG, caregivers reported a higher presence of dysphoria, apathy, and aberrant motor activity comparing base line and T1 after 6 months, whereas the perceptions of these neuropsychiatric symptoms score were preserved in EG (except for a significant decreased in apathy score). NPI total interaction revealed that EG decreased significant their NPI score while no alteration was seen in CG comparing the baseline and following the intervention period.

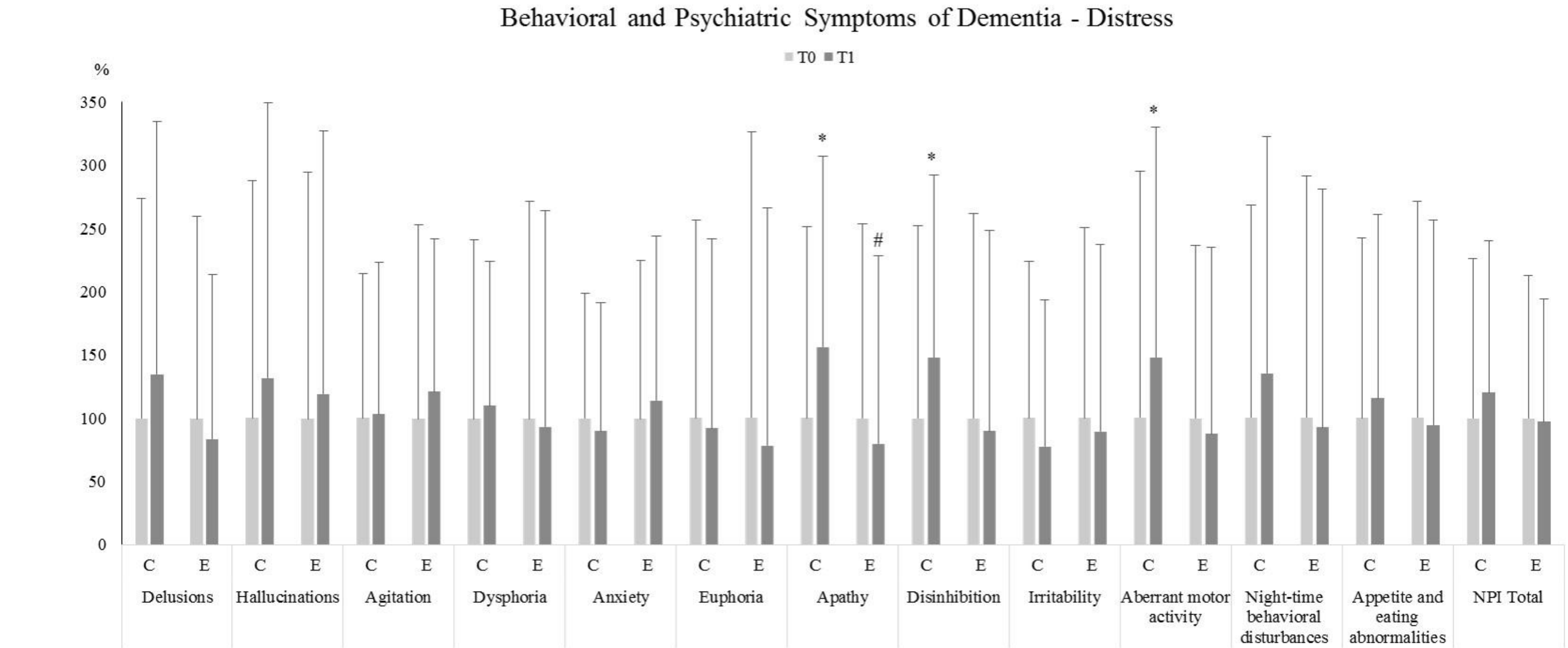
Behavioral and Psychological Symptoms of Dementia **-** *Distress*

BPSD distress scores reported by the caregivers at baseline and following exercise intervention are shown in Figure 4. For the apathy dimension a significant group by time interaction was observed. Among CG, the caregiver's distress due to apathy increased whereas among EG decreased at follow-up comparing with baseline. A significant interaction forthe disinhibition and aberrant motor activity dimensions showed a decreased in CG not seen in EG comparing baseline and T1.



	Delusions	Hallucinations	Agitation	Dysphoria	Anxiety	Euphoria	Apathy	Disinhibition	Irritability	Aberrant motor activity	Night-time behavioral disturbances	Appetite and eating abnormalities	NPI Total
p Group	0.692	0.917	0.708	0.0579	0.851	0.980	0.152	0.244	0.696	0.396	0.676	0.729	0.663
p Time	0.817	0.733	0.834	0.465	0.152	0.248	0.066	0.637	**0.018**	0.444	0.742	0.912	0.325
p Interaction	0.056	0.680	0.522	**0.033**	0.497	0.921	**<0.001**	0.565	0.789	**0.014**	0.283	0.068	**0.043**

Figure 3. Effects of an exercise intervention on caregivers' perception of neuropsychiatric symptoms score (NPI) of institutionalized older adults with dementia. n= 26 in the CG and n= 38 in the EG. Results were expressed as percentage of T0. *vs T0; # vs CG ($p \leq 0.05$). Significant ($p \leq 0.05$) main effects of Group, Time and/or their interaction are indicated. T0 baseline values, before the exercise intervention; T1 after 6 months of the exercise intervention.

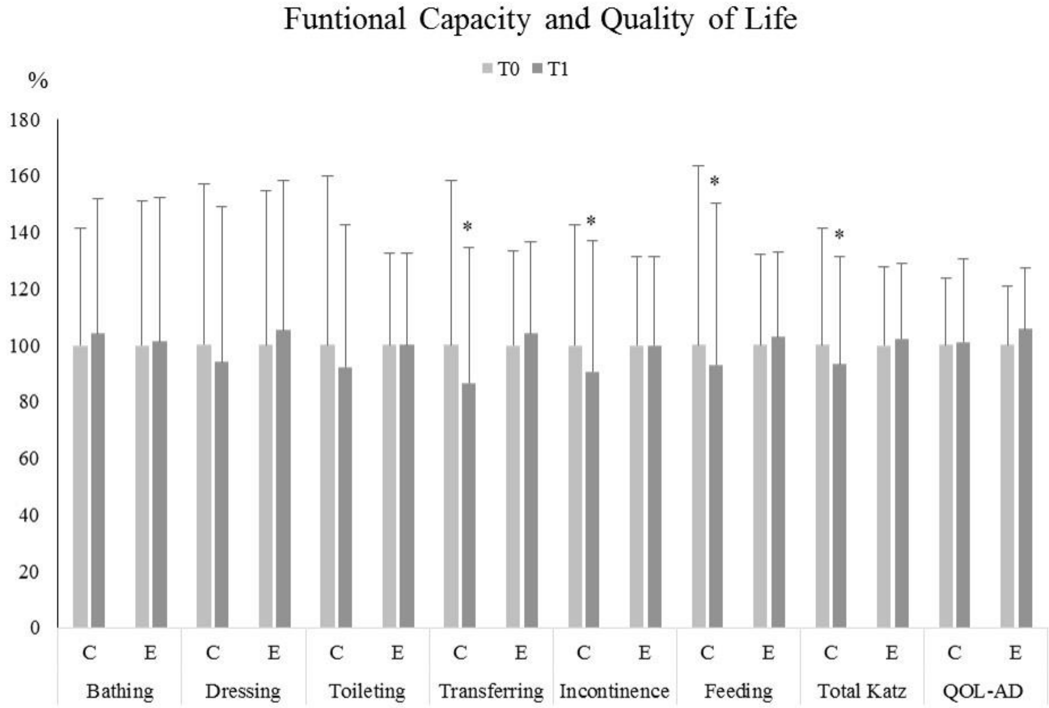


	Delusions	Hallucinations	Agitation	Dysphoria	Anxiety	Euphoria	Apathy	Disinhibition	Irritability	Aberrant motor activity	Night-time behavioral disturbances	Appetite and eating abnormalities	NPI Total
p Group	0.510	0.893	0.774	0.826	0.680	0.883	0.292	0.442	0.849	0.431	0.623	0.795	0.675
p Time	0.740	0.080	0.348	0.969	0.628	0.343	0.411	0.288	0.298	0.417	0.613	0.688	0.367
p Interaction	0.080	0.679	0.535	0.393	0.176	0.695	**0.006**	**0.028**	0.699	0.052	0.271	0.137	0.129

Figure 4. Effects of an exercise intervention on caregivers' neuropsychiatric symptoms distress of institutionalized older adults with dementia. n= 26 in the CG and n= 38 in the EG. Results were expressed as percentage of T0. *vs T0; # vs CG ($p \leq 0.05$). Significant ($p \leq 0.05$) main effects of Group, Time and/or their interaction are indicated. T0 baseline values, before the exercise intervention; T1 after 6 months of the exercise intervention.

Functional Capacity and Quality of Life

Figure 5 shows the functional capacity and QoL perceived by the caregivers at baseline and following an exercise intervention for each group. For the transferring, feeding and total Katz dimensions a significant interaction between groups and time was observed. Among CG, the values of these variables decreased comparing the baseline and the follow-up while in EG remained unaltered after the exercise intervention. No significant main effects were observed for total QoL-AD.



	Bathing	Dressing	Toileting	Transferring	Incontinence	Feeding	Total Katz	QOL-AD
p Group	0.906	0.689	0.707	0.408	0.620	0.666	0.592	0.676
p Time	0.320	0.838	0.273	0.240	0.125	0.611	0.252	0.117
p Interaction	0.609	0.074	0.186	**0.001**	0.065	**0.030**	**0.001**	0.344

Figure 5. Effects of an exercise intervention on caregivers' perception of functional capacity of and QoL institutionalized older adults with dementia. Data are mean ± standard deviation; n= 26 in the control group (CG) and n= 38 in the exercise group (EG). Results were expressed as percentage of T0. *vs T0; # vs EG ($p \leq 0.05$). Significant ($p \leq 0.05$) main effects of Group, Time and/or their interaction are indicated. T0 baseline values, before the exercise intervention; T1 after 6 months of the exercise intervention.

Discussion

Exercise programs may be relevant for PwD living in nursing homes, since they spend a protracted period in the nursing home (Welch et al., 1992) with a high rate of functional decline (Schmeidler et al., 1998) and they are frequently physically inactive (Ballard et al., 2001, Rolland et al., 2007). Although exercise interventions are low cost, feasible and can be easily implemented, there is lack of physical activity opportunities in institutions.

The caregivers as the person with more contact with PwD are the most appropriate ones to evaluate the outcomes of an exercise intervention. Therefore, the present study highlighted the caregiver's perception of an exercise intervention as a possible strategy to mitigate symptoms and alleviate disease progression in institutionalized PwD.

The hypothesis that a 6-month exercise program can promote a positive caregivers' perception concerning its effects on BPSD and functional capacity in institutionalized older adults with mild to moderate dementia was confirmed. This study, also tested the hypothesis if a 6-month exercise program can promote a positive caregivers' perception of the importance of an exercise intervention on QoL, but this hypothesis was not confirmed.

