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Is lower physical fitness associated with diminished global cognitive function in older adults with suggestive cognitive impairment? A cross-sectional study

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Is lower physical fitness associated with diminished global cognitive function in older adults with suggestive cognitive impairment?

A cross-sectional study

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Palavras-chave: AGING, FUNCTIONAL CAPACITY, MAJOR NEUROCOGNITIVE DISORDER, DEMENTIA, ELDERLY.

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Resumo

O envelhecimento afeta todos os órgãos e sistemas do corpo, comprometendo o domínio biológico, físico e social. As alterações relacionadas com o envelhecimento no sistema nervoso resultam em alterações cognitivas que podem induzir a perturbações neurocognitivas, como delírio, perturbações neurocognitivas ligeiras e perturbações neurocognitivas major. Para além da disfunção cognitiva, o envelhecimento está associado à redução da capacidade funcional e da aptidão física. Nos últimos anos, evidências tem vindo a sugerir uma associação entre a aptidão física e a função cognitiva global. **Objetivo:** Analisar a associação entre a aptidão física e a função cognitiva global em idosos, utentes de lares de idosos, com possível défice cognitivo grave. **Métodos:** Setenta e cinco idosos (76% mulheres, 78,00 ± 8,13 anos) utilizadores de lares de idosos do Porto, Portugal, foram avaliados quanto à função cognitiva global (através da versão portuguesa do *Montreal of Cognitive Assessment)* e quanto à aptidão física (através do *Senior Fitness Test* e da força de preensão manual). Foi efetuada uma regressão linear múltipla, com o método *enter*, incluindo variáveis biológicas e variáveis de aptidão física, para verificar a existência de uma associação entre a aptidão física e a função cognitiva global. **Resultados:** Não houve diferenças significativas entre os homens e mulheres para as variáveis da aptidão física e na função cognitiva global ($p>0,05$). O modelo de regressão foi estatisticamente significativo [(5.68) =5.817; $p<0.001$; $R^2=0.300$; $R^2_a=0.248$; $f^2=0.43$], e explicou ~30 % da variação da função cognitiva global. A flexibilidade dos membros superiores ($\beta=0.276$; $p=0.017$) explicou ~9.5% da variação da função cognitiva global, enquanto a força de preensão manual esquerda ($\beta=0.305$; $p=0.008$) explicou ~7.8% da mesma. **Conclusão:** A flexibilidade dos membros superiores e a força de preensão manual são fatores preditores independentes de uma melhor função cognitiva global. Estes resultados reforçam a necessidade de implementação de estratégias para melhorar/sustentar a aptidão física entre os idosos com possível défice cognitivo major.

Palavras-chave: envelhecimento, capacidade funcional, perturbação neurocognitiva major, idosos, lares de idosos.

Abstract

The aging process affects all body organs and systems resulting in a decrease in biological, physical, and social domains. Age-related changes in nervous system and brain structure leads to cognitive changes, triggering neurocognitive disorders, such as delirium, mild neurocognitive disorders, and major neurocognitive disorders. Besides cognitive dysfunction, aging is associated with the reduction in functional capacity and physical fitness. In recent years, evidence has been suggesting the association among physical fitness and global cognitive function. **Aim:** Analyze the association between physical fitness and global cognitive function among older adults, users of nursing homes, with suggestive severe cognitive impairment. **Methods:** Seventy-five older adults (76% women, 78.00 ± 8.13 years) users of nursing homes from Porto, Portugal, were assessed for global cognitive function (using the Portuguese version of the Montreal of Cognitive Assessment) and physical fitness (using Senior Fitness Test and Handgrip Dynamometer). Multiple linear regression, with enter method, including biological variables plus physical fitness variables was performed to check the association between physical fitness and global cognitive function. **Results:** Older men and women were not significant different for physical fitness variables and global cognitive function ($p>0.05$). The regression model was statistically significant [$F(5.68)=5.817$; $p<0.001$; $R^2=0.300$; $R^2_a=0.248$; $f^2=0.43$] and explained 30.0 % of global cognition function variation. Upper body flexibility ($\beta=0.276$; $p=0.017$) explained 9.5% of global cognition function variation and left handgrip strength ($\beta=0.305$; $p=0.008$), 7.8%. **Conclusion:** Upper body flexibility and handgrip strength are predictors of better global cognitive function highlighting the need to implement strategies to improve/sustain physical fitness amongst older adults with suggestive severe cognitive impairment.

Keywords: aging, functional capacity, major neurocognitive disorder, elderly, nursing homes.

List of Abbreviations

Aβ – β-amyloid

ADL – Activities of Daily Living

APP – Amyloid Percursor Protein

APO-E – Apolipoprotein E

BMI – Body Mass Index

DNA – Deoxyribonucleic Acid

DSM-5 – Diagnostic and Statistical Manual of Mental Disorders 5

IADL – Instrumental Activities of Daily Living

MCI – Mild Cognitive Impairment

MoCA – Montreal of Cognitive Assessment

WHO – World Health Organization

CHAPTER 1

GENERAL INTRODUCTION

General Introduction

Along the last decades, there has been observed an important reduction in mortality and increase in life expectancy, which result from an interplay between technology, medicine, public health, science, amongst others factors (Bárrios et al., 2020; Fillit et al., 2016).

The aging process affects all body systems (Raz & Daugherty, 2018), resulting in a reduction in biological, physical, and social domains, that together compromise functional and cognitive capacities of older people (Dziechciaż & Filip, 2014; Milanovic et al., 2013). In the literature, there is still no consensus about the theories of aging, however, studies have showed that aging results from a gradual and progressive accumulation of cell and tissue damages, that leads to adverse health outcomes related to age, such as frailty and disability (Fillit et al., 2016; Rodríguez-Mañas et al., 2012).

Aging is also characterized by many other changes such as decreased and slowed reflexes, progressive decrease and loss of vibratory sensation, progressive deterioration of visual acuity, hearing impairment by middle ear affectation and, in some cases, total hearing loss, and changes in taste and smell (Schott, 2017).

Changes in cognitive function

As the years go by, the nervous system suffers a normal process of aging (Schott, 2017), with the brain experiencing many changes in terms of metabolism and physiological mechanisms (Raz & Daugherty, 2018). These modifications lead to a brain volume reduction, dysmorphology, cellular senescence of neurons and microglia, and myelin breakdown (Bartzokis, 2004). Consequently, age-related cognitive changes are associated with deficits in autophagy, impairing protein homeostasis and organelle renewal (Glatigny et al., 2019). Not all cognitive domains are affected in the same way along aging. For instance, in normal healthy aging, memory and processing speed are downregulated, while vocabulary can be improved (Harada et al., 2013; Wisdom et al., 2012).

Most of difficulties in cognitive domains are associated with the lost in the speeding process, that is define as “the speed with which cognitive activities are performed” (Harada et al., 2013).

Changes in Cognitive Domains

Attention includes selective attention, divided attention, and working memory. Attention decreases along aging, and it results from a decrease in the capability to select, retain and manipulate relevant information during tasks performance by the older adults (Harada et al., 2013; O'Brien et al., 2013).

Memory is compound by semantic, episodic, implicit, procedural, and declarative memories. Memory is one off the most affected cognitive domains in older adults, and its reduction is probably associated with the decrease in speeding process, as mentioned above (Harada et al., 2013). The memory depends on the synaptic plasticity and age-related memory loss has come to be associated with changes in Deoxyribonucleic Acid (DNA) methylation and decrease in levels of histone acetylation in hippocampus (Dahan et al., 2020; Maity et al., 2021).

Language suffers impairments with aging, however, studies have shown some controversial results in its components. For instance, compression remains stable, vocabulary improves along lifetime, nomination only seems to be affected after 70 years and verbal fluency decreases (Harada et al., 2013; Shafto & Tyler, 2014; Verhaeghen, 2003).

Executive function is a very complex cognitive domain that includes planning, organization, cognitive flexibility, abstraction, and problem solving. Executive function declines with age and, consequently, affects the capacity of the older adults to be independent and successful in their activities of daily living (ADL) (Harada et al., 2013). Executive dysfunction is associated with neurodegenerative disease and is caused by changes in pre-frontal cortex (Lee et al., 2019; Yegla et al., 2019).

