PHYSICAL ACTIVITY AND COGNITIVE PERFORMANCE IN CANCER SURVIVORS - A CROSS-SECTIONAL STUDY

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Abstract

Cancer survivorship poses challenges beyond remission, with cancer-related cognitive impairment (CRCI) often affecting memory, attention, and executive function, impacting daily functioning and quality of life. Physical activity (PA) has shown positive effects on cognitive performance, with studies reporting improvements in cognitive function after high-intensity exercise and enhanced memory recall following moderate exercise. However, evidence regarding PA's effects in cognition on cancer survivors remains mixed, possibly due to the reliance on self-report cognitive questionnaires and the limited number of studies examining the influence of factors like depression and cognitive reserve (CR) on PA in this population. Therefore, this study aims to explore the relationship between regular ongoing physical activity and cognitive performance, and how it influences cognitive reserve and depression in cancer survivors.

The sample of this study comprised 154 breast and lung cancer survivors. PA was self-reported and categorized by PA intensity levels. CR was measured with the TeLPI and the CRIq. Cognitive domains were evaluated as composite scores for attention and processing speed (APS), executive function (EF), and learning and memory (LM). For subjective cognitive complaints, the FACT-COG-v3 was used, while depressive symptoms were measured using the HAM-D.

Results show no significant differences in cognitive performance across PA intensity levels. However, the very active PA group was positively associated with the leisure-time subscale of CRIq. No significant correlations were found between PA and depressive symptoms, although its severity was negatively associated with subjective cognitive complaints. These findings highlight the complexity of CRCI and the need for further longitudinal research to explore the effects of PA on cognition in this population and the influence of other possible factors such as CR.

Resumo

A sobrevivência ao cancro apresenta desafios além da remissão, com comprometimentos cognitivos (CRCI) que afetam o funcionamento diário e a qualidade de vida nesta população. A atividade física (AF) demonstrou efeitos positivos na cognição, com melhorias na cognição após AF de alta intensidade e melhor recordação após AF moderada. Contudo, a evidência sobre os efeitos da AF nesta população ainda é mista, possivelmente devido a vários estudos utilizarem apenas instrumentos de autorrelato e à falta de estudos que examinam a influência de fatores como sintomas depressivos e reserva cognitiva (RC) na AF nesta população. Assim, este estudo tem como objetivo explorar a relação entre a AF regular e contínua e o desempenho cognitivo, bem como a forma como ela influencia a reserva cognitiva e o afeto, em sobreviventes de cancro.

A amostra deste estudo inclui 154 sobreviventes de cancro da mama e pulmão. A AF foi caracterizada após entrevista clínica e separada por intensidade. A RC foi medida através do TeLPI e da CRIq. Os domínios cognitivos foram avaliados através de compositos para atenção e velocidade de processamento (AVP), função executiva (FE) e aprendizagem e memória (AM). Para as queixas cognitivas subjetivas foi utilizada a FACT-Cog-v3, e os sintomas depressivos foram avaliados com a HAM-D.

Os resultados não mostram diferenças significativas no desempenho cognitivo entre os níveis de intensidade da AF. No entanto, o grupo ativo de AF foi positivamente associado à subescala de tempo-livre da CRIq. Não foram encontradas correlações significativas entre a AF e sintomas depressivos, embora a gravidade dos sintomas tenha sido negativamente associada a queixas cognitivas subjetivas. Os resultados destacam a complexidade da CRCI e a necessidade de estudos longitudinais que explorarem os efeitos da AF na cognição nesta população.

"Quero arroz doce" - Isabel Calçado

Avó, mãe e paciente terminal com tumor cerebral

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1. Introduction

After cancer treatment, survivors often face challenges that extend beyond disease remission (Hardy et al., 2018). A common side effect reported by cancer survivors includes cognitive difficulties and mood disorders, such as depression (Campbell et al., 2019; Lange et al., 2019). Improving and preventing these is crucial for ensuring a better quality of life for these patients. Significant efforts have been made in these areas, and terms like “cancer-related cognitive impairment” (CRCI) have emerged. However, the study of its mechanisms is still not fully understood (Campbell et al., 2020; Wefel et al., 2004, 2011, 2012).

Understanding the relationship of physical exercise on cognitive performance and its influence on mood, in cancer survivors, is important, as its benefits span cardiovascular health, stress reduction, and cognitive function enhancement making it a promising safe and highly accessible intervention for preventing and managing CRCI (Chen & Nakagawa, 2023; Chieffi et al., 2017). Furthermore, its role on neurobiological processes emphasises its importance in promoting overall well-being (Chen & Nakagawa, 2023; Scarmeas & Stern, 2003), as well as its potential role as a proxy for cognitive reserve (Chen & Nakagawa, 2023; Scarmeas & Stern, 2003; Stern, 2002). While the benefits of physical exercise for other cancer side effects hold strong evidence, the available research on its role on the cognitive performance of cancer survivors is limited (Campbell et al., 2019; Cheng et al., 2022; Koevoets et al., 2022). Many studies present inconsistent results and, therefore, this study aims to assess how regular ongoing physical exercise, as reported by the participants, influences cognitive reserve and affect, particularly depression, in cancer survivors.