The present study attempted to adapt an exercise program for PwD, living in institutional settings to the physical exercise recommendations of American College of Sports Medicine (ACSM) and American Heart Association (AHA) for older adults (Nelson et al., 2007, Chodzko-Zajko et al., 2009). The exercise intervention integrated several important physical abilities to perform the ADLs, and involving playful and social group activities. Corroborating other studies that applied similar training programs in terms of duration, frequency and type of population (Rolland et al., 2007, Roach et al., 2011, Sampaio et al., 2016), improvements were seen in all the physical fitness components evaluated in the group that participate in the 6 months' exercise intervention (figure 2). It is possible that these positive results were linked with low scores seen before the intervention. These results also suggested that the exercise intervention was adjusted to the characteristics of our population and enough to induce physical adaptations. This underlines that the adaptation of the physical activity recommendations to this population, allows them to improve their levels of physical fitness.

Although some studies reveled positive outcomes of exercise intervention on cognitive function, most of these studies were conducted in older adults without dementia (Colcombe & Kramer, 2003). In fact, in this special population physical exercise showed controversial results, with studies suggesting no alterations in general cognition in comparison with control group (Forbes et al., 2015). Our intervention did not alter significantly the general cognition in comparison with control group. Probably, as suggested by Lautenschlager & Cox (2013) to improve brain function and cognition, exercise intervention should be more extended in time.

BPSD are an intrinsic feature of dementia that is often treated with antipsychotics. Current person-centered philosophies of care in dementia, encourage non-pharmacological therapies as alternative and/or complementary interventions for minimize BPSD (Turner, 2005), including exercise programs. Literature points out controversial results, while Forbes et al. (2015) found no clear evidence of the positive effects of exercise intervention on BPSD, other authors affirm that exercise interventions can be beneficial to reduce some of the BPSD (Cerga-Pashoja et al., 2010, Thuné-Boyle et al., 2012). Besides the controversy, these studies agree that further work is needed to comprehend the potential of exercise as non-pharmacological therapy to manage BPSD (Thuné-Boyle et al., 2012 2015). Evidence suggests that exercise may affect various BPSD in different ways (Cerga-Pashoja et al., 2010). Indeed, effects of exercise seem to be more beneficial on depressed mood, agitation and reduce “wandering” (Cerga-Pashoja et al., 2010). The results from our study seem to be in line with these evidences, generally EG maintain their BPSD scores similarly to the scores reported on baseline, while the CG worsen depression, apathy, aberrant motor behavior scores (figure 3). Importantly, in our study the caregiver’s perceived a decreased of the total BPSD in the EG after the 6 months’ exercise intervention.

From our knowledge, no studies have addressed the caregiver's perspective about the impact of exercise intervention in their BPSD distress. In our study, formal caregiver´s distress triggered by apathy, disinhibition and aberrant motor behavior increased in CG while after 6 months of an exercise intervention no alterations were seen regarding these distress causes in EG (figure 4). Evidences suggests that disruptive behaviors and a low ADL levels among residents with dementia expose formal caregivers to demanding physical and emotional distress (Miyamoto et al., 2010), leading to poorer QoL (Brodaty & Donkin, 2009). Thus, our results could suggest that exercise programs in institutionalized PwD may be useful as a strategy of BPSD- distress management. Strategies to alleviate the burden felt by formal caregivers leads to higher job satisfaction, increase their QoL and consequently improved staff attitudes and caring behaviors and, over time, resident well-being (Lintern et al., 2000).

Functional status is related to institutionalization (Fried et al., 2009). Among other reasons, in most cases, older adults move to a nursing home when their functional capacity is diminish affecting their independency to perform ADL (Scocco et al., 2006). In institutional settings, assistance in ADL for older adults living are often delivered in a standardized and depersonalized way that undermines independence (Secker et al., 2003). Particularly in PwD, less opportunities to perform ADL and the lack of physical activity opportunities exacerbates the functional decline in the institutional settings (Egerton & Brauer, 2009). Corroborating these evidences, the present study showed a progressive decline in total functional capacity score and some of their domains including, transferring, feeding, and incontinence outcomes in the group without exercise intervention. Altering this tendency, the EG was capable of preserving their total functional capacity after the 6 months of exercise intervention (figure 5). Other studies have verified that exercise programs implemented in institutions can induce positive outcomes concerning the functional capacity of PwD (Santana-Sosa et al., 2008, Venturelli et al., 2011, Forbes et al., 2015).

It has been suggested that in institutional settings the participation in a wide range of activities improves the QoL of PwD (Edvardsson et al., 2014). In fact, activity engagement may contribute to the pleasure and enjoyment, the sense of connection and belonging and the retain a sense of autonomy and personal identity (Phinney & Ong, 2007). Importantly, caregivers also consider aspects such as social relationships, physical movement, attachment and affect, control over life, and contributing to the community as important for PwD QoL (Cahill & Diaz-Ponce, 2011, Moyle et al., 2011). A 3 months home-based exercise randomize control trial (Teri et al., 2003) and 16 weeks institutional setting exercise program (Williams & Tappen, 2007), both for older adults with Alzheimer´s Disease shown some evidences that exercise program can improve QoL. However, we did not found alterations on QoL following 6 months of EG or CG from the perspective of the caregivers (figure 5).

BPSD are commonly associated with reduction in the QoL for the older adult with dementia (Colerick & George, 1986) and increase of caregiver stress (Finkel et al., 1997). Therefore, we would expect an alteration of QoL in CG and a possible preservation in EG. Although in the majority of the studies regarding, functional capacity and QoL evaluation of institutionalized PwD have been partially or fully reported by the formal caregivers, the fact that this is the perspective of the caregiver have not been highlighted. In fact, it seems relevant to empathize their perception since dementia care can contribute (due to disruptive behavior and limited capacity of performing ADL) for the burden of formal caregivers (Brodaty et al., 2003, Zimmerman et al., 2005). Additionally, from the authors knowledge, no previous studies had explored the effects of 6 months' exercise intervention on BPSD score and caregivers distress in institutional settings. Higher levels of stress and poorer levels of well-being of formal caregiver's impact negatively on the quality of care they provide and consequently have a negative effect on institutionalized PwD well-being (Cheung & Chow, 2006). Therefore, interventions for residents with dementia perceived as positive by the formal caregiver may increase the well-being both of themselves and, by extension, those they care for. The results of our study showed that formal caregivers perceived some of the benefits of the engagement to exercise program in institutionalized PwD.

The main limitation of this study was the small sample size and the lack of randomization for group assignment. Recruiting voluntary people diagnosed with dementia willing to commit with a 6-month´ intervention was challenging and several institutions were therefore involved.

Conclusions

In sum, this study confirms that 6 months of exercise program can promote a positive caregivers' perception concerning its importance on functional capacity and BPSD in institutionalized older adults with mild to moderate dementia. Moreover, this study suggests that an exercise intervention in institutionalized PwD may be useful as a strategy of BPSD- distress management, alleviating the burden felt by formal caregivers. Although no QoL improvement was observed, these results indicate that formal caregivers perceived the engagement in the exercise program in institutionalized PwD as positive. This can be relevant for better well-being of both PwD and formal caregivers is institutional settings.

Acknowledgments

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GENERAL DISCUSSION

Setup justification and overview of the main findings

The overall aim of this thesis was to understand the effectiveness of exercise as a non-pharmacological intervention aiming at delaying the progression of physical, cognitive and psychological declines due to dementia, particularly among nursing homes residents. Recently, the number of studies related with this research topic is growing. Although the American College of Sports Medicine (ACSM) and other important sports medicine and exercise science organizations provide some physical activity recomendations for people with dementia, specifically Alzheimer´s disease, no formal guidelines have been published yet. Consequently, studies comprising exercise for older adults with dementia use a variety of methodologies producing very diverse outcomes (Forbes et al., 2015; Heyn et al., 2004). The existing body of evidence is mainly based on cross-sectional studies or based on experimental setups using isolated endurance training, although combined aerobic and strength training programs, may have a larger effect on cognition than aerobic or resistance training alone (Kirk-Sanchez & McGough, 2014; Smith et al., 2010). Thus, a rising attention should be address to exercise type, intensities and volumes, following the diagnosis of the disease, needed to optimize cognitive and physical fitness required to perform ADL autonomously. In our study we aimed to design and implement an intervention that could be attractive for the participants, but also safe and efficient. To accomplish this goal, we took into account the current ACSM recommendations, and we examined which physical fitness component(s) could be more relevant (if any) for this specific population (Study 1). Although the relationship between higher levels of physical activity and functional capacity has been previously established (Manini & Pahor, 2009), the association between the specific components of the physical fitness and ADL are still unclear, particularly among older adults with dementia. In addition, studies regarding the impact of physical fitness on cognition mainly investigate aerobic fitness (Forbes et al., 2015). Consequently, the interaction between different physical fitness levels, cognitive function and functional capacity is still not well understood. As physical fitness modulates cognitive function and functional capacity, and as these are important for QoL (Forbes et al., 2015), it is relevant to study the interaction between physical fitness components and the perceived QoL in this population. Thus, the interaction between different physical fitness components, cognitive function, functional capacity and QoL in older adults with dementia was investigated in paper 1. Overall, we found associations between different components of physical fitness with cognitive function, physical capacity and QoL. These findings contribute for the possible general benefits of a ME intervention in institutionalized older people with dementia.

Bearing that in mind, in paper 2 we evaluated the effects of 6 months ME intervention, in institutionalized older people with AD and dementia, (respectively, Study 2 and 3). In both samples, 6 months of ME interventions had a positive impact, improving the different dimensions of physical fitness in institutionalized older people both in AD and dementia (study 2 and study 3). These results are particularly important, as it may counteract the age-related decline of physical fitness that isamplified by the progression of the dementia and the institutionalization. Consequently, ME can contribute to minimize the loss of ability to perform ADLs, preserving autonomy for longer (Blankevoort et al., 2010). Several studies tried to understand the potentialities of the impact of physical exercise on cognition. This connection has been studied across lifespan (Hillman et al., 2008) and in special populations including older adults with dementia (Forbes et al., 2015). The most studied are based onaerobic and muscle strength exercise programs (Forbes et al., 2015), with several systemic mechanisms proposed to explain the benefits of exercise on brain health and cognition. Importantly, recent evidence highlight that combined (aerobic, strength training) programs, may have a larger effect on cognition than aerobic exercise alone (Kirk-Sanchez & McGough, 2014; Smith et al., 2010). Moreover, evidence shows that cognition and mobility are intertwined (Montero-Odasso et al., 2015). Cognition plays a key role in the control of gait initiation, planning, execution and the adaptation of these movements to meet motivational and environmental demands (Rossignol et al., 2006). Thus, the stimuli of this motor behavior may counteract dementia related cognitive decline. Therefore, older adults with dementia should benefit not only from both strength and aerobic exercise but also from an agility/dynamic balance and flexibility training given by a ME intervention. Exercise-induced cognition preservation was only achieved in the pilot study (study 2), when compared with the CG. While in the third study, no significantly alterations were seen in MMSE score for both groups. This is in line with other studies that demonstrate no clear evidences of exercise effects on cognition of older adults that already developed dementia and related diseases (for refs see Forbes et al., 2015).