Neurocognitive Disorders

According to Diagnostic and Statistical Manual of Mental Disorders – 5 (DSM-5), neurocognitive disorders can be classified in three syndromes: delirium, mild neurocognitive impairment, and major neurocognitive disorders, such as dementia (APA, 2014).

Delirium is characterized by an atypical function in the attention domain, which cause difficulties in focusing and orienting in physical space. This disorder develops sharply throughout the day (APA, 2014).

Mild cognitive impairment (MCI) is a state between normal and major neurocognitive disorders. People with MCI have an irregular cognitive function, at least in one cognitive domain, but with no interference on their capacity to perform ADL independently (Jongsiriyanyong & Limpawattana, 2018; Sachdev et al., 2014). The MCI can be subdivided into MCI amnesic, MCI single-domain non-amnestic, MCI multiple-domain amnestic, and MCI multiple-domain non-amnestic (Jongsiriyanyong & Limpawattana, 2018).

Major neurocognitive disorder is the most severe neurocognitive disorder. It is also known as dementia. This pathology is characterized by a decrease in cognitive function and performance in at least one cognitive domain that affect and impair the performance of ADL independently (Sachdev et al., 2014). Dementia represents an enormous burden for people with this health condition and for their caregivers. According to the World Health Organization (WHO), dementia is rapidly growing worldwide (Wortmann, 2012), affecting around 50 million people around the world with the tendency to worsen with increasing ageing (WHO, 2019).

Severe neurodegenerative diseases can be subdivided into Alzheimer's disease, vascular dementia, Lewy body dementia, and frontotemporal dementia (Brown et al., 2014).

Alzheimer's disease is the most common form of dementia and may account for 60-70% of all severe neurodegenerative diseases (WHO, 2023). This subtype of dementia develops by the accumulation of β-amyloid (Aβ) peptide in senile plaques, because of proteolytic cleavage of an amyloid precursor protein (APP) on hippocampus, neocortex, and cerebrovascular and intracellular deposition of phosphorylated-tau in neurofibrillary tangles (Chen et al., 2017; Raz et al., 2016). The symptoms of Alzheimer's disease appear gradually and progressively, with the most noticeable symptom being memory loss (Eratne et al., 2018). Clinical manifestations of Alzheimer's disease differ between individuals, and are dependent on disease its severity and progression, ranging from MCI to severe impairment affecting several cognitive domains (Atri, 2019; Eratne et al., 2018).

Vascular dementia is a consequence of a cerebrovascular injury (Schneider, 2022) caused by hypoxia/ hypoperfusion, combined with metabolic dysfunction and cerebrovascular hemodynamics (Raz et al., 2016). These vascular injuries affect the hemispheric white matter leading to an axonal loss and demyelination that has a crucial role in cognitive impairment and brain atrophy (Iadecola, 2013). The development of vascular dementia through a brain injury depends on factors such as the size and location of the injury (Schneider, 2022).

Lewy body dementia develops due to the development of Lewy bodies, an intracytoplasmic neuronal inclusion, which are a result of the aging process (Schneider, 2022). These Lewy bodies are found in cortical neurons and defined by phosphorylated alpha-synuclein protein and are associated with cognitive impairment (Schneider, 2022). This type of dementia is associated with Parkinson's disease, since the presence of Lewy bodies in cortical neurons is a marker for the development of Parkinson's disease (Schneider, 2022). Its symptoms include motor changes, such as gradual loss of balance and frequent involuntary movements (which increased the risk of fall), as well as rigidity and bradykinesia (Knopman et al., 2003).

Frontotemporal dementia is associated with a severe degeneration in the frontal and temporal lobes, causing changes in behaviors and language impairments (Schneider, 2022). The most common symptoms of frontotemporal dementia are a gradual change in behavior (namely lack of empathy - derogatory language, impulsivity, apathetic behavior), lack of interest in social activities and social disinhibition (sharing of personal information and inappropriate sexual comments), and appearance of addictive behaviors (smoking, alcohol, or illicit substances) (Finger, 2016).

The diagnosis of neurocognitive disease, mild or severe, requires the collection of detailed information about the person, including a clinical history, blood tests and radiological examinations (Hatfield et al., 2009). In addition, assessments of cognitive function through simple screening tests or more complex cognitive tests are essential (Hatfield et al., 2009). One of the screening instruments used for the detection of mild or severe neurodegenerative diseases is the Montreal Cognitive Assessment – MoCA (Freitas et al., 2014). The MoCA, is a high sensitivity’s instrument, with good psychometric properties designed to detect mild neurocognitive disease and severe neurocognitive disease (Duro et al., 2010; Freitas et al., 2014). The MoCA can be organized into six cognitive domains – executive function, visuospatial capability, short-term memory, attention, concentration and working memory, language, and temporal-spatial orientation. MoCA is already validated for Portuguese population (Freitas et al., 2014).

Risk factors for neurocognitive disorders

Risk factors related to neurocognitive disorders can be divided into sociodemographic, genetic, medical, psychiatric and environmental (Hugo & Ganguli, 2014).

Age, sex (women) and low levels of education are the most important sociodemographic risk factors for major neurocognitive disorders (Hugo & Ganguli, 2014). Regarding genetic risk factors, the Apolipoprotein E – APO-E polymorphism on chromosome 19 is the best-established gene associated with higher risk to develop dementia (Campbell et al., 2013; Hugo & Ganguli, 2014). Pathologically, the diseases with a higher probability of developing cognitive decline hypertension and coronary heart disease, cardiorespiratory disease, and cardiovascular diseases – stroke and inflammatory processes (Campbell et al., 2013; Hugo & Ganguli, 2014). People who suffer from a psychiatric disease, such as depression (Kessing, 2012), anxiety (Campbell et al., 2013), post-traumatic stress have more probably to develop a neurocognitive disorder (Hugo & Ganguli, 2014).

Finally, there are evidenced showing that the exposure to air pollution and vitamin D deficiency are environmental risk factors associated with dementia onset (Killin et al., 2016).

Prevention of cognitive decline

In recent years there has been an increase in the number of people diagnosed with neurocognitive diseases (Tipton & Graff-Radford, 2018). Although the enormous scientific effort, no treatment has yet been found (Kouloutbani et al., 2019), so it is essential to prevent the onset or worsening of this pathology (Tipton & Graff-Radford, 2018). An active and healthy lifestyle (ensured through the performance of regular physical activity, healthy dietary habits, smoking absenteeism, and low alcohol consumption) represents a preventive strategy in postponing dementia onset and its aggravation (Grande et al., 2020; Tipton & Graff-Radford, 2018).

Physical inactivity and sedentariness are two of the most influence modifiable risk factor for cognitive decline (Cheng, 2016; Denkinger et al., 2012). Several authors studied the benefits of physical activity in cognitive decline prevention, and study's findings shows that physical activity improves global cognitive function, memory, and executive function (Dominguez et al., 2021; Nuzum et al., 2020).

Studies analyzing the role of physical activity in brain function highlight the neuroprotective modulator effect from regular physical activity (Cheng, 2016; Machado et al., 2017).

The WHO guidelines for physical activity and sedentary behavior recommend that older adults should perform 150 to 300 minutes of moderate-intensity aerobic physical activity or at least 75 to 150 minutes vigorous-intensity aerobic physical activity or an equivalent combination throughout the week (WHO, 2020). The WHO also recommends at least 2 days a week of muscle-strengthening activities at moderate or superior intensity, involving all major muscle groups (WHO, 2020).

A balanced nutrition profile has been also associated with a better cognitive function. Considering that cognitive impairment is linked with an increased oxidative stress and inflammatory processes (Horvat et al., 2016; Weaver et al., 2002), the consumption of antioxidant nutrients prevents the rapid progression of cognitive decline (Tipton & Graff-Radford, 2018). In addition, both MCI and severe neurocognitive disease appear to be associated with vitamin deficits, particularly vitamin C, D, and E (Tipton & Graff-Radford, 2018). The Mediterranean Diet can prevent many diseases, including neurocognitive disease (Dominguez et al., 2021; Tipton & Graff-Radford, 2018).