2. Literature Review

Cancer is a complex disease that significantly impacts millions of individuals worldwide. According to the IARC (2024), 20 million individuals were affected by cancer in 2022, which resulted in approximately 9.7 million deaths, with the most prevalent types being breast and lung cancer (International Agency for Research on Cancer, 2024). However, in the past decade, advances in cancer screening, detection and treatments have led to a better prognosis, resulting in lower mortality rates and an increase in cancer survivors (Shapiro, 2018).

2.1 - Survivorship in Cancer

The concept of cancer survivorship is multifaceted and includes the entire trajectory from initial diagnosis to the end of life (Shapiro, 2018; Vaz-Luis et al., 2022). It can be divided into four phases: The acute survival phase starts at diagnosis and includes the active treatment period; the transitional survivorship phase marks the phase were patients distance themselves from medical care; in the extended survival phase, cancer survivors may live with cancer as a chronic condition or remain in remission; and finally, permanent survivorship refers to those free of cancer and treatment, yet still dealing with long-term persistent side effects from cancer and its treatment (Shapiro, 2018; Vaz-Luis et al., 2022). These long-term effects are experienced by approximately two-thirds of cancer survivors and begin during treatment, persisting afterward, with some late effects arising post-treatment (Shapiro, 2018; Vaz-Luis et al., 2022).

Unfortunately, these issues frequently go unnoticed by healthcare systems, neglecting these long-term physical, psychological, and supportive care needs of the patients. This often occurs due to factors such as limited healthcare resources, lack of systematic follow-up programs that address the complex, ongoing needs of cancer survivors, and financial barriers to accessing care (Cardoso et al., 2021). As a result, many patients are discharged without proper support for their ongoing problems (Jefford et al., 2022; Shapiro, 2018). Physical symptoms, such as pain and fatigue are common among cancer survivors, and they might also experience insomnia and cognitive difficulties (Hardy et al., 2018; Lange et al., 2019; Vaz-Luis et al., 2022).

The quality of life and mortality rates of cancer survivors are significantly impacted by mental health conditions, such as anxiety and depression, which often exacerbate physical symptoms (Shapiro, 2018; Vaz-Luis et al., 2022). For instance, depression may increase the perception of physical pain, making it more difficult for patients to engage in physical activities that could help alleviate some symptoms (Mitchell et al., 2013; Wakefield et al., 2015). Additionally, psychological issues including anxiety and depression affect about 40% of cancer survivors and can last for years after the initial diagnosis (Mitchell et al., 2013; Vaz-Luis et al., 2022; Wakefield et al., 2015).

Furthermore, financial concerns are a prevalent issue for many cancer survivors, as worries about work and finances often accompany the physical and psychological challenges (Kirchhoff & Jones, 2021). The concept of "financial toxicity", which describes the negative financial impact directly associated with cancer and its treatment, emerged because of the growing financial burden that the rising costs of cancer treatments have placed on patients and their families (Carrera et al., 2018; Kirchhoff & Jones, 2021).

2.2 - Cancer-Related Cognitive Impairment (CRCI)

The term cancer-related cognitive impairment (CRCI) refers to cognitive difficulties experienced either by central or non-central nervous system (CNS) cancer patients throughout the disease's course. In non-CNS cancer patients, where cognitive difficulties may not be immediately expected given the lack of direct impact on the CNS, such difficulties are nonetheless prevalent and can significantly affect a patient's quality of life (Hardy et al., 2018). The most affected cognitive domains in non-CNS cancer patients are attention, learning and memory, processing speed, and executive function (Campbell et al., 2020; Hardy et al., 2018; Janelsins et al., 2014; Lange et al., 2019). Usually, these cognitive impairments increase during treatment and can last for months or years afterwards, varying in intensity from mild to moderate (Fernandes et al., 2019; Hardy et al., 2018; Lange et al., 2019). For example, a study conducted by Janelsins and colleagues (2018) revealed persistent declines in memory, attention, and executive function in breast cancer patients up to six months after completing chemotherapy.