Further work is also needed to comprehend the effects of exercise in BPSD. Although Forbes et al. (2015) found no clear evidence of the positive effects of exercise intervention on BPSD, other authors affirm that exercise interventions can be beneficial to reduce some of the BPSD (Cerga-Pashoja et al., 2010; Thuné-Boyle et al., 2012). The results from our study seem to be in line with these evidences, as caregiver's perceived a decreased of the total BPSD in the EG after the 6 months' exercise intervention, while the group without intervention got worsen in some BPSD comparing with the baseline values (Study 3). Similar trend was observed in CG, with caregivers BPSD-distress whereas no alterations were seen regarding in caregivers BPSD-distress score, in EG after the 6 moths of intervention. This may suggest that exercise programs in institutionalized older adults with dementia may be useful as a strategy of BPSD- distress management. The study 3 also shown that the ME intervention may contribute for the preservation of the ability to perform ADL, while the functional capacity of the CG became increasingly compromised. Limitations in ADLs become more evident, gradually leading to the loss of autonomy. Although this study failed to stand more positive scores in the QoL, our ME intervention seems capable of induce generally positive and valuable results.

Strengths and limitations

Strengths of this doctoral thesis include the focus on institutionalized older adults with dementia. The increase of age-related diseases such as AD and the others neurocognitive disorders set Dementia as a health priority public (WHO, 2012).

This particular population is typical frail, having low opportunities of being physically active. Literature points out for the need of developing non-pharmacological interventions and evidences have shown that exercise may have some beneficial effects on older adults with dementia, but further work is needed (Forbes et al., 2015). Therefore, this thesis explores the effects in important dimensions of older adult with dementia of ME intervention (study 2 and 3). The positive results may suggest that ME interventions could be a feasible instrument to manage dementia and relevant health promotion in institutional settings.

Another strength is the low number of participants in each exercise session (5-8) was important to ensure the efficiency of the ME intervention. Due to the small groups, it was possible to stablish a more personal interaction with each participant and manage in a more effective way any BPSD. Those were important points for the high participant attendance and low drop-out rate of our sample, which not only allowed us to maintain a consistent number of participants to conduct the full 6 months' exercise intervention.

Most importantly, some of the participants enjoyed so much the exercise sessions that they would reproduce some of the exercises by themselves spontaneity, this lead to some institutions that had the intervention to continue having session of exercises. In a specific institution after the intervention it was set weekly a session of chair-based exercise for residents, with and without dementia and formal caregivers.

A main limitation of this study was the recruiting process. Only 15 out of 21 institutions contacted accept to participate in the study and the under-diagnosis of dementia in Portugal (Santana et al., 2015) leaded to small potential participants in the study. Due to the small sample size, the randomization for group assignment was not possible. Although only 3 exercise trainers conducted the classes and 1 supervisor ensured the homogeneity between exercise sessions and assessments, working with different settings with different conditions may have been a limitation.

Controlling the intensity of the exercise sessions was another limitation, due to dementia most of the participants refuse to use heart rate monitors, and using perceived exertion scales were not reliable. The control of intensity had to be done using a mix model: perceived exertion scales and external signs of fatigue.

In the ME interventions, we used chair-based exercises most of the time. With this, and as a strength, we were able to minimize the probability of falls and ensured the safety of the exercises session. As limitation, chair-based exercise diminishes the variety of possible exercises, making it more challenging to increase intensities, specifically aerobic exercise and to train lower-body flexibility. Even though, alterations in those physical fitness components were seen in study 2 and 3, possibly due to low score at the baseline, before exercise intervention.

As a strength, we used instruments that allowed us to apply and replicate in different settings to assess anthropometry variables (BMI, WC) and physical fitness (SFT) components, instruments widely used in international studies, which allowed the comparison of the results with other studies. It is important to highlight that studies with institutionalized older adults with dementia are scarce. Being aware of the subjectivity of instruments used it was always the same evaluator to make the assessments. As limitations these subjective instruments have a lower level of reliance comparing with other more objective instruments, including DEXA (for anthropometric assessment), isokinetic evaluation (for strength), oxygen consumption (VO_2max or peak) by spirometry (for aerobic assessment) and dynamometer (for flexibility assessment), among others.

Directions for future research

Further work in exercise type, intensity, volumes and underlying mechanisms should be address to allow a better understanding of the effects of exercise in dementia and to develop more efficient exercises programs.

There is a need to raise awareness in the health system providers, institutional settings specialized in older adults' care, formal and informal caregivers for the potential benefits of ME intervention in older adults with dementia. This could lead to higher number of participants allowing more robust scientific outcomes and older adults having access to the benefits of training. Developing ME intervention in research settings, can be crucial for more accurate results.

The use of objective measurements instruments for assessment and to motorize the training could contribute substantially to develop this area of research. As the ultimate goal it is to reach as many older adults with dementia as possible, different types of exercise programs (home-base, in community-setting, in institutions) should be developed, so they could be implemented according to the different needs, and specific training for exercise professionals has to be ensured by universities and another educational entities.

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CONCLUSIONS

Considering the overall findings that emerged from the original studies we highlight the following conclusions:

Study 1 suggests that although aerobic endurance stands out as the key factor of physical fitness in association with cognitive function, functional capacity and QoL, every component of physical fitness seems to be singular and irreplaceable. Thus, exercise interventions aiming to preserve cognitive function, functional capacity and to maintain QoL, in institutionalized older adults with dementia, should combined aerobic exercise, flexibility, strength and agility/balance training.

Study 2 this study confirms that 6 months of ME intervention can improve all physical fitness components (aerobic capacity, lower and upper limbs strength and flexibility, agility/balance) and can preserve cognitive function in institutionalized older adults with AD.

Study 3 this study showed that a 6 months of exercise intervention can promote a positive caregivers' perception concerning its importance on functional capacity and BPSD of institutionalized older adults with mild to moderate dementia. These results indicate that formal caregivers positively perceived the engagement of institutionalized PwD in the exercise program. This can be relevant for better well-being of both PwD and formal caregivers in institutional settings.

Effectiveness of exercise as a non-pharmacological interventions aiming at delaying the progression physical, cognitive and psychological declines due to dementia, particularly among institutionalized, often disabled adults with dementia.

The results suggest expanding the use of exercise as a therapeutic strategy to attenuate the negative effects of dementia-related pathologies. Although aerobic endurance stands out as the key factor of physical fitness in association with cognitive function, functional capacity and QoL, we believe that the contributing of every component of physical fitness is singular and irreplaceable!

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[Appendix 1]

ETHICS OPINION

U.PORTO
FACULDADE DE DESPORTO
UNIVERSIDADE DO PORTO

Ethics Committee

ETHICS OPINION

Process **CEFADE 02.2014**

The Ethics Committee of the Faculty of Sport from the University of Porto analyzed the project entitled “Exercício Físico e o Idoso com Demência: os efeitos da participação em programas de exercício físico sobre a cognição, sintomas neuropsiquiátricos, aptidão física, capacidade funcional, risco de quedas e qualidade de vida” presented by MSc. Arnaldina Lopes Sampaio. Considering the project’s characteristics, as well as the competence of the research team, the Ethics Committee addresses a positive opinion, because the ethical principles that govern this type of scientific work are respected.

Porto and Faculty of Sport, 29 of January from 2014

The chairman of the Ethics Committee,

José Alberto Ramos Duarte

[Appendix 2]

WRITTEN INFORMED CONSENT

FACULDADE DE DESPORTO
UNIVERSIDADE DO PORTO

Carta de Consentimento

Eu, abaixo-assinado, declaro que participo voluntariamente no trabalho de doutoramento intitulado: "Exercício Físico e o Idoso com Demência: os efeitos da participação em programas de exercício físico sobre a cognição, sintomas neuropsiquiátricos, aptidão física, capacidade funcional, risco de quedas e qualidade de vida", da aluna Arnaldina Sampaio, coordenado pela Professora Doutora Joana Carvalho, do curso de Doutoramento em Actividade Física e Saúde da Faculdade de Desporto da Universidade do Porto.

Tomei conhecimento que, de acordo com as recomendações da Declaração de Helsínquia, a informação ou explicação que me foi prestada pelo responsável desta investigação incidiu sobre os objectivos, procedimentos e implicações do referido estudo e que tais não acarretam riscos evidentes para a minha saúde, podendo eu, em qualquer momento, abandonar a pesquisa caso não me sinta satisfeito.

Porto, ____ de _____ de 201_

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Assinatura do Voluntári

[Appendix 3]

EFFECTS OF A MULTICOMPONENT EXERCISE PROGRAM IN INSTITUTIONALIZED ELDER WITH ALZHEIMER´S DISEASE

Article

Effects of a multicomponent exercise program in institutionalized elders with Alzheimer's disease

Dementia
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Abstract

This study examined the effect of a Multicomponent Training (MT) intervention on cognitive function, functional fitness and anthropometric variables in institutionalized patients with Alzheimer's disease (AD). Thirty-seven institutionalized elders (84.05 ± 5.58 years) clinically diagnosed with AD (mild and moderate stages) were divided into two groups: Experimental Group (EG, $n = 19$) and Control Group (CG, $n = 18$). The EG participated in a six-month supervised MT program (aerobic, muscular resistance, flexibility and postural exercises) of 45–55 minutes/session, twice/week. Cognitive function (MMSE), physical fitness (Senior Fitness Test) and anthropometric variables (Body Mass Index and Waist Circumference), were assessed before (M1), after three months (M2) and after six months (M3) of the experimental protocol. A two-way ANOVA, with repeated measures, revealed significant group and time interactions on cognitive function, chair stand, arm curl, 2-min step, 8-foot up-and-go (UG), chair sit-and-reach (CSR) and back scratch tests as well as waist circumference. Accordingly, for those variables a different response in each group was evident over the time, supported by a significantly better EG performance in chair stand, arm curl, 2-min step, UG, CSR and back scratch tests from M1 to M3, and a significant increase in MMSE from M1 to M2. The CG's performance decreased over time (M1 to M3) in chair stand, arm curl, 2-min step, UG, CSR, back scratch and MMSE. Results suggest that MT programs may be an important non-pharmacological strategy to improve physical and cognitive functions in institutionalized AD patients.