Changes in Physical Fitness

Besides cognitive dysfunction, strong evidence has shown that aging is associated with the reduction in functional capacity and physical fitness (Hesseberg et al., 2016; Nascimento et al., 2019). Among physical fitness attributes, those related with health are body composition, muscle strength, cardiorespiratory fitness, agility, dynamic balance, and flexibility (Hesseberg et al., 2016; Varesco et al., 2021). Physical fitness reduction later in life is mainly associated with primary aging (Varesco et al., 2021) and with the low levels of physical activity (Silva et al., 2019). The decrease in physical fitness in older adults affect the functional capacity and independence, limiting simple ADL such as dressing, standing up, taking a shower, climbing stairs, walking small distances, among others (Garatachea & Lucia, 2013; Hesseberg et al., 2016).

Older adults have a less efficient repair process (Fillit et al., 2016; Mitnitski et al., 2013) and the presence of frailty phenotypes characteristics, such as weight loss, exhaustion, weakness, slower walking speed and low physical activity leads to higher levels of deficits (Fried et al., 2001; Rockwood et al., 2007).

Changes in skeletal muscle

The physiologic age-related changes in skeletal muscle include a gradual reduction of number and size of muscle fibers, denervation and reduced reinnervation capacity (Nilwik et al., 2013). These changes lead to a decline in muscle strength and muscle power (Goodpaster et al., 2006; Lord et al., 2018). Simultaneous changes in the skeletal muscle capacity associated with risk of negative outcomes is described as sarcopenia (Dao et al., 2020).

Regarding to functionality, the loss of muscle strength and flexibility limit the performance of many ADL, such as walking outdoor and climbing stairs (Rantakokko et al., 2013). A systematic review and meta-analysis (Wang et al., 2020) showed that a low muscle mass and low muscle strength, including handgrip strength, are associated with worsening ADL and instrumental activities of daily living (IADL) and consequently more dependence.

Changes in cardiorespiratory fitness

Cardiorespiratory fitness is the ability of the cardiovascular, musculoskeletal, and pulmonary systems to supply oxygen to the muscles to sustain a physical effort (Bassett & Howley, 2000; Hoffman, 2014; Pica, 2008; Sözen, 2020). Maximal cardiorespiratory fitness decreases with aging because of many physiological and structural changes in the cardiac system (increase connective tissue, reduction of elastin content, increased blood pressure, decreased left ventricular volume and systolic volume, and decreased in maximal heart rate) (Alvis & Hughes, 2015; Jugdutt, 2014; Selman et al., 1999), pulmonary system (decreased lung volume, alveolar surface area and bronchiole diameter and, consequently, deficits in the ventilation-perfusion mechanism that leads to decreased ability to perform gas exchange) (Alvis & Hughes, 2015; Chan & Welsh, 1998; Sharma & Goodwin, 2006; Sprung et al., 2006), and musculoskeletal tissue (decreased capacity of the respiratory muscles and compliance of the chest wall, decreased muscle mass and strength, reduction in mitochondrial content and consequently in oxidative phosphorylation, among other) (Alvis & Hughes, 2015; Chan & Welsh, 1998; Curcio et al., 2020; Sharma & Goodwin, 2006; Sprung et al., 2006).

Changes in flexibility

An adequate flexibility, especially of upper body is fundamental to performed ADL (Oosterwijk et al., 2018; Pieniazek et al., 2007). According to the current literature, flexibility decreases significantly in older adults (Holland et al., 2002; Milanovic et al., 2013), which may be explained by the fact that aging affects the bones and connective tissues (Holland et al., 2002).

The decrease in flexibility leads to disability and, as consequence, difficulties in performing activities independently, including locomotion, climbing stairs, hygiene, bathing, dressing, among other (Holland et al., 2002).

Association between Physical Fitness and Cognitive Function

In recent years, there has been positive evidence among physical fitness and global cognitive function (Nascimento et al., 2019; Pérez-Sousa et al., 2021; Sampaio et al., 2020; Zhao et al., 2022).

A cross-sectional analysis (Daimiel et al., 2020) with 6874 participants showed that higher levels of physical fitness were associated with better score in all cognitive function domains, including executive function and language. Another cross-sectional study (Zhao et al., 2022) including 107 older people showed an association between upper body strength and cardiorespiratory fitness with better cognitive function. Others authors also agreed that the loss of cognitive function could be affected by low levels of physical fitness later in life (Pérez-Sousa et al., 2021). Although some researchers reported the association between physical fitness and global cognitive function amongst older adults with preserved cognitive function (Angevaren et al., 2008) and MCI (Hesseberg et al., 2016), the number of studies observing the association in people with major cognitive disorders is still lacking (Sampaio et al., 2020). In addition, it remains unclear which physical fitness components better predict global cognitive function in older adults with major cognitive disorders.

The increase in major neurocognitive disorders incidence, as well as the augmentation in institutionalization rates of the older adults in nursing homes (Bárrios et al., 2020; Nascimento et al., 2019), boosts the need to understand the association between physical fitness and global cognitive function, prompting the development of strategies to counteract the aggravation of this disease.

CHAPTER 2

IS LOWER PHYSICAL FITNESS ASSOCIATED WITH DIMINISHED GLOBAL COGNITIVE FUNCTION IN OLDER ADULTS WITH SUGGESTIVE COGNITIVE IMPAIRMENT? A CROSS-SECTIONAL STUDY

Is lower physical fitness associated with diminished global cognitive function in older adults with suggestive cognitive impairment?

A cross-sectional study

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Abstract

This study aims to analyze the association between physical fitness and global cognitive function among older adults with suggestive severe cognitive impairment who are users of nursing homes. Seventy-five older adults (76% women, 78.00 ± 8.13 years) users of nursing homes were assessed for global cognitive function using Montreal of Cognitive Assessment and physical fitness using Senior Fitness Test and handgrip dynamometer. Multiple linear regression, with enter method, including biological variables plus physical fitness variables was performed. Older men and women were not significant different for physical fitness and global cognitive function ($p>0.05$). The regression model was statistically significant [$F(5.68)=5.817$; $p<0.001$; $R^2=0.300$; $R^2_a=0.248$; $f^2=0.43$] and explained 30.0 % of global cognition function variation. Upper body flexibility ($\beta=0.276$; $p=0.017$) explained 9.5% of global cognition function variation and left handgrip strength ($\beta=0.305$; $p=0.008$), 7.8%. Upper body flexibility and handgrip strength are predictors of better global cognitive function highlighting the need to implement strategies to improve/sustain physical fitness amongst older adults with suggestive severe cognitive impairment.

Keywords: aging, functional capacity, major neurocognitive disorder, elderly.

Introduction

The aging process affects all body organs and systems (Raz & Daugherty, 2018), compromising the functional and cognitive capacities later in life (Dziechciaż & Filip, 2014; Milanovic et al., 2013). Over time, the brain undergoes numerous physiological and structural changes (Raz & Daugherty, 2018), resulting in a decrease in brain volume, dysmorphology, cellular senescence of neurons and microglia, as well as myelin breakdown (Bartzokis, 2004). People suffering major cognitive disorders, such as dementia, experience a loss of autonomy and independency in performing ADL (Davenport et al., 2012).

Besides cognitive dysfunction, strong evidence has shown that aging is associated with a reduction in functional capacity and physical fitness (Hesseberg et al., 2016). Among physical fitness attributes, those related with health include body composition, muscle strength, cardiorespiratory fitness, agility, dynamic balance, and flexibility (Hesseberg et al., 2016; Varesco et al., 2021). The decline in physical fitness later in life is primarily associated with aging (Varesco et al., 2021) and low levels of physical activity (Silva et al., 2019). The decrease in physical fitness among older adults affects their functional capacity and independence, limiting their ability to perform simple ADL such as dressing, standing up, taking a shower, climbing stairs, and walking short distances (Garatachea & Lucia, 2013; Hesseberg et al., 2016).

In recent years, there has been positive evidence linking physical fitness and global cognitive function (Pérez-Sousa et al., 2021; Sampaio et al., 2020; Zhao et al., 2022). For instance, a baseline cross-sectional analysis (Daimiel et al., 2020) performed in older adults with or without cognitive impairment demonstrated that higher levels of physical fitness are associated with better scores in all cognitive function domains, including executive function and language. Accordingly, a cross-sectional study (Zhao et al., 2022) also suggested an association between upper body strength and cardiorespiratory fitness with better cognitive function in older adults with normal cognitive function or cognitive impairment. In line with this, some results also suggests that the decline in cognitive function may be influenced by the levels of physical fitness among older adults (Pérez-Sousa et al., 2021). Others have also suggested that the association between physical fitness and global cognitive function in later life, is especially marked in older adults with preserved cognitive function (Angevaren et al., 2008) and mild cognitive decline (Hesseberg et al., 2016). Based on the available literature, one might notice that there is still few studies examining the association between physical fitness and cognitive function in individuals with major cognitive disorders (Sampaio et al., 2020). Additionally, it remains unclear which specific physical fitness attributes better predict global cognitive function, particularly among older people in Portugal. Thus, the present study aims to analyze the association between global cognitive function and physical fitness among older adults with suggestive major cognitive impairment who are users of nursing homes.

Materials and Methods

Study Design and Participants

This is a cross-sectional observational study comprising an intentional and non-probabilistic sample selected by the convenience sampling method (Marôco, 2018).

Participants were recruited from four nursing homes located in the north region of Portugal. Inclusion criteria were age ≥ 65 years old, being daily users of nursing homes and capacity of walking autonomously without any kind of assistive device or human assistance. Exclusion criteria were preserved cognitive function (Montreal of Cognitive Assessment – MoCA ≥22 points) or mild cognitive impairment (MoCA≥17 points). Study protocol was approved by the ethics board of the Faculty of Sports, university of Porto (24th March 2018; Number: CEFADE 02.2018).

Procedures

Four nursing homes (Sousela, Rebordosa, Carvalhosa, and Paranhos) were conveniently selected and contacted to integrate this study. All of them accept to receive the research team for an initial visit. In this visit, the research project and study aims were presented, as well as the potential risks associated with measurements. After obtaining the legal representative consent of each institution, researchers contact the social workers of each institution to get potential participants. In nursing homes, social workers are responsible for providing authorizations for older adults to participate in activities, and thus, they sign a formal consent. In addition, all potential participants also sign the formal consent regardless their cognitive status. All procedures were conducted in accordance with Helsinki Declaration.

Sample size was calculated a *priori* with G*Power version 3.1. The chosen parameters were family t-tests, multiple linear regression analysis, two tails, medium effect size of 0.2, alpha error probability of 0.05, power of 0.95, and 8 potential predictors. The needed sample size was 68 participants.

Measurements

Participants were assessed in one single appointment and the evaluation process took about 1 hour. Before the contact with the participants, sociodemographic data and clinical information were provided by the social workers. Subsequently, each participant was assessed for anthropometric, physical fitness, and cognitive function, following the above-cited order.

Sociodemographic and Clinical Information

Sociodemographic (sex, age, marital status, and years of education) and clinical information (presence of hypertension, diabetes and/ or dyslipidemia, and medication) were obtained through a questionnaire applied in form of interview to the social workers, who provide answers based on participants´ clinical registries.

Anthropometrics

Body weight (kg) was measured using a calibrated scale (Tanita, Innerscan BF-522W, Japan). Height (cm) was measured using a calibrated stadiometer (SECA 213, Hamburg, Germany). Body mass index (BMI) was calculated as the weight (kg) divided by the squared height (m^2), and classified according to Lipschitz, as underweight (BMI < 22 kg/m^2), normal weight (BMI ≥ 22kg/m2 and < 27kg/m^2), and overweight (BMI ≥ 27 kg/m^2) (Lipschitz, 1994).

Physical Fitness

Physical fitness was measured by the Senior Fitness Test (Rikli & Jones, 2013) and handgrip strength (Therapists, 1992). The Senior Fitness Test includes tests for lower body strength (30-sec seat and stand test), upper body strength (30-sec elbow flexion), cardiorespiratory fitness (6-min walking test), lower body flexibility (chair sit and reach test), upper body flexibility (back scratch test) and agility and dynamic balance (8-ft up-and-go test) (Rikli & Jones, 2013). In brief, lower body strength was measured using a 43-cm chair. Participants were asked to do the maximum possible chair raises in 30-sec, with arms folded across the chest. Upper body strength was measured using a 2.27 kg and 3.36 kg dumbbells for the women and men, respectively. In this test, older adults were asked to execute the maximum of elbows flexions in 30-sec time. Cardiorespiratory fitness was measured with a 6 min walking test. Participants were asked to walk the longer distance in a 15 m. Lower body flexibility was measured using a 50 cm ruler and the participants were asked to extend one leg and slowly bend toward the foot, keeping the spine erect, and then was measured the distance between the foot and the hand. Upper body flexibility was also measured using a 50 cm ruler and the participants were asked to place one hand on their shoulder and the other hand behind their back and try to touch both hands, then the distance between the right and left hand was measured. To evaluated agility and dynamic balance, the participants were asked to stand up from a 43 cm chair, walk 2.44 m and return to the seat position, as fast as possible.

Handgrip strength was measured with Jamar Hydraulic Hand Dynamometer (Duluth, Minnesota, USA). Participants were sitting on a comfortable chair, with elbow flexed at 90° and arm in neutral position. It was asked to participants to hold the dynamometer and squeeze it as hard as possible. Three measurements, on both hands, were taken with 1 minute rest between each, and with alternating hands to prevent muscle fatigue (Pitcher & Miles, 1997; Therapists, 1992). Different measures of handgrip strength were considered in the analysis. First, the mean value calculated for each hand (mean of left and right hand). Second, handgrip asymmetry, that was calculated by dividing the strongest handgrip score (kg) by the strongest handgrip score of the other hand (kg) (McGrath et al., 2022). Based in the difference between upper body sides handgrip strength asymmetry, participants were categorized in groups as 0.0-10.0%, 10.1-20.1%, 20.1-30.0% or >30.0% (McGrath et al., 2021).

Cognitive Function

The MoCA was used to evaluate the cognitive function among older adults and its evaluation took around 15 minutes. MoCA was designed to detect lower cognitive function and major cognitive disorders, and results range from 0 to 30. A score lower than 17 points indicates possible major cognitive disorder, results between 17 and 21 points are suggestive of MCI, while 22 points or higher indicates a preserved cognitive function (Freitas et al., 2014). MoCA has a high sensitivity with good psychometric properties (Freitas et al., 2014).

Statistical Analysis

Data was analyzed with the IBM SPSS Statistics software, version 28 (IBM, Chicago, IL, United States) and the significance level was set at 0.05 (Marôco, 2018). Data normality was evaluated according to Kolmogorov-Smirnov (Marôco, 2018). For variables with normal distribution, descriptive statistics are as mean and standard deviation (SD). For those variables not normally distributed, descriptive statistics is presented as medians and interquartile range (IQR). Nominal and ordinal qualitative variables were analyzed by absolute (n) and relative frequency (%) (Marôco, 2018). Between groups comparisons were performed with Mann-Whitney test (for continuous variables), and chi-square test (for categorical variables). Comparison of handgrip strength between hands were performed with Wilcoxon Signed Ranks Test. Partial correlation, adjusted for sex, age and BMI, was used to analyze the relationship between physical fitness and global cognitive function to find the fitness physical variables that may be candidates as independent predictors of cognitive function. Subsequently, multiple linear regression, with stepwise method, was performed to find physical fitness variables with significant correlation that are potentially independent predictors of global cognitive function. After that, it was executed the first model of a multiple linear regression, with enter method, including sex, age, and BMI. These variables present biological plausibility to predict cognitive function. The second model of multiple linear regression, with enter method, included the biological variables from the first model plus physical fitness variables that presented a significant correlation with global cognitive function. All assumptions in all multiple linear regressions were checked. Multicollinearity was verified through VIF (1.020), homoscedasticity, normality of the data, and linear relationship between the dependent and independent variable, residue analysis was made by Durbin-Watson (Marôco, 2018).