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Keywords
Alzheimer's disease, cognitive function, functional fitness, exercise, aging

Introduction

The world's population is ageing at an exponential rate, accompanied by an increase of age-related pathologies (Castro-Caldas & Mendonça, 2005) such as dementia and Alzheimer's disease (AD). The World Health Organization (WHO) estimates that 47.5 million people worldwide are living with dementia, a figure that might increase to 75.6 million by 2030, and to 135.5 million by 2050 (WHO, 2015). In Europe, 8.7 million people lived with dementia in 2012, including 182,526 Portuguese citizens (Alzheimer Europe, 2013). AD is the most common cause of dementia and may contribute to 60–70% of cases. After age 65, the risk of this neurocognitive disorder doubles every five years (Prince et al., 2013).

The benefits of moderate exercise in relation to chronic degenerative diseases are well known (Barnes et al., 2007), contributing towards the prevention and reduction of morbidity and mortality of the elderly (Barnes et al., 2007). Regular exercise reduces vascular risk, obesity, levels of inflammation markers and it improves metabolism (Rovio et al., 2005). Besides improving general health status, strong evidence shows that functional fitness and cognitive function in older adults can be improved by regular physical activity (Heyn, Abreu, & Ottenbacher, 2004).

Functional fitness is universally accepted as an indicator of health status and quality of life in older adults (Justine, Hamid, Mohan, & Jagannathan, 2011). It comprises aerobic capacity, muscle strength, and static/dynamic balance agility and flexibility (Justine et al., 2011). During the aging process, there is a natural decline of physical functioning that is amplified by the progression of AD, including the loss of ability to perform Activities of Daily Living (ADLs), thus leading to higher levels of dependency (Noro & Aro, 1996).

Due to cognitive-behavioral functioning impairment and compromised ability to perform ADLs inherent to AD progression (Melrose et al., 2011), older adults with AD tend to lose their autonomy. This has devastating consequences for both the diagnosed individual and the entire family, who both are no longer able to cope with these demands. As a result, patients often require institutionalization (Brodaty et al., 2014). Usually, institutional settings lack physical activity opportunities, a situation that further emphasizes the decline of functional fitness contributing in turn to a faster progression of AD.

Although there are a growing number of publications on exercise programs for people with dementia, the studies reveal a wide variety of methodologies applied to different stages of dementia, resulting in inconsistent or even contradictory outcomes (Heyn et al., 2004).

The majority of studies have assessed the effectiveness of aerobic training on cognitive function and brain health. The literature points out that aerobic training can increase blood flow in the brain and regulate neurotrophic factors which, in turn, have been associated with improvements of cognitive functions, neurogenesis, angiogenesis and brain plasticity (Rovio et al., 2005). Aerobic training is also associated with higher cortical tissue on the temporal, parietal and frontal lobes, which are the key areas associated with cognition (Colcombe & Kramer, 2003) and brain activation patterns (Voss et al., 2011). Fewer exercise intervention studies have examined the effects of resistance training on cognitive function. However, there is some evidence that resistance-only training contributes to functional plasticity in brain regions associated with executive function and increased levels of IGF-1, thought to be related to the preservation of cognitive function (Cassilhas et al., 2007).

Thus, Multicomponent Training (MT),[1] such as combined aerobic exercise and strength training programs, may have a larger effect on cognition than aerobic or resistance training alone (Kirk-Sanchez & McGough, 2014; Smith et al., 2010). Although MT has been less investigated, studies have shown that it is an effective approach to improve functional fitness in healthy older adults (Justine et al., 2011), and is also beneficial for cognitive function in older adults with cognitive impairment (Suzuki et al., 2013).

The present study was designed to determine the effect of multicomponent training on cognitive and functional fitness in institutionalized AD patients following three and six months of training. Due to its wide applicability and feasibility, it is pertinent to assess to what extent MT (integrating several important physical abilities to perform the ADLs, and involving playful and social group activities and cognitive stimulation) can contribute to AD therapy as a low cost alternative to mitigate symptoms, alleviate disease progression (thus allowing the preservation of physical and brain health of patients with AD) and offset the lack of physical activity opportunities in institutions.

Hypothesis

A six-month MT program can promote cognitive and physical functions in institutionalized older adults with mild to moderate AD.

Methods

Study design

Nine nursing homes took part in this quasi-experimental non-randomized study. Four nursing homes implemented the MT training intervention for six months (Experimental Group (EG)); while five haven't participated in structured physical activity program and maintained with their normal routine, during the same period (Control Group (CG)).[2]

Participants

Of 12 nursing homes invited, nine nursing homes in suburban areas Viseu, Portugal, accepted to be part of this study. Participants were recruited from these institutions, 49 older adults from both genders clinically diagnosed with AD, aged 69–94 years, volunteered to participate in this study.

The eligible subject pool was restricted to older adults with the following characteristics: age ≥65 years, not engaged in any regular exercise training in the last year, institutionalized for more than six months, diagnosis of AD at mild or moderate stage according to Clinical Dementia Rating (CDR) (Morris, 1993) and lack of any diagnosed or self-reported musculoskeletal or cardiovascular disorders that contraindicate participation in moderate exercise and testing. A 70% minimum attendance rate to the exercise sessions was required for participants in the EG.

After initial screening, all participants, formal caregivers, and institutions received a complete explanation of the purpose, risks and procedures of the study. A written informed consent was provided. The investigation was in full compliance with the Helsinki declaration (World Medical Association, 2009) and the nine institutions where the intervention took place approved all methods and procedures. The Ethical Commission of the Faculty of Sports of the University of Porto also approved this study. The participants' flow diagram is represented in Figure 1.

Exercise intervention

The EG completed a six-month MT program following the recommendations of the American College of Sports Medicine (ACSM) (Nelson et al., 2007), including aerobic, muscle strengthening, flexibility, balance and postural exercises with two sessions per week on non-consecutive days. Sessions contained 4–7 participants and took place in specific rooms with peaceful and pleasant music environment. Sessions lasted for 45–55 minutes and were conducted by the same exercise trainer in all settings. The sessions were divided into three main parts: Warm-up (5–10 minutes, including postural and stretching

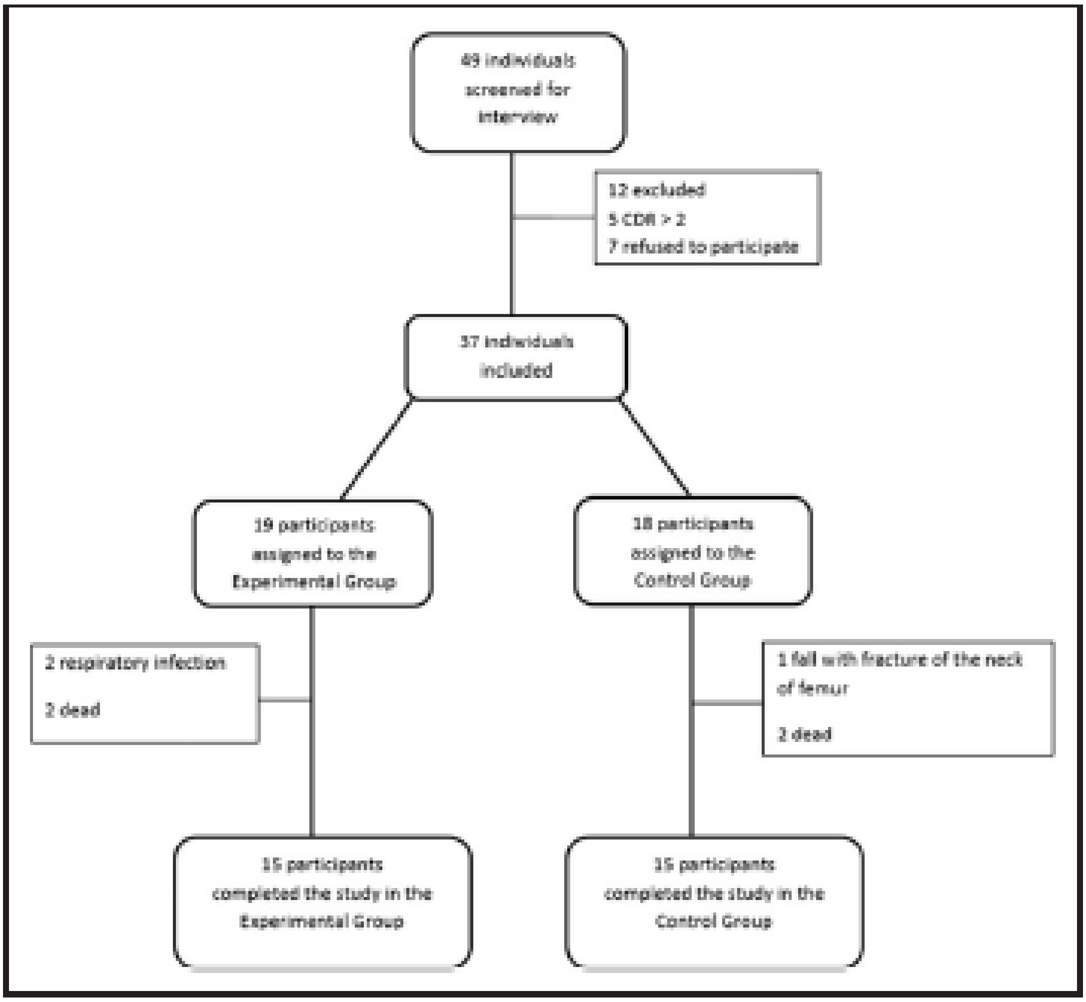

Figure 1. Participants flow diagram from initial screening to the end of the study.

exercises for general activation), specific training (30–35 minutes, including 15 minutes of moderate aerobic exercises + 15–20 minutes motor and muscular tasks for strength and coordination/balance training) and cool down (5 minutes with respiratory and flexibility exercises). In order to make the exercise program more efficient and attractive, we established regular similar routines that prioritized enjoyable and familiar exercises (as simulating walking, running, biking, rowing) (Teri, Logsdon, & McCurry, 2008). Due to the frailty condition of the participants and for safety reasons, sessions were mainly chair-based and routines of functional exercises with low coordination requirements were emphasized so participants could achieve the session's goals.

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics of the participants were provided by the nursing homes where they were residing. Their sociodemographic and clinical characteristics are given in Table 1.

Outcome measures

All following measures were assessed at baseline and after three and six months of experimental protocol.

Table 1. Characteristics of the participants.

	Exercise group ($n = 19$)	Control group ($n = 18$)	p[a]
Age (years)	84.8 ± 5.9	83.3 ± 5.3	0.418
Men, No. (%)	4 (21.1%)	5 (27.8%)	0.685
Marital status			0.693
Single/Widower	16 (84.2%)	14 (77.8%)	
Married	3 (15.8%)	4 (22.2%)	
Educational level (years)	2.58 ± 2.8	4.00 ± 4.0	0.166
Profession (%)			0.508
Domestic/Agricultural	10 (52.6%)	12 (66.7%)	
Others	9 (47.6%)	6 (33.3%)	
Diagnosis, No. (%) (others than AD)			
Hypertension	12 (63.2%)	13 (72.2%)	0.728
Heart disease	5 (26.3%)	8 (44.4%)	0.313
Diabetes mellitus	3 (15.8%)	6 (33.3%)	0.269
Depression	7 (36.8%)	4 (22.2%)	0.476
Medication, No.	7.79 ± 1.75	8.3 ± 2.11	0.448
Blood pressure, mmHg			
Systolic	137.63 ± 17.79	144.11 ± 15.66	0.249
Diastolic	75.52 ± 15.18	81.89 ± 13.56	0.188
Clinical Dementia Rating scale	1.68 ± 0.48	1.67 ± 0.49	0.911
Baseline			

Note: [a]Student's t-test or Mann-Whitney for continuous variables; Chi-squared or Fisher's exact test (two-tailed) for categorical variables.