The magnitude of the relationship was observed with the effect size checked as $f^2 = \frac{R^2}{1-R^2}$, and considerate as small (0.02-0.14), moderate (0.15-0.34), and large (>0.35) (Cohen, 1988).

Results

One hundred and twenty-eight older adults were invited to participate in the study. From those, 8 declined to participate, 4 didn´t met inclusion criteria and 41 met exclusion criteria. Thus, the final sample was constituted by 75 older adults (78% female, 78 ±8,13 years) from Sousela (n=20), Rebordosa (n=22), Carvalhosa (n=10), and Paranhos (n=23). The study flowchart is in Figure 1.

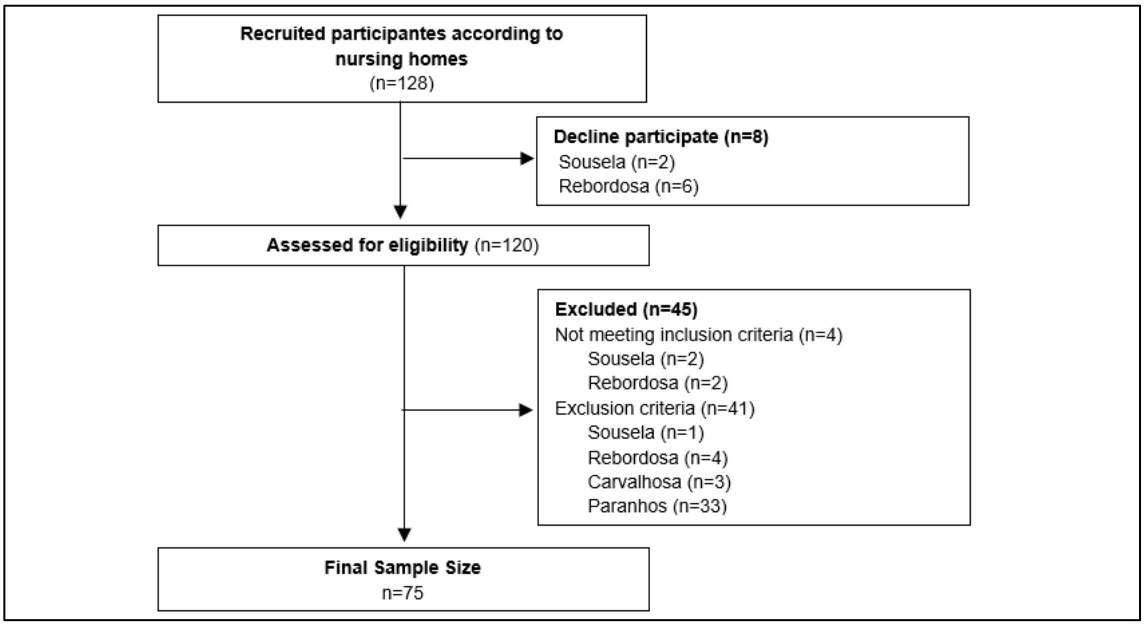

Figure 1|Study Flowchart

Table 1 shows descriptive statistics and between sex comparisons for sociodemographic, clinical information, anthropometrics, physical fitness, and cognitive function parameters. The age range was between 65 to 98 years old. The prevalence of hypertension and diabetes were 46.7%, and 37.3%, respectively. Regarding BMI classification, 61.3% were overweight. Men and women were not different for sociodemographic, clinical conditions, physical fitness parameters, and cognitive function (p>0.05).

Table 1 | Overall and between sexes comparisons for sociodemographic, clinical information, anthropometrics, physical fitness, handgrip strength asymmetry and cognitive function.

Variables	**Overall (*N*: 75)**	**Male (*N*: 18)**	**Female (*N*: 57)**	**Statistical inference**
Sociodemographic				
Age, years	78.00 [72.00-84.00]	80.50 [71.25-84.25]	78.00 [72.00-84.00]	U = 504.50, *p* = 0.916
Clinical conditions				
Hypertension (%)	46.7	33.3	50.9	X^2(1) = 1.69; *p* = 0.193
Dyslipidemia (%)	26.7	27.8	26.3	X^2(1) = 0.02; *p* = 0.903
Diabetes (%)	37.3	33,3	38.6	X^2(1) = 0.16; *p* = 0.687
Anthropometrics				
Weight	68.00 [61.00-75.00]	74.50 [68.00-80.50]	66.00 [58.45-74.00]	U = 272.50, *p* = 0.003
Height	1.53 [1.49-1.60]	1.65 [1.59-1.69]	1.50 [1.48-1.55]	U = 136.50, *p* < 0,001
BMI, kg/m²	28.45 [26.12-31.96]	27.49 [25.20-30.22]	28.65 [26.41-32.32]	U = 437.00; *p* = 0.399
Underweight (%)	5.30	0.00	7.00	
Normal weight (%)	33.30	44.40	29.80	X^2(2) = 2.27; *p* = 0.322
Overweight (%)	61.30	55.60	63.20	
Physical Fitness				
Lower body strength, repetitions	9.00 [7.00-13.00]	8.50 [6.00-11.25]	9.00 [7.00-13.00]	U = 431.00, *p* =0.307
Upper body strength, repetitions	10.00 [7.00-14.00]	8.50 [7.00.11.25]	11.00 [6.00-15.00]	U = 442.00, *p* = 0.377
Cardiorespiratory fitness, seconds	240.00 [142.00-327.00]	207.50 [134.50-308.75]	240.00 [145.50-330.10]	U = 466.50, *p* = 0.564
Lower body flexibility, cm	0.00 [-10.00-0.00]	0.00 [-15.75-0.00]	0.00 [-10.00-0.00]	U = 493.50, *p* = 0.804
Upper body flexibility, cm	-31.00 [-40.00- -18.00]	-37.50 [-45.75- -27.50]	-26.00 [-40.00- -17.50]	U = 369.00, *p* = 0.074
Agility/ dynamic balance, seconds	7.60 [5.53-12.53]	8.11 [6.42-11.92]	7.35 [5.48-13.22]	U = 490.50, *p* = 0.780
Handgrip – right hand	13.90 [9.60-17.73]	17.50 [11.30-21.84]	12.67 [9.30-16.30]	U = 356.00, *p* = 0.052
Handgrip – left hand	12.80 [8.80-16.87]	16.09 [7.88-27.47]	12.33 [8.86-16.30]	U = 391.50, *p* = 0.132
HGS Asymmetry 10.1%-20.0% (%)	33.30	38.90	31.60	
HGS Asymmetry 20.1%-30.0% (%)	28.00	27.80	28.10	X^2(2) = 0.394; *p* = 0.821
HGS Asymmetry >30.0% (%)	38.70	33.30	40.40	
MoCA				
Global cognitive function, score	10.00 [6.00-14.00]	11.00 [6.75-14.25]	9.00 [5.50-14.50]	U = 460.50, *p* =0.513

Notes. Values are mean ± SD (continuous variables), median [interquartile range], or percentage (categorical variables). BMI, body mass index; χ 2 , Chi square test; U, Mann–Whitney U test. Senior fitness test, Senior Fitness Test. MoCA, Montreal of Cognitive Assessment. Cm, centimeters.

Results from the partial correlation, adjusted for sex, age and BMI, showed that lower (*r*=0.340; *p*=0.004) and upper body strength (*r*=0.245; *p*=0.039), cardiorespiratory fitness (*r*=0.305; *p*=0.010), upper body flexibility (*r*=0.329; *p*=0.005), handgrip strength of the right (*r*=0.303; *p*=0.010) and left sides (*r*=0.356; *p*=0.002) and handgrip strength asymmetry (*r*=-0.245; *p*=0.040) were associated with global cognitive function. Thus, they were candidates as independent predictors of global cognitive function. On the contrary, lower body flexibility (*r*=0.138; *p*=0.253) and agility and dynamic balance (*r*=-0.081; *p*=0.504) were not associated with global cognitive function. .