Dementia stage

The CDR test (Morris, 1993) was used only at baseline to distribute the participants according to their cognitive stage. CDR is an instrument that assesses the existence and prevalence of the various stages of dementia. It comprises six cognitive-behavioral items covering memory, orientation, judgment and problem solving, community activities, home and hobbies, and personal care. The cut-off points were CDR = 1 (mild dementia stage) and CDR = 2 (moderate dementia stage).

Anthropometry

Anthropometric variables included Body Mass Index (BMI) and Waist Circumference (WC). BMI was determined using the standard formula: weight divided by height squared (kg/m^2). Body weight was measured to the nearest 0.1 kg with a digital weight scale. Participants were weighed barefoot wearing light clothing. Height was measured to the nearest 1 mm with a standard stadiometer. Participants were required to maintain the Frankfurt plane, standing as tall as possible with hands hanging by their sides, and taking a deep breath before the measurement. WC was assessed at the midpoint between iliac crest and the bottom of the ribcage using a spring-loaded measuring tape.

Functional fitness

The Senior Fitness Test (Rikli & Jones, 2013) battery for older adults was used to assess functional fitness associated with maintaining physical independence in later life. The test items included: chair-stand test—to assess lower-body strength; arm curl test—to measure upper-body strength; 2-min step test—to assess aerobic endurance; chair sit-and-reach test—to assess lower-body flexibility; back scratch test—to assess upper-body flexibility; and 8-foot up-and-go (UG) test—to assess agility and dynamic balance.

Cognitive function

The Mini-Mental State Examination (MMSE) was used for a global cognitive evaluation (Folstein, Folstein, & McHugh, 1975). It is a widely used method for assessing cognitive mental status. This instrument is clinically used to detect and follow the course of an illness and can also be used as a research tool to screen for cognitive disorders and follow cognitive changes in epidemiological studies. It assesses orientation, attention, immediate and short-term recall, language and the ability to follow simple verbal and written instructions. Furthermore, it provides a total score that categorizes the individual on a scale of cognitive function (Folstein et al., 1975). Ranging from 0 to 30. MMSE normative values consider the subject educational level. Operational cut-off values for the Portuguese population are 22 (for 0 to 2 years of literacy), 24 (for 3 to 6 years of literacy), and 27 (for more than 6 years of literacy) (Morgado et al., 2009).

Statistical analysis

All statistical analyses were conducted with the SPSS IBM Statistical Software version 20.0 for Windows with a significance level of 0.05. For the baseline comparisons between

EG and CG, data for all participants are presented as absolute (proportions) and relative (percentages) frequencies for categorical values, as means with standard deviation (SD) for interval data. The Chi-square test or Fisher exact test was used to compare categorical data, and Student's *t*-test or non-parametric Mann–Whitney was applied for interval data (Table 1).

A two-way (group and time) factorial ANOVA, with repeated measures on one factor (time) was used to determine the differences between and within the EG and the CG for dependent variables. Bonferroni Post-hoc analysis was used to determine the differences between the three time-points.

Results

Recruitment

The process of recruitment and screening of participants lasted for two months. Of the 49 participants who were assessed for eligibility, 12 were excluded. A severe stage of dementia was the reason for the exclusion of five individuals and seven older adults declined to participate in the study after being informed of the details.

The intervention included 37 participants, divided into two groups: EG ($n=19$; mean age $=84.8\pm5.9$ years) and CG ($n=18$; mean age $=83.3\pm5.3$ years). In the EG, two participants dropped out due to respiratory infections and two died. In the CG, three dropouts were registered, one due to a fall and a femoral neck fracture, and two due to death. Thus, the dropout rate from the initial assessment and group's allocation until the end of the study was 18.9%, resulting in 15 participants for both groups. Figure 1 shows the participant flow from screening to the end of the study.

Attendance rate for the EG was calculated by dividing the number of exercise sessions completed by participants by the full amount of sessions they were expected to perform throughout the study. The attendance levels were 85% or over. The reasons for missing exercise sessions were behavioral disorders (33.3%), acute diseases (26.7%), unwillingness to participate in a particular exercise session (20%) and other reasons (20%). The dropouts occurred between the 12th and 46th session from a total of 48 MT sessions.

Subject characteristics

The sociodemographic and clinical characteristics of participants at baseline are shown in Table 1. No significant differences at baseline were found between the groups.

The 37 participants in the study were predominately females (75.7%) and single or widowed (81.1%). Apart from AD, in both groups (EG and EC), participants were mainly diagnosed with hypertension, minor heart condition, diabetes mellitus, and depression. The CDR (EG $=1.68\pm0.48$: CG $=1.67\pm0.49$) allowed ensuring that the stage of dementia of all participants ranged between mild ($n=12$) and moderate ($n=25$).

The number of participants who did not complete the study was similar in each group ($p=0.737$). Dropout participants had no statistically significant differences compared to the other older adults in any descriptive parameters. None of the reasons for dropping out (including deaths) were directly or indirectly related to possible adverse effects of the exercise program.

Changes in body composition, functional fitness, and cognitive function in the EG and the CG are reported in Table 2.

Table 2. Pre-test, three-month test, and post intervention test outcomes for body composition, functional fitness, and cognitive variables.

Variable	Exercise group (M ± SD) Pre-test (M1)	Exercise group 3-Month test (M2)	Exercise group 6-Month test (M3)	Control group (M ± SD) Pre-test (M1)	Control group 3-Month test (M2)	Control group 6-Month test (M3)	p (Group)	p (Time)	p (Interaction)
BMI (kg/m²)	27.7 ± 3.2	27.5 ± 3.2	27.3 ± 3.3	27.8 ± 5.8	27.9 ± 6.2	27.9 ± 6.7	0.828	0.766	0.641
WC (cm)	98.5 ± 6.3	96.9 ± 6.7°	93.5 ± 8.2°°,°°°	99.4 ± 14.8	99.8 ± 15.6	100.7 ± 16.9	0.412	0.027*	< 0.001*
Chair stand	5.7 ± 3.7	8.5 ± 3.9°	9.5 ± 5°°°	6.2 ± 3.1	5.8 ± 3.2	5.2 ± 2.8	0.103	< 0.001*	<0.001*
Arm curl	9.6 ± 4	11.2 ± 4.1°	11.8 ± 4.1°°°	8.9 ± 4	8.0 ± 3.6	7.2 ± 3.7°°°	0.045*	0.672	<0.001*
CSR	−19.7 ± 9.6	−14.4 ± 11.5°	−13.3 ± 9.9°°°	−22.8 ± 8.5	−25.7 ± 9.1	−27.1 ± 8.9°°°	0.008*	0.569	<0.001*
Back scratch	−42.8 ± 2.2	−32 ± 10.6°	−29.7 ± 1°°°	−41.6 ± 8.7	−43.3 ± 8.4	−43.5 ± 8.7	0.001*	0.002*	0.022*
UG	27.5 ± 32.8	24.6 ± 6.7	23.1 ± 22.5	24.9 ± 10	27.3 ± 12.5	30.1 ± 15.4	0.769	0.658	0.029*
2 min Step	59 ± 38	78.6 ± 42.4°	86.4 ± 46.2°°°	51.1 ± 26.7	46.9 ± 27.9	38.3 ± 25.1	0.021*	0.102	<0.001*
MMSE	14.9 ± 6	16.6 ± 6.5°	15.3 ± 6	16.1 ± 4.2	14.9 ± 5	13.3 ± 4°°°	0.822	0.036*	0.008*

Note: °Statistically significant difference from M1 to M2 ($p < 0.05$); °°Statistically significant difference from M2 to M3 ($p < 0.05$); °°°Statistically significant difference between M1 and M3 ($p < 0.05$); *Statistically significant difference.

Anthropometry

In the baseline values, no significant group differences were found in BMI and WC. For WC a different response in each group was evident over time, supported by a significant decrease of WC in the EG from M1 to M2 ($p < 0.05$) and from M2 to M3 ($p < 0.05$). During the intervention, the CG presented a subtle, though not statistically significant, increase in the WC test. There was a significant main effect of time on WC ($p = 0.027$) and of group and time interactions on WC ($p < 0.001$). No changes—neither significant interactive nor main effects of time and group—were observed for BMI.

Functional fitness

No significant group differences were found at baseline for all functional fitness variables. Different responses in each group became evident over time. A significantly better performance in the EG in the Chair Stand test from M1 to M2 ($p < 0.05$) and from M1 to M3 ($p < 0.05$) was found. Also, significant main effects of time ($p < 0.001$) and interaction ($p < 0.001$) were observed in the chair-stand test. The CG had a worse performance in the chair-stand test over time, although not statistically significant. The EG improved its performance over the time, being statistically significant from M1 to M2 and from M1 to M3 on arm-curl test ($p < 0.05$), CSR test ($p < 0.05$) back-scratch test ($p < 0.05$), and 2-min step test ($p < 0.05$). The CG had a statistically significant decrease in their performance, between M1–M3, on arm-curl test ($p = 0.047$) and CSR test ($p = 0.020$). Thus, there were significant interactive and main effects of group on arm-curl test ($p = 0.045$), CSR test ($p < 0.05$) back-scratch test ($p < 0.05$) and 2-min step test ($p = 0.021$). In the back-scratch test significant interactive ($p = 0.022$) and main effects of time ($p = 0.002$) and group ($p < 0.001$) were observed. From M1 to M2 ($p < 0.05$) and from M1 to M3 ($p < 0.05$), the EG significantly improved their performance in this test. In the UG test, groups responded differently resulting in a significant interaction from M1 to M3 ($p = 0.029$).

Cognitive function

At the baseline, no significant group differences were found in cognitive function. A significant increase in MMSE from M1 to M2 ($p = 0.016$) was observed in the EG, while a significant decrease of performance of the CG was observed over time M1 to M3 ($p = 0.016$). Analysis revealed significant group and time interactions on MMSE ($p = 0.008$) and significant main effects of time for this same variable ($p = 0.036$).

Discussion

The present study tested and confirmed the hypothesis that a six-month MT program can improve cognitive and physical functions in institutionalized older adults with mild to moderate AD.

As expected, anthropometric measurements (BMI and WC) showed that, at baseline, participants were generally overweight. Indicators of obesity and overweight have been associated with dementia (Dahl et al., 2010; Luchsinger et al., 2004) and with poor neurocognitive outcomes (Whitmer et al., 2005). Medical conditions frequently related to obesity and overweight (dyslipidemia, hypertension, type 2 diabetes) are also known contributors to cognitive decline and dementia (Hayden et al., 2006; Skoog et al., 2006). However, several clinical settings have also reported associations between lower BMI and dementia at mild severity, increasing with advancing disease severity and duration (White et al., 1998). Although no significant changes were observed for BMI in both groups, the EG's WC significantly decreased after three months and again at the end of the intervention, whereas the EG's WC increased during the intervention period. Reducing WC may have relevant health implications, as it has been highly correlated with visceral fat (Molarius et al., 1998). Despite being a frequent and widely accepted measurement of adiposity in young and middle-aged adults (Schreiner et al., 1996), considering age-related changes in fat and fat-free mass in elderly populations (Harris et al., 2000), the influence of BMI on health risks and dementia has been controversial. The literature points out that WC is as good as measure of excess adiposity as BMI among older adults or even better (Leitzmann et al., 2011).

Normal aging is also characterized by the functional fitness decline. With increased physical impairment, the ability to perform ADL decreases (Zhu & Chodzko-Zajko, 2006). In elderly patients with AD functional decline becomes more pronounced and while the disease progresses, physical function becomes increasingly compromised. Limitations in ADLs become more evident, gradually leading to the loss of autonomy. Our data show that the CG follows this trend, with a decline in all dimensions of functional fitness. In opposition, our MT program seems capable of preventing this tendency.

Age-related loss of muscle mass and strength (sarcopenia) are magnified by the lack of physical activity opportunities in the institutional settings leading to frailty faster (Santana-Sosa, Barriopedro, Lopez-Mojares, Perez, & Lucia, 2008). The CG followed this trend, with their performance declining in both lower and upper limbs strength tests, being significant in the arm-curl test (upper limbs strength test) from M1 to M3. A significant improvement in the upper and lower muscle strength tests was observed in the EG from M1 to M2 and from M1 to M3. Thus, our results are in accordance with the literature that considers the increment of physical activity as an important therapeutic tool for the attenuation of this loss (Santana-Sosa et al., 2008). Particularly, frailer older adults with some physiological impairment can improve their levels of strength remarkably (Chandler et al., 1998).

Ageing has a similar effect on flexibility. The decline of this capacity ranges from 20% (hip) to 40% (ankle flexion) by 70 years of age (ACSM, 2009). As a consequence, the risks of injury, falling, and back pain, increases (ACSM, 2009). Our data show that the EG was able to significantly improve their flexibility after three and six months, in both upper and lower limbs. Other studies support these results (Toraman & Ayceman, 2005), showing that the decrease of flexibility can be mitigated or even reversed through physical exercise (Batista et al., 2009).

Regarding the UG test, EG improved their performance during the intervention while a significant decrease was observed in the CG, although this difference was not statistically significant. Agility, balance (Toraman & Ayceman, 2005), and lower limb muscular strength (Santana-Sosa et al., 2008) are the capacities that are important to perform the UG test. All these capacities were trained and were included in our MT intervention. Therefore, MT boosts better results than one type of training that contemplates only one of these capabilities.

According to the literature, an increase in aerobic fitness, as observed in the present study, raises the blood flow and cerebral perfusion preserving critical areas of cognition in older adults (Cotman et al., 2007). Higher levels of aerobic capacity are associated with reduced whole-brain atrophy in persons with AD, thus enhancing the cognitive function (Colcombe & Kramer, 2003). They also reduce the risk of cardiovascular and all-cause mortality (Zhu & Chodzko-Zajko, 2006). The MT program was able to improve significantly the participant's aerobic fitness after three and six months. These results are supported by previous studies that have shown significant improvements in aerobic capacity after MT (Takeshima et al., 2007; Toraman & Ayceman, 2005) in non-demented older adults.

The improvements observed in the present study have significance for functional fitness which has consistently been linked with better health status, the ability to perform ADL and consequently with better quality of life (Forbes et al., 2013). Similar results were observed by Santana-Sosa et al. (2008), who conducted a 12-week MT program for patients with AD which succeeded in inducing significant improvements in patients' functional performance.

The Seattle Protocols, a series of evidence-based interventions conducted by Teri et al. (2008), showed that physical activity is beneficial and feasible for community-residing individuals with dementia and cognitive impairment (Teri et al., 2008).

The benefits of chronic exercise on cognitive function have been reported (Kaliman et al., 2011; Stevens & Killeen, 2006), studies found it to be linked to positive changes in brain structures, affecting angiogenesis, neurogenesis, and up-regulation of neuroprotective molecules as well as brain volume and functional architecture (Kaliman et al., 2011).

However, others studies have reported that exercise has no effect on cognition (Holliman et al., 2001; Steinberg et al., 2009). In this study, we observed a significant increase in MMSE from M1 to M2 and from the M1 to M3 in the EG. The literature provides evidence that supports the trend from M1 to M2 and from M2 to M3. We believe that, despite the benefits of physical exercise on cognition that could justify better results in the EG from M1 to M2, the neurogenerative nature of AD may justify the decline from M2 to M3. However, between M1 and M3, the results show a slight and not statically significant improvement in the cognitive function, in the EG while the CG had a statistical significant decrease of this function in the same period of time. These data suggest that MT exercise programs can improve (as in M1 to M2) or at least help preserve cognitive abilities for a longer period of time (as in M1 to M3).

The main limitation of this study was the small sample size, the lack of randomization for group assignment and dietary assessment. Recruiting voluntary AD older adults willing to commit with a six-month intervention was challenging and several institutions were therefore involved. Although the same exercise trainer supervised all classes, working with different settings with different conditions may have disturbed the homogeneity between exercise sessions.

It is important to highlight the low drop-out rate of our sample, which not only allowed us to maintain a consistent number of participants to conduct the full six months exercise program, but also reinforces the idea that mild to moderate AD older adults can and should be engaged in MT exercise program in order to improve or maintain functional and cognitive performance.

Besides the proliferation of different types of intervention for AD older adults, the key strength of our study is that our MT program attempted to adapt the physical exercise recommendations of ACSM for older adults (Nelson et al., 2007) to a population with highly specific characteristics (elderly with AD, in institutional settings). We believe that the positive results are also linked with extremely low level of physical activity and physical fitness at the baseline. According to the literature, exercise can produce short-term, highly improvements even frailer older adults (Fiatarone et al., 1994). Thus, we believe that our results underline that the adaptation of these recommendations is viable and allows this population to enjoy the benefits of improved levels of physical and cognitive functioning associated to physical exercise.

In sum, this study confirms that six months of MT program can positively affect physical and cognitive functions in institutionalized older adults with AD. Due to the frailty of the participants, higher physical fitness contributes for a better performance of ADL and delay the deterioration inherent to AD. Additionally, due its wide application and feasibility, the implementation and dissemination of such exercise program, as a low-cost alternative therapy, could be an important instrument for relevant health promotion policies such as national dementia plans.

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Notes

1. MT is generally defined as a combination of strength training, aerobic endurance, coordination, balance, and flexibility, and is recommended by current PA guidelines for older adults (Carvalho et al., 2008).
2. Participants were assigned to the different groups according to the results of the CDR test. After screening the stage of dementia of all participants, the allocation of the institutions was based on the homogeneity of participants in the initial and moderate stage of dementia in the EG and the CG.

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[Appendix 4]

CLINICAL DEMENTIA RATING

Questionário de Avaliação Clínica da Demência

Perguntas sobre a memória para o doente:

1. Tem problemas de memória ou raciocínio? ☐ Sim ☐ Não
2. Há poucos instantes, o seu (parceiro, etc.) contou-me um acontecimento que se passou recentemente. Quer contar-me o que aconteceu? (Se for necessário, obtenha pormenores tais como o local, hora, pessoas envolvidas, qual foi a duração, quando acabou e como o doente ou outras pessoas chegaram lá).

No espaço de 1 semana

1,0 – Correcto (em grande parte) ____________________
0,5 ____________________
0,0 – Incorrecto (em grande parte) ____________________

No espaço de 1 mês

1,0 – Correcto (em grande parte) ____________________
0,5 ____________________
0,0 – Incorrecto (em grande parte) ____________________

3. Vou dar-lhe um nome e um endereço para memorizar durante alguns minutos. Repita este nome e endereço: (Repita até a frase ser repetida correctamente ou até um máximo de três tentativas).

Elementos	1	2	3	4	5
	João	Borges,	Rua do Mercado,	42	Guimarães
	João	Borges,	Rua do Mercado,	42	Guimarães
	João	Borges,	Rua do Mercado,	42	Guimarães

(Sublinhe os elementos repetidos de forma correcta em cada uma das tentativas).

4. Quando nasceu? ____________________
5. Onde nasceu? ____________________
6. Qual foi a última escola que frequentou?
   Nome ____________________
   Cidade ________________ Classe ____________
7. Qual foi a sua ocupação/emprego principal (ou do seu parceiro, caso não tivesse emprego)? ____________________
8. Qual foi o seu último emprego principal (ou do seu parceiro, caso não tivesse emprego)? ____________________
9. Quando se reformou (ou o seu parceiro) e porquê? ____________________
10. Repita o nome e endereço que lhe pedi para memorizar:

Elementos	1	2	3	4	5
	João	Borges,	Rua do Mercado,	42	Guimarães

(Sublinhe os elementos repetidos correctamente).

Questionário de Avaliação Clínica da Demência

Perguntas sobre a orientação para o doente:

Registe literalmente a resposta do doente a cada pergunta

1. Qual é a data de hoje? ☐ Correcto ☐ Incorrecto

   ____

2. Qual é o dia da semana? ☐ Correcto ☐ Incorrecto

   ____

3. Qual é o mês? ☐ Correcto ☐ Incorrecto

   ____

4. Qual é o ano? ☐ Correcto ☐ Incorrecto

   ____

5. Qual é o nome deste local? ☐ Correcto ☐ Incorrecto

   ____

6. Em que terra nos encontramos? ☐ Correcto ☐ Incorrecto

   ____

7. Que horas são? ☐ Correcto ☐ Incorrecto

   ____

8. (Na sua opinião), o doente sabe quem é o informante? ☐ Correcto ☐ Incorrecto

   ____

Perguntas sobre o discernimento e resolução de problemas para o doente:

Instruções: Caso a resposta inicial do doente não mereça uma avaliação de 0, insista no assunto para identificar o melhor entendimento do problema por parte do doente. Marque com um círculo a resposta que mais se aproxima.

Semelhanças:

Exemplo: "Em que aspecto se assemelha um lápis a uma caneta? (instrumentos de escrita)

Em que aspecto se assemelham estas coisas?" Resposta do doente

1. nabo……couve-flor ______________________________
   (0 = vegetais)
   (1 = alimentos comestíveis, seres vivos, podem ser cozinhados, etc.)
   (2 = respostas não pertinentes; diferenças; compram-se)

2. escrivaninha……estante de livros __________________________
   (0 = mobiliário, mobiliário de escritório; ambos servem para guardar livros)
   (1 = em madeira, pernas)
   (2 = não pertinentes; diferenças)

Diferenças:

Exemplo: "Qual é a diferença entre açúcar e vinagre? (doce vs. azedo)

Qual é a diferença entre estas coisas?"