Table 2 shows the two multivariate models. In the first model, age was statistically significant (β=-0.316; t=-2.828; *p*=0.006; f^2=0.15). The other biological variables included in the model were not statistically significant [sex (β=-0.117; t=-1.041; *p*=0.302); BMI (β=0.125; t=1.115; *p*=0.269)]. The second model was statistically significant [F(5.68)=5.817; p<0.001; R^2=0.300; R^2_a=0.248; f^2=0.43] and explained 30.0 % of global cognitive function variation. In the second model, the physical fitness variables that were independent predictors were upper body flexibility (β=0.276; t=2.446; *p*=0.017) and left handgrip strength (β=0.305; t=2.753; *p*=0.008). No other physical fitness component reached a significant level (*p*>0.05). Upper body flexibility explained 9.5% of the global cognitive function variation while left handgrip strength, 7.8%.

Table 2 | Multivariate relationship between physical fitness and global cognitive function.

Parameters	**R^2 increment %**	**Beta**	***p*-value**
Model 1 (R^2: 0.127)			
Sex	0.90	- 0.117	0.302
Age, years	9.20	-0.316	0.006
BMI, kg/m^2	2.60	0.125	0.269
Model 2 (R^2: 0.300)			
Sex	0.90	- 0.075	0.506
Age, years	9.20	- 0.181	0.101
BMI, kg/m^2	2.60	0.132	0.202
Upper Body flexibility – Back Scratch Test	9.50	0.276	0.017
Handgrip – left hand	7.80	0.305	0.008

Beta: standardized coefficients

Discussion

This study analyzed the association between physical fitness and global cognitive function among older adults with suggestive major cognitive impairment who are users of nursing homes. The multiple linear regression had a large effect size and explained 30% of global cognitive function variation. In the final model, upper body flexibility and left-hand grip strength were independent predictors of global cognitive function, explaining, respectively, 9.5% and 7.8% of global cognitive function variation.

Amongst the variables with biological plausibility, age was the only one that reach the significant level and explained 9.2% of the variation of global cognitive function. This is line with previous studies that pointed out age as the most important risk factor for major cognitive disorder (Hugo & Ganguli, 2014). For example, in a systematic review and meta-analysis (Cao et al., 2020) that analyzed the prevalence of major cognitive disorder in different geographics regions, showed that major cognitive disorder risk augments linearly as the age decades augments. Although sex and BMI didn’t reach a significantly level, we kept both in our models considering what scientific evidence highlights about their effect on cognition (Laitala et al., 2011; Li & Singh, 2014). Regarding sex, the actual literature shows that the prevalence of major neurocognitive disorder is higher among women (Hugo & Ganguli, 2014). In addition, the biological plausibility of obesity as a risk factor for major cognitive disorder is also well known because of its relationship with cardiometabolic conditions, such as hypertension, diabetes and cardiovascular diseases (Riaz et al., 2018) that lead to brain damages along time (Pasqualetti et al., 2022; Pugazhenthi et al., 2017).

In our study, upper body flexibility was a predictor of global cognitive function, explaining 9.5% of its variation. According to our knowledge, only few studies have analyzed the association between flexibility and cognitive function, and the available scientific evidence is not consensual in regards the association between flexibility and cognitive function (Hesseberg et al., 2016; Sampaio et al., 2020). In line with our results, Sampaio, et al (2020) found a significant association between upper body flexibility and global cognitive function in older adults from four Portuguese nursing homes (Sampaio et al., 2020). In this study, researchers included 102 older adults diagnosed with a major neurocognitive disorder and flexibility was assessed as we did. Nonetheless, Sampaio and colleagues did not show how much upper body flexibility explained global cognitive function. Contrary to our results, the study from Hesseberg et al (2016) also performed a multiple linear regression model aiming to observe the association between cognitive function and physical fitness components, and the association between upper body flexibility and cognitive function were not significant (Hesseberg et al., 2016). The relationship between upper body flexibility and cognitive function may be, albeit partially, explained considering that upper body flexibility is crucial to perform many ADL independently, including activities like dressing, hygiene, and bathing (Holland et al., 2002; Stathokostas et al., 2013). In addition, the scientific evidence is not yet consensual with regard to the consequences of low level of upper body flexibility in others health-related outcomes (Stathokostas & Vandervoort, 2016). One novelty of our study is that we report how much of global cognitive function is explained by upper body flexibility, and between studies comparability is not possible once others did not show this variation. Nonetheless, it is important to observe that upper body flexibility explained more global cognitive function than age (9.7% versus 9.5%, respectively), highlighting the huge importance that upper body flexibility might exert in cognitive function. This must be ascertained in longitudinal studies.

Left handgrip strength was also an independent predictor of global cognitive function, and it explained 7.8% of global cognitive function variation. Previous studies have also showed a strong association between handgrip strength and cognitive function in older adults with preserved cognitive function (Chou et al., 2019), and mild or major cognitive disorder (Shaughnessy et al., 2020). The above-mentioned studies show different handgrip strength parameters, however, they only used the value from one hand (the strongest or the dominant side), instead using values from both hands as we did. In our study, we tested right and left sides and handgrip asymmetry, but only the left handgrip strength was an independent predictor. We cannot find a reason for this.

The loss of muscle strength tendentially occurs along aging (Zammit et al., 2019) leading to a decrease in functional capacity (Evans & Campbell, 1993) and cognitive function (Clouston et al., 2013). According to some authors, muscle strength is an indicator of integrity of central nervous system (Anstey, 1999) and handgrip strength is also an indicator of vitality (MacDonald et al., 2004).

Recently, the association between handgrip strength and neurocognitive brain health was examined through a cohort study of 190 406 adults in the United Kingdom (Duchowny et al., 2022). In this study, results showed that handgrip strength was associated with markers of cognitive aging (odds of major cognitive disorders development and reduction in cognition functions, such as fluid intelligence, prospective memory).

Contrary to our expectations, we did not find significant associations between lower body strength, cardiorespiratory fitness, and agility and dynamic balance with global cognitive function. Differently from our results, other researchers found a significant association between global cognitive function and cardiorespiratory profile (Farnsworth Von Cederwald et al., 2022), body strength (Hesseberg et al., 2020; Sobol et al., 2016) and agility (Sampaio et al., 2020). In our study, the lack of a significant association might be a consequence of our small sample size. Therefore, it is suggested future studies with larger samples from different geographical regions from Portugal aiming to characterize the Portuguese population in a more generalized way.

This study has strengths that must be mentioned. Several authors suggested the need to study the association between physical fitness components with cognitive function in older adults, and in the current literature there is a scarcity of studies in Portuguese older adults' users of nursing homes. Another strength is the utilization of validated instruments for Portuguese older adults. In addition, our study reported the percentage improvement that each variable contributes to the model. Lastly, our study analyzed and reported the effect size of the regression model considered for this study.

However, this study also had some limitations. This is an observational, cross-sectional study, it hinders the establishment of causal inferences and suggests associations only. The sample size was small and potentially non-representative from the population. Third, we did not control our analysis from daily physical activity levels, that represents an important determinant of physical fitness. Finally, we did not measure difficulty that older adults had to perform ADL or IADL.

Our results add evidence of the positive association between some components of physical fitness and global cognitive function in people with suggestive major neurocognitive disease. The clinical implication is regarding the components of physical fitness that can predict global cognitive function. That said, this study highlights the need to improve muscle strength and flexibility through the implementation of physical exercise programs in nursing homes which attend older adults with major cognitive disorder. These exercise programs can potentially counteract the disease progression and preserve physical independency.

Conclusion

The study findings indicate a significantly association between physical fitness and global cognitive function, highlighting the need to implement strategies to improve/sustain physical fitness amongst older adults with suggestive major cognitive impairment.

In a more general scope, this study alerts to a need to improve physical fitness and functional capacity in older adults' users of nursing homes, as a possible strategy to preserve their independence and global cognitive function.

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CHAPTER 3

GENERAL DISCUSSSION

General Discussion

This study examined the association between global cognitive function and physical fitness components in older adults with suggestive major neurocognitive disorder who are users of nursing homes.