3. mentira……erro ______________________________
   (0 = um é intencional, o outro não)
   (1 = um é mau, o outro é bom – ou explica apenas um)
   (2 = tudo o resto, semelhanças)

4. rio……canal ______________________________
   (0 = natural - artificial)
   (2 = tudo o resto)

Cálculos:

5. Quantos centavos perfazem um escudo? ☐ Correcto ☐ Incorrecto
6. Quantas moedas de 50 centavos perfazem 13,50 escudos? ☐ Correcto ☐ Incorrecto
7. Subtraia 3 a 20 e continue a subtrair 3 a cada número novo até ao fim. ☐ Correcto ☐ Incorrecto

Discernimento:

8. Depois de chegar a uma cidade que não conhece, de que forma tentaria localizar um amigo que gostaria de visitar?

   (0 = tentar a lista telefónica; telefonar a um amigo comum)
   (1 = telefonar à polícia, telefonar para as Informações (normalmente não facultam endereços)
   (2 = nenhuma resposta clara)

9. Avaliação do doente relativamente à sua incapacidade e posição na vida e a sua percepção das razões porque está presente neste exame (mesmo que já tenha avaliado este aspecto, classifique aqui):

   ☐ Bom discernimento ☐ Discernimento parcial ☐ Pouco discernimento

[Appendix 5]

MINI MENTAL STATE EXAMINATION

Mini Mental State Examination (MMSE)

1. Orientação (1 ponto por cada resposta correcta)

Em que ano estamos? ______
Em que mês estamos? ______
Em que dia do mês estamos? ______
Em que dia da semana estamos? ______
Em que estação do ano estamos? ______

Nota:____

Em que país estamos? ______
Em que distrito vive? ______
Em que terra vive? ______
Em que casa estamos? ______
Em que andar estamos? ______

Nota:____

2. Retenção (contar 1 ponto por cada palavra correctamente repetida)

"Vou dizer três palavras; queria que as repetisse, mas só depois de eu as dizer todas; procure ficar a sabê-las de cor".
Pêra ______
Gato ______
Bola ______

Nota:____

3. Atenção e Cálculo (1 ponto por cada resposta correcta. Se der uma errada mas depois continuar a subtrair bem, consideram-se as seguintes como correctas. Parar ao fim de 5 respostas)

"Agora peço-lhe que me diga quantos são 30 menos 3 e depois ao número encontrado volta a tirar 3 e repete assim até eu lhe dizer para parar".
27_ 24_ 21 _ 18_ 15_

Nota:____

4. Evocação (1 ponto por cada resposta correcta.)

"Veja se consegue dizer as três palavras que pedi há pouco para decorar".
Pêra _______
Gato _______
Bola _______

Nota:____

5. Linguagem (1 ponto por cada resposta correcta)

a. "Como se chama isto? Mostrar os objectos:
Relógio ____
Lápis______

Nota:____

b. "Repita a frase que eu vou dizer: O RATO ROEU A ROLHA"

Nota:____

c. "Quando eu lhe der esta folha de papel, pegue nela com a mão direita, dobre-a ao meio e ponha sobre a mesa"; dar a folha segurando com as duas mãos.
Pega com a mão direita____
Dobra ao meio ____
Coloca onde deve____

Nota:____

d. "Leia o que está neste cartão e faça o que lá diz". Mostrar um cartão com a frase bem legível, "FECHE OS OLHOS"; sendo analfabeto lê-se a frase.
Fechou os olhos____

Nota:____

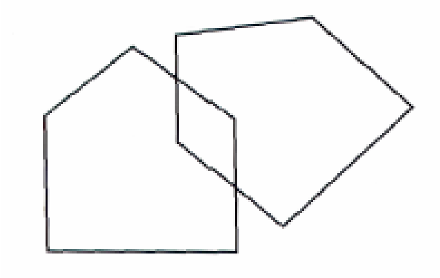
e. "Escreva uma frase inteira aqui". Deve ter sujeito e verbo e fazer sentido; os erros gramaticais não prejudicam a pontuação.

Frase:

Nota:____

6. **Habilidade Construtiva** (1 ponto pela cópia correcta.)

Deve copiar um desenho. Dois pentágonos parcialmente sobrepostos; cada um deve ficar com 5 lados, dois dos quais intersectados. Não valorizar tremor ou rotação.



Cópia:

Nota:____

TOTAL(Máximo 30 pontos):____

<u>**Considera-se com defeito cognitivo**</u>: • analfabetos ≤ 15 pontos
• 1 a 11 anos de escolaridade ≤ 22
• com escolaridade superior a 11 anos ≤ 27

[Appendix 6]

KATZ INDEX

Avaliação Funcional

Escala de Actividades de Vida Diária . Índice de Kazt

Índice de Katz apresentado por Sequeira (2007)

Índice de Katz	Independente	Independente com supervisão	Independente com ajuda	Dependente
Controlo de esfíncteres	4	3	2	1
Banho	4	3	2	1
Utilização da casa de banho	4	3	2	1
Mobilidade	4	3	2	1
Vestir/despir	4	3	2	1
Alimentação	4	3	2	1

[Appendix 7]

NEUROPSYCHIATRIC INVENTORY

Nome: ____ Data ____/____/____

Idade: ________ Sexo: M F Entrevistador (iniciais): ______________________

Prestador de cuidados: conjuge ☐ filha(o) ☐ outro: ______________________

Reside com o paciente: Sim ☐ Não ☐

Percentagem de assistência prestada pelo entrevistado: <25%; 25-50%; 50-75%; >75%

INVENTÁRIO NEUROPSIQUIÁTRICO (INP)

Universidade da Califórnia, Los Angeles (UCLA)

Idade	N/A	Não	Frequente (F)	Gravid. (G)	FxG	Desgaste
Manifestações neuropsiquiátricas						
Delírios	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Alucinações	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Agitação	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Depressão/disforia	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Ansiedade	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Euforia/elação	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Apatia/indiferença	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Desinibição	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Irritabilidade/labilidade	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Comportamento motor aberrante	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
				Nota total INP	____	________
Alterações neurovegetativas	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Comportamento nocturno	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5
Apetite/alteração alimentar	x	0	1 2 3 4	1 2 3	____	1 2 3 4 5

[Appendix 8]

QUALITY OF LIFE – ALZHEIMER´S DISEASE SCALE

QOL – AD *versão portuguesa*

(Versão de entrevista para doente)

Aplicada por entrevistador de acordo com as instruções.

Fazer um círculo à volta das respostas:

1- Saúde Física	Fraco	Razoável	Bom	Excelente
2- Energia	Fraco	Razoável	Bom	Excelente
3- Humor/ Disposição	Fraco	Razoável	Bom	Excelente
4- Condições de vida	Fraco	Razoável	Bom	Excelente
5- Memória	Fraco	Razoável	Bom	Excelente
6- Família	Fraco	Razoável	Bom	Excelente
7- Casamento	Fraco	Razoável	Bom	Excelente
8- Amigos	Fraco	Razoável	Bom	Excelente
9- Em geral, como se sente	Fraco	Razoável	Bom	Excelente
10- Capacidade de realizar tarefas em casa	Fraco	Razoável	Bom	Excelente
11- Capacidade de fazer coisas para se divertir	Fraco	Razoável	Bom	Excelente
12- Dinheiro	Fraco	Razoável	Bom	Excelente
13- A Vida como um todo	Fraco	Razoável	Bom	Excelente

QOL – AD *versão portuguesa*

(Versão de questionário para familiar ou prestador de cuidados)

As questões seguintes dizem respeito à Qualidade de Vida do doente:

Quando pensa sobre a vida do doente, podemos considerar vários aspectos, alguns dos quais estão abaixo mencionados. Por favor, pense em cada um dos itens e classifique a qualidade de vida actual do doente, como ele a consideraria, em cada área usando uma de quatro palavras: **fraco, razoável, bom, excelente**. Classifique estes itens com base na vida do doente no momento presente (ou seja, nas últimas semanas). Se tiver questões acerca de qualquer item, por favor peça ajuda à pessoa que lhe forneceu este questionário.

Faça um círculo à volta das respostas:

1- Saúde Física	Fraco	Razoável	Bom	Excelente
2- Energia	Fraco	Razoável	Bom	Excelente
3- Humor/ Disposição	Fraco	Razoável	Bom	Excelente
4- Condições de vida	Fraco	Razoável	Bom	Excelente
5- Memória	Fraco	Razoável	Bom	Excelente
6- Família	Fraco	Razoável	Bom	Excelente
7- Casamento	Fraco	Razoável	Bom	Excelente
8- Amigos	Fraco	Razoável	Bom	Excelente
9- Em geral, como se sente	Fraco	Razoável	Bom	Excelente
10- Capacidade de realizar as tarefas em casa	Fraco	Razoável	Bom	Excelente
11- Capacidade de fazer coisas para se divertir	Fraco	Razoável	Bom	Excelente
12- Dinheiro	Fraco	Razoável	Bom	Excelente
13- Vida como um todo	Fraco	Razoável	Bom	Excelente

INSTRUÇÕES PARA A PONTUAÇÃO DA QOL:

A pontuação é atribuída a cada item da seguinte forma: fraco =1; razoável =2, Bom =3, excelente =4;

A pontuação total é a soma dos 13 itens.

Para cálculo de pontuação conjunta: (2 x pontuação escala doente + pontuação escala cuidador): 3.

[Appendix 9]

SENIOR FITNESS TEST

DESCRIÇÃO DOS TESTES DA BATERIA SENIOR FITNESS TEST (SFT)

Levantar e Sentar na Cadeira

Objectivo:

Avaliar a força e resistência dos membros inferiores.

Equipamento:

Cronómetro, cadeira com encosto (sem braços), com altura de assento aproximadamente de 43cm. Por razões de segurança, a cadeira deve ser colocada contra uma parede, ou estabilizada de qualquer outro modo, evitando que se mova durante o teste.

Protocolo:

O teste inicia-se com o participante sentado no meio da cadeira, com as costas direitas e os pés afastados à largura dos ombros e totalmente apoiados no solo. Um dos pés deve estar ligeiramente avançado em relação ao outro para ajudar a manter o equilíbrio. Os braços estão cruzados ao nível dos punhos e contra o peito. Ao sinal de "partida" o participante eleva-se até a extensão máxima (posição vertical) e regressa à posição inicial de sentado. O participante é encorajado a completar o máximo de repetições num intervalo de tempo de 30s. O participante deve sentar-se completamente entre cada elevação. Enquanto controla o desempenho do participante para assegurar o maior rigor, o avaliador conta as elevações correctas. Chamadas de atenção verbais (ou gestuais) podem ser realizadas para corrigir um desempenho deficiente.