Previously studies showed the positive associations between higher values of body strength (Hesseberg et al., 2020; Sobol et al., 2016), cardiorespiratory fitness (Farnsworth Von Cederwald et al., 2022), agility and dynamic balance agility (Sampaio et al., 2020) and upper body flexibility (Sampaio et al., 2020) with global cognitive function in people with and without neurocognitive disorders.

Contrary to our expectations, our cross-sectional observational study did not find significant associations between body strength, cardiorespiratory fitness, and agility and dynamic balance with global cognitive function in older adults with suggestive major cognitive disorders. Conversely, we demonstrated that upper body flexibility (measured by the specific tests from the Senior Fitness Test battery) and left-hand grip strength (measured by handgrip dynamometer) were independent predictors of global cognitive function by MoCA scores, explaining, respectively, 9.5% and 7.8% of global cognitive function variation.

Regards upper body flexibility, the evidence is still not consensual, with some authors corroborating with our results (Sampaio et al., 2020), while others failing in showing the association between the two variables (Hesseberg et al., 2016). Upper body flexibility is affected and affects independence in performing ADL (Holland et al., 2002; Stathokostas et al., 2013), and the lack of independence is associated with the major neurocognitive disorders (Stineman et al., 2012).

Besides upper body flexibility, this study also presents a significantly association between left handgrip strength and global cognitive function. These results go according to the actual evidence (Chou et al., 2019; Shaughnessy et al., 2020). Surprisingly, the right handgrip strength was not significantly associated with global cognitive function, and we cannot find a reason for that. This relationship between handgrip strength and global cognitive function can be explained by the fact that handgrip strength is considered by some authors an indicator of vitality (MacDonald et al., 2004).

One strength of our study is the characteristics of our sample. Indeed, it is difficult to get access to these kind of participants, besides the aging population (Bárrios et al., 2020), the increase in age-related dementia (Wortmann, 2012), and the significant influx of elderly people in nursing homes. Another study strength is the utilization of the Portuguese version of MoCA, considering that is an instrument with high sensitivity with good psychometric properties and adapted for Portuguese people (Freitas et al., 2014). In addition, it is also important to note that in our study we carried out a detailed statistical analysis, presenting important results, such as the effect size of the regression model used, as well as the percentage with which each biological and physical fitness variable predicts global cognitive function.

It is also worth noting that this study also has limitations. First, considering that this is an observational cross-sectional study, it can only suggest association between those variables, whereas in a longitudinal study it is possible to establish causal inferences that justify these associations. Another limitation is the small size, as well as the fact that the nursing homes are located very close to each other and consequently do not represent the general elderly population in Portugal. Finally, we did not control our analysis based on levels of daily physical activity, nor did we measure the difficulty the sample had in carrying out ADL.

This is an important study in the sense that provides important clinical implications about the need to maintain and improve the physical fitness components, such as upper body flexibility and handgrip strength of older adults with suggestive major neurocognitive disorder.

To better understand the associations between physical fitness and cognitive function, as well as the causal relationships between both variables, it is suggested that future longitudinal studies must be carried out with a high sample size and covering different geographic areas. Furthermore, it would be equally interesting to carry out future investigations aiming to observe the associations between physical fitness and each one of the cognitive domains.

CHAPTER 4

CONCLUSION

Conclusion

The present study aims to analyze the association between global cognitive function and physical fitness among older adults who are users of nursing homes, with suggestive major cognitive impairment.

The finding of this study indicates that upper body flexibility and handgrip strength are predictors of better global cognitive function.

More generally, this study highlighting the need to implement strategies to improve/sustain physical fitness amongst older adults with suggestive severe cognitive impairment who are user of nursing homes.

CHAPTER 5

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Annexes

Annex I: Declaration of Helsinki

VAM Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the: 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General Assembly, Venice, Italy, October 198; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996; 52nd WMA General Assembly, Edinburgh, Scotland, October 2000; 53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added); 55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added); 59th WMA General Assembly, Seoul, Republic of Korea, October 2008; 64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WM encourages others who are involved in medical research involving human subjects to adopt this principle.

General principle

3. The Declaration of Geneva of the WMA binds the physician with the words, “The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that “A physician shall act in the patient’s best interest when providing medical care.”
4. It is the duty of the physician to promote and safeguard the health, well-being, and rights of patients, including those who are involved in medical research.

The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include studies involving human subjects.
6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures, and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, their safety, effectiveness, efficiency, accessibility, and quality.
7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.
8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.
9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and con identicality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.
10. Physicians must consider the ethical, legal, and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal, or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.
11. Medical research should be conducted in a manner that minimizes possible harm to the environment.
12. Medical research involving human subjects must be conducted only by individuals with the appropriate.
13. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientist education, training, and qualifications. Research on patients or healthy volunteers requires the

supervision of a competent and appropriately qualified physician or other health care professional.

14. Groups that are underrepresented in medical research should be provided appropriate access to participation in research. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.
15. Appropriate compensation and treatment for subjects who are harmed because of participating in research must be ensured.

Risks, Burdens and Benefits

16. In medical practice and in medical research, most interventions involve risks and burdens.

    Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.
17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

    Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed, and documented by the researcher.
18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

Vulnerable Groups and Individuals

19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection.

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

Scientific Requirements and Research Protocols

21. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.
22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

    The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

    In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

Research Ethics Committees

23. The research protocol must be submitted for consideration, comment, guidance, and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards, but these must not

be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

Privacy and Confidentiality

24. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

Informed Consent

25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.
26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

    After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

27. When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.
28. For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.
29. When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject’s dissent should be respected.
30. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.
31. The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the

patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

Use of Placebo

33. The benefits, risks, burdens, and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

    Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

    Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

    and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

    Extreme care must be taken to avoid abuse of this option.

Post-Trial Provisions

34. In advance of a clinical trial, sponsors, researchers, and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

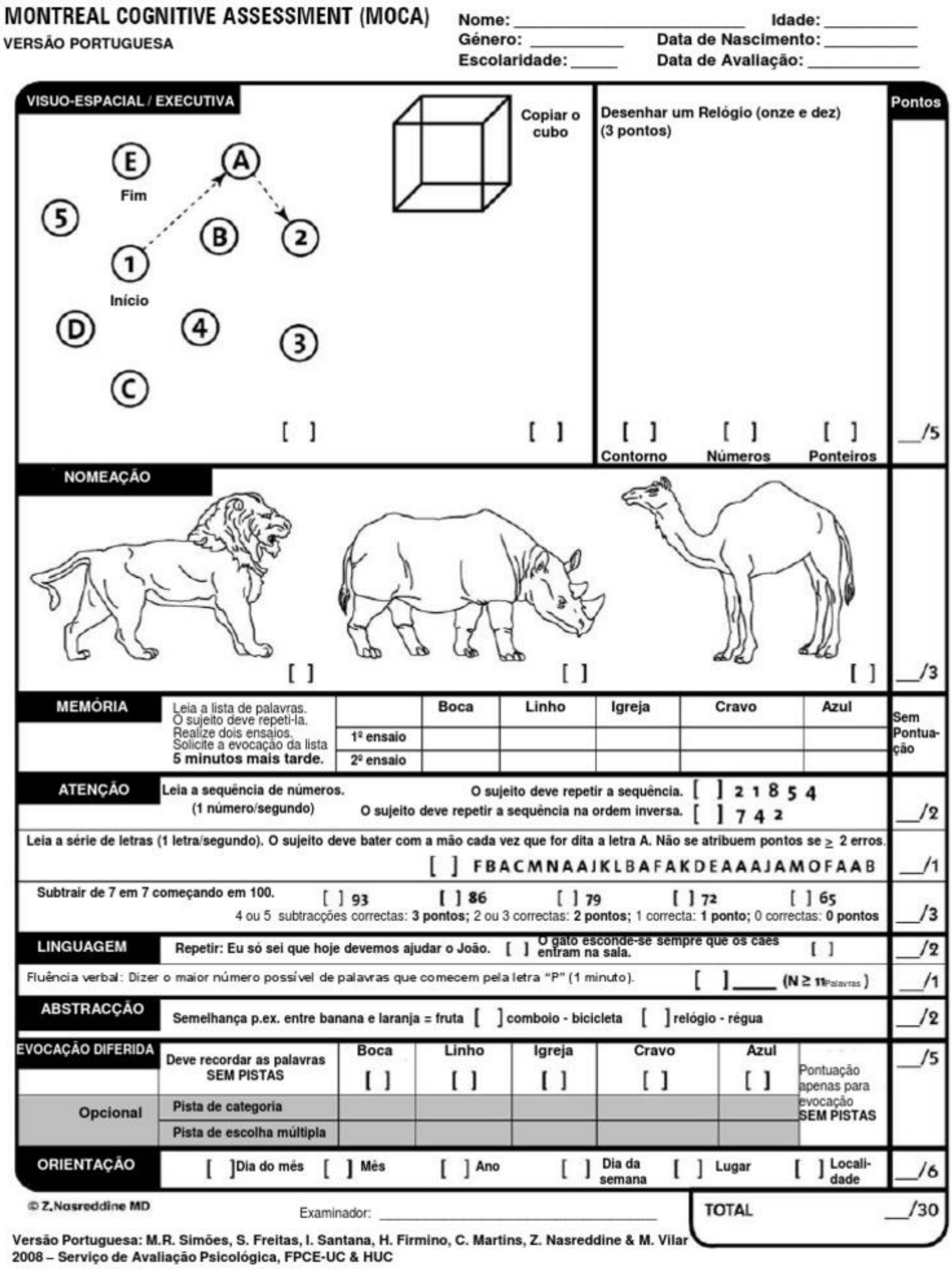
Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.
36. Researchers, authors, sponsors, editors, and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