Prática / ensaio:

Após uma demonstração realizada pelo avaliador, um ou dois ensaios podem ser efectuados pelo participante visando uma execução correcta. De imediato segue-se a aplicação do teste.

Pontuação:

A pontuação é obtida pelo número total de execuções correctas num intervalo de 30s. Se o participante estiver a meio da elevação no final dos 30s, esta deve contar como uma elevação.

Flexão do Antebraço

Objectivo:

Avaliar a força e resistência do membro superior.

Equipamento:

Relógio de pulso ou outro qualquer que possua ponteiro de segundos, cadeira com encosto (sem braços) e halteres de mão (2,27 kg para mulheres e 3, 63 kg para homens).

Protocolo:

O participante está sentado numa cadeira, com as costas direitas, com os pés totalmente assentes no solo e com o tronco totalmente encostado. O haltere está seguro na mão dominante. O teste começa com o braço em extensão ao lado da cadeira, perpendicular ao solo. Ao sinal de "iniciar" o participante roda gradualmente a palma da mão para cima, enquanto faz a flexão do cotovelo no sentido completo do movimento; depois regressa à posição inicial de extensão. Especial atenção deverá ser dada ao controlo da fase final da extensão do cotovelo.

O avaliador ajoelha-se (ou senta-se numa cadeira) junto do participante no lado do braço dominante, colocando os seus dedos no bicípite do executante, de modo a estabilizar a parte superior do braço, e assegurar que seja realizada uma flexão completa (o antebraço do participante deve apertar os dedos do avaliador). É importante que a parte superior do braço permaneça estática durante o teste.

O avaliador pode precisar de colocar a sua outra mão atrás do cotovelo de maneira a que o executante saiba quando atingiu extensão total, evitando movimentos de balanço do antebraço. O relógio deve ser colocado de maneira totalmente visível.

O participante é encorajado a realizar o maior número possível de flexões num tempo limite de 30s, mas sempre com movimentos controlados tanto na fase de flexão como de extensão. O avaliador deverá acompanhar as execuções de forma a assegurar que o peso é transportado em toda a amplitude do movimento – da extensão total à flexão total.

Cada flexão correcta é contabilizada, com chamadas de atenção verbais sempre que se verifique um desempenho incorrecto.

Prática / ensaio:

Após demonstração por parte do avaliador deverão ser realizadas, uma ou duas tentativas pelo participante para confirmar uma realização correcta, seguindo-se a execução do teste durante 30s.

Pontuação:

A pontuação é obtida pelo número total de flexões correctas realizadas num intervalo de 30s. Se no final dos 30s o antebraço estiver em meia-flexão, deve contabilizar-se como uma flexão total.

Sentado e Alcançar

Objectivo:

Avaliar a flexibilidade dos membros inferiores.

Equipamento:

Cadeira com encosto (aproximadamente 43cm de altura até ao assento) e uma régua de 45cm. Por razões de segurança, a cadeira deve ser colocada contra uma parede para que se mantenha estável (não deslize para a frente) quando o participante se sentar na respectiva extremidade.

Protocolo:

Começando numa posição de sentado, o participante avança o seu corpo para a frente, até se encontrar sentado na extremidade do assento da cadeira. A prega entre o topo da perna e as nádegas deve estar ao nível da extremidade do assento. Com uma perna flectida e o pé totalmente assente no solo, a outra perna (a perna de preferência) é estendida na direcção da coxa, com o calcanhar no chão e o pé flectido (aproximadamente 90º). O participante deve ser encorajado a expirar à medida que flecte para a frente, evitando movimentos bruscos, rápidos e fortes, nunca atingindo o limite da dor.

Com a perna estendida (mas não hiper-estendida), o participante flecte lentamente para a frente até à articulação da coxo-femoral (a coluna deve manter-se o mais direita possível, com a cabeça no prolongamento da coluna, portanto não flectida), deslizando as mãos (uma sobre a outra, com as pontas dos dedos sobrepostas) ao longo da perna estendida, tentando tocar os dedos dos pés. Deve tocar nos dedos dos pés durante 2s. Se o joelho da perna estendida começar a flectir, solicitar ao participante que se sente lentamente até que o joelho fique na posição estendida antes de iniciar a medição.

Prática / ensaio:

Após demonstração realizada pelo avaliador, o participante é questionado sobre a sua perna preferencial. O participante deve ensaiar duas vezes, seguindo-se a aplicação do teste.

Pontuação:

Usando uma régua de 45 cm, o avaliador regista a distância (cm) até aos dedos dos pés (resultado mínimo) ou a distância (cm) que consegue alcançar para além dos dedos dos pés (resultado máximo). O meio do dedo grande do pé, na extremidade do sapato, representa o ponto zero. Registar ambos os valores encontrados com a aproximação de 1cm, e fazer um círculo sobre o melhor resultado. O melhor resultado é usado para avaliar o desempenho. Assegure-se de que regista os sinais – ou + na folha de registo.

Atenção:

O avaliador deve ter em atenção as pessoas que apresentam problemas de equilíbrio, quando sentadas na extremidade da cadeira.

A perna preferida é definida pelo melhor resultado. É importante trabalhar os dois lados do corpo ao nível da flexibilidade, mas por questões de tempo apenas o lado hábil tem sido usado para definição de padrões.

Sentado, caminhar 2,44m e voltar e sentar

Objectivo:

Avaliar a mobilidade física – velocidade, agilidade e equilíbrio dinâmico.

Equipamento:

Cronómetro, fita métrica, cone (ou outro marcador) e cadeira com encosto (aproximadamente 43cm de altura).

Montagem:

A cadeira deve ser posicionada contra a parede ou de outra forma que garanta a posição estática durante o teste. A cadeira deve também estar numa zona desobstruída, em frente a um cone à distância de 2,44m (medição desde a ponta da cadeira até à parte interior do marcador). Deverá haver pelo menos 1,22m de distância livre à volta do cone, permitindo ao participante contornar livremente o cone.

Protocolo:

O teste é iniciado com o participante totalmente sentado na cadeira (postura erecta), mãos nas coxas, e pés totalmente assentes no solo (um pé ligeiramente avançado em relação ao outro). Ao sinal de "partida" o participante eleva-se da cadeira (pode empurrar as coxas ou a cadeira), caminha o mais rápido possível à volta do cone (por qualquer dos lados) e regressa à cadeira. O participante deve ser informado de que se trata de um teste "por tempo", sendo o objectivo caminhar o mais depressa possível (sem correr) à volta do cone e regressar à cadeira. O avaliador deve funcionar como um assistente, mantendo-se a meia distância entre a cadeira e o cone, de maneira a poder dar assistência em caso de desequilíbrio. O avaliador deve iniciar o cronómetro ao sinal de "partida" quer a pessoa tenha ou não iniciado o movimento, e pará-lo no momento exacto em que a pessoa se senta.

Prática/ensaio:

Após demonstração, o participante deve experimentar uma vez, realizando duas vezes o exercício. Deve chamar-se a atenção do participante de que o tempo é contabilizado até este estar completamente sentado na cadeira.

Pontuação:

O resultado corresponde ao tempo decorrido entre o sinal de "partida" até ao momento em que o participante está sentado na cadeira. Registam-se os dois valores até aos 0,1s. O melhor resultado é utilizado para medir o desempenho.

Alcançar atrás das costas

Objectivo:

Avaliar a flexibilidade dos membros superiores (ombro).

Equipamento:

Régua de 45cm.

Protocolo:

Na posição de pé, o participante coloca a mão dominante por cima do mesmo ombro e alcança o mais baixo possível em direcção ao meio das costas, palma da mão para baixo e dedos estendidos (o cotovelo apontado para cima). A mão do outro braço é colocada por baixo e atrás, com a palma virada para cima, tentando alcançar o mais longe possível numa tentativa de tocar (ou sobrepor) os dedos médios de ambas mãos.

Prática/ensaio:

Após demonstração por parte do avaliador, o participante é questionado sobre a sua mão de preferência. Sem mover as mãos do participante, o avaliador ajuda a orientar os dedos médios de ambas as mãos na direcção um do outro. O participante experimenta duas vezes, seguindo-se duas tentativas do teste. O participante não pode entrelaçar os dedos e puxar.

Pontuação:

A distância da sobreposição, ou a distância entre as pontas dos dedos médios é medida ao cm mais próximo. 0s resultados negativos (-) representam a distância mais curta entre os dedos médios; os resultados positivos (+) representam a medida da sobreposição dos dedos médios. Registam-se duas medidas. O “melhor” valor é usado para medir o desempenho. Certifique-se de que marca os sinais – e + na ficha de pontuação.

A mão de preferencia é definida segundo o melhor resultado encontrado. É importante trabalhar os dois lados do corpo ao nível da flexibilidade, mas por questões de economia de tempo tem sido usada apenas a “melhor” pontuação para definir a norma.

Dois minutos de *step* no próprio lugar

Objectivo:

Avaliar a resistência aeróbia (teste alternativo ao de andar seis minutos).

Equipamento:

Cronómetro, fita métrica ou pedaço de corda com 75cm e marcador.

Montagem:

A altura adequada (mínima) para o joelho do participante realizar o *step* é ao nível do ponto médio entre a rótula (ponto médio) e a crista ilíaca (topo do osso ilíaco). Este ponto pode ser determinado usando uma fita métrica, ou simplesmente esticando o bocado de corda entre a rótula e a crista ilíaca, dobrando-a depois para determinar o ponto médio. O monitor corrige a altura do joelho ao longo do teste com uma régua presa à cadeira ou à parede, marcando a altura adequada do joelho.

Protocolo:

Ao sinal de "partida" o participante inicia o *step* no mesmo lugar, realizando o maior número possível de *steps* no período de tempo estipulado. O avaliador conta o número de *steps* efectuados, servindo de apoio em caso de desequilíbrio e assegurando que o participante mantenha o joelho na altura adequada. Logo que a altura adequada do joelho não possa ser mantida, o participante é informado para parar ou apenas descansar até recuperar. O teste poderá ser retomado se ainda não tiver terminado o período de 2 minutos. Se necessário, pode ser colocada uma mão na mesa ou na parede para ajudar a manter o equilíbrio.

Prática/ensaio:

O participante deve experimentar numa ocasião anterior ao dia do teste, para que possa criar o seu ritmo. No dia do teste, o avaliador deve fazer uma demonstração do procedimento e permitir ao participante que pratique rapidamente para assegurar a compensação do protocolo. Os participantes devem ser encorajados verbalmente no sentido de obterem o desempenho máximo.

Pontuação:

A pontuação é calculada a partir do total de *steps* realizados em 2 minutos. Apenas *steps* completos deverão ser contados, isto é, cada vez que o joelho atinge a altura mínima. No sentido de disponibilizar uma assistência periódica, os sujeitos devem ser informados do tempo intermédio (1 minuto) e quando faltarem 30s.