Unproven Interventions in Clinical Practice

37. In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician’s judgement it offers hope of saving life, re-establishing health, or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.

Annex II: Montreal Cognitive Assessment (MoCA)



MONTREAL COGNITIVE ASSESSMENT (MOCA)
VERSÃO PORTUGUESA

Nome: ______________________ **Idade:** __________
Género: __________ **Data de Nascimento:** __________
Escolaridade: _____ **Data de Avaliação:** ____________

Pontos

VISUO-ESPACIAL / EXECUTIVA

[ ]

Copiar o cubo [ ]

Desenhar um Relógio (onze e dez) (3 pontos)

[ ] Contorno [ ] Números [ ] Ponteiros ___/5

NOMEAÇÃO

[ ] [ ] [ ] ___/3

MEMÓRIA

Leia a lista de palavras. O sujeito deve repeti-la. Realize dois ensaios. Solicite a evocação da lista **5 minutos mais tarde.**

	Boca	Linho	Igreja	Cravo	Azul
1º ensaio					
2º ensaio					

Sem Pontuação

ATENÇÃO Leia a sequência de números. (1 número/segundo)

O sujeito deve repetir a sequência. [ ] 2 1 8 5 4
O sujeito deve repetir a sequência na ordem inversa. [ ] 7 4 2 ___/2

Leia a série de letras (1 letra/segundo). O sujeito deve bater com a mão cada vez que for dita a letra A. Não se atribuem pontos se ≥ 2 erros.

[ ] FBACMNAAJKLBAFAKDEAAAJAMOFAAB ___/1

Subtrair de 7 em 7 começando em 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 ou 5 subtracções correctas: **3 pontos;** 2 ou 3 correctas: **2 pontos;** 1 correcta: **1 ponto;** 0 correctas: **0 pontos** ___/3

LINGUAGEM Repetir: Eu só sei que hoje devemos ajudar o João. [ ] O gato esconde-se sempre que os cães entram na sala. [ ] ___/2

Fluência verbal: Dizer o maior número possível de palavras que comecem pela letra "P" (1 minuto). [ ]____ (N ≥ 11 Palavras) ___/1

ABSTRACÇÃO Semelhança p.ex. entre banana e laranja = fruta [ ] comboio - bicicleta [ ] relógio - régua ___/2

EVOCAÇÃO DIFERIDA

		Boca	Linho	Igreja	Cravo	Azul	
	Deve recordar as palavras SEM PISTAS	[ ]	[ ]	[ ]	[ ]	[ ]	Pontuação apenas para evocação SEM PISTAS
Opcional	Pista de categoria						
	Pista de escolha múltipla						

___/5

ORIENTAÇÃO [ ] Dia do mês [ ] Mês [ ] Ano [ ] Dia da semana [ ] Lugar [ ] Localidade ___/6

© Z.Nasreddine MD

Examinador: ______________________

TOTAL ___/30

Versão Portuguesa: M.R. Simões, S. Freitas, I. Santana, H. Firmino, C. Martins, Z. Nasreddine & M. Vilar
2008 – Serviço de Avaliação Psicológica, FPCE-UC & HUC

Appendixes

Appendix I: Declaração do Consentimento Informado

Caro senhor(a),

No âmbito do 2º ciclo de Atividade Física, Exercício e Saúde, no ramo de Atividade Física e Exercício para a Terceira Idade, a realizar na Faculdade de Desporto da Universidade do Porto, estou a realizar um estudo dos níveis de atividade física, aptidão física e saúde em idosos de Centros de Dia, cujo objetivo principal é identificar a influência da atividade física e aptidão física nas competências cognitivas, socio-emocionais e higiene do sono. Durante todo o estudo será garantido o anonimato e a confidencialidade de todos os dados recolhidos, assim como a sua utilização apenas para meios de investigação.

Deste modo, os dados serão recolhidos a partir dos seguintes métodos:

- Questionário Sociodemográficos e informações clínicas
- Avaliação da Aptidão Física e Medidas Antropométricas
- Avaliação da Função Cognitiva

Eu, abaixo-assinado, ____ (nome completo), compreendi a informação que me foi fornecida, por escrito e verbalmente, sobre o estudo dos níveis de atividade física, aptidão física e saúde em pessoas na terceira idade, conduzida pela Faculdade de Desporto, da Universidade do Porto e pela qual é pedida a minha participação. Sei que poderei desistir do estudo a qualquer momento, sem ter de dar justificações e sem que isso me possa trazer quaisquer consequências.

Nestas circunstâncias,

☐ Aceito livremente participar, fornecendo dados listados abaixo para as finalidades de investigação científica no âmbito deste estudo, tal como me foi apresentado pela investigadora responsável.

- Questionário Sociodemográfico e informações clínicas
- Avaliação da Aptidão Física e Medidas Antropométricas
- Avaliação da Função Cognitiva

(Se não consentir a recolhas de dados de uma ou mais categorias, por favor risque a categoria)

Data ___ / ___ / ______

Participante:

____

Assistente Social:

____

Appendix II: Declaração da instituição

U.PORTO
FACULDADE DE DESPORTO
UNIVERSIDADE DO PORTO

== Declaração ==

Declaro para os devidos efeitos que o estudo dos níveis de atividade física, aptidão física e saúde em idosos de Centros de Dia resulta de uma colaboração entre a Faculdade de Desporto da Universidade do Porto e da presente instituição e que ambas as partes se responsabilizam por assegurar e disponibilizar os meios necessários para permitir a realização do estudo.

Esta instituição assegurará a avaliação dos critérios de elegibilidade para a participação no estudo dos idosos selecionados.

Diretor(a) da Instituição

Appendix III: Questionário Sociodemográfico

Questionário Sociodemográfico

Nome: ____

Idade: ___________ Sexo: ____________ Data: _______________

Nacionalidade: _____________________________

Localidade: ________________________________

Instituição: ____

Estado Civil: Casado/a ___ Solteiro/a ___ União de Facto ___ Viúvo/a ___ Divorciado/a ___

Nº de filhos: _____

Habilitações Literárias: ____

Principal profissão desempenhada na vida: ____

Vive na própria casa? Sim ____ Não ____

Se não, onde vive? ____

Vive acompanhado? Sim ____ Não ____

Se sim, com quem? ____

Tem alguma doença: Sim ____ Não ____

Se sim, qual: ____

Toma alguma medicação: Sim ____ Não ____

Se sim, qual: ____

Teve alguma queda: Sim ____ Não ____

Se sim, quando? ____