The exact mechanisms behind CRCI are still unclear. It has been suggested that chemotherapy may cause neurotoxic effects on the brain and, as a result, CRCI was originally referred to as *chemo-brain* or *brain fog* (Campbell, 2020; Janelsins et al., 2014; Wefel et al., 2004). However, studies also report that radiotherapy and endocrine therapy can also cause CRCI and those terms were changed to adopt a wider view of the condition (Campbell et al., 2020; Hardy et al., 2018; Janelsins et al., 2014; Lange et al., 2019). As such, CRCI is a complex condition and recent studies show that it can be influenced by a multitude of variables, such as genetics, age, cognitive reserve, social and psychological factors, making it challenging to identify a specific cause for its onset (Hardy et al., 2018; Lange et al., 2019). Cognitive reserve is a protective factor in which the brain maintains cognitive function despite brain lesions or degeneration (Stern, 2002). CR is often attributed to lifelong intellectual activities, such as work and education, and other factors, for example, reading and physical exercise (Scarmeas & Stern, 2003; Stern, 2002). Lower reserve can lead to a greater vulnerability to cognitive changes, especially following chemotherapy or other cancer treatments (Ahles et al., 2010). For instance, in a study conducted by Ahles and collaborators (2010), both older age and low cognitive reserve were significant factors contributing to declines in processing speed among women following chemotherapy, highlighting the importance of these factors in shaping cognitive outcomes post-treatment.

CRCI can significantly impact the quality of life and mental health of both cancer patients and survivors (Campbell et al., 2020; Koevoets et al., 2022). In a study developed by Fernandes and collaborators (2019), patients with CRCI reported difficulties in word finding during conversations that led to avoidance of social interactions, impacting their relationships. Additional studies highlighted the negative impact of CRCI on work, resulting in financial difficulties and early retirement (Lange et al., 2019; Reid-Arndt et al., 2010).

It is crucial for healthcare systems to address the effects of CRCI in cancer survivors, as cognition is closely linked to daily functioning and a person's identity. Impairments in cognition and functionality can burden patients and their quality of life. This can lead to reduced independence, confidence, and participation in social roles and work, resulting in *financial toxicity*, negatively impacting their personal, social, and professional life (Carrera et al., 2018; Kirchhoff & Jones, 2021; Marzorati et al., 2024).

2.3 – CRCI and Physical Activity

Although there are no established interventions for CRCI, there has been a growing concern to identify strategies to prevent and manage it. Psychoeducation, pharmacological and mindfulness-based interventions, cognitive behavioural therapy, cognitive training, and rehabilitation have been the interventions most used and investigated (Lange et al., 2019). However, most studies have shown that these interventions have limited effectiveness on cognition and show contradictory results, primarily because they rely solely on subjective measurements to confirm cognitive deficits (Campbell et al., 2020; Cheng et al., 2022; Lange et al., 2019). Therefore, it is essential to identify other factors that can be used for more practical and accessible interventions to support cancer survivors and simultaneously use objective and subjective measurements to effectively evaluate and address cognitive changes (Campbell et al., 2020).

One of these factors can be physical activity, as it plays a fundamental role in overall well-being, representing a safe, non-pharmacological intervention that can be easily implemented (Vehmanen et al., 2022). In addition, it can be also a cost-free intervention to help alleviate the financial burden of cancer survivors. Moreover, exercise impacts almost every system in the body, helping decrease the risk of cardiovascular diseases, controlling cholesterol levels, improving heart function, lowering stress levels, and enhancing neuroplasticity (Campbell et al., 2019). Physical activity has also been shown to improve cognitive function, including attention, processing speed, and memory, in various populations, such as older adults and individuals with certain psychiatric or degenerative conditions (Koevoets et al., 2022; Northey et al., 2018; Smith & Merwin, 2021; Zimmer et al., 2016). For instance, aerobic and strength training have demonstrated improvements in the quality of life for individuals with depression and anxiety conditions (Bedillion et al., 2019; Smith & Merwin, 2021).

Additionally, physical activity has been known to help maintain cognitive health and reduce the risk of neurodegenerative diseases (Chieffi et al., 2017). For example, a study conducted by Baker and collaborators (2010) showed a positive effect of aerobic exercise on cognitive function in adults with Mild Cognitive Impairment (MCI). Engaging in regular physical activities throughout life can also delay cognitive decline and promote neurobiological processes, such as increased neuronal activation, cerebral blood flow, and metabolism (Chen & Nakagawa, 2023; Chieffi et al., 2017). These processes, central to neuroplasticity, are also closely linked with the concept of cognitive reserve (Chieffi et al., 2017; Erickson et al., 2013). This overlap between the effects of physical activity and the underlying mechanism of cognitive reserve explains why physical activity has increasingly been regarded as a proxy for cognitive reserve (Cheng, 2016; Chieffi et al., 2017). In the context of CRCI, the overlap between physical activity and CR mechanisms is particularly significant. By enhancing neuroplasticity and cognitive reserve, physical activity may mitigate the cognitive challenges associated with cancer treatments, offering a promising avenue for intervention and cognitive health preservation in cancer survivors (Ahles et al. 2010, Hardy et al., 2018).

Physical activity is already established as a secure and effective way to prevent and manage other adverse effects of cancer treatments, as it can alleviate psychological distress, prevent functional decline, and positively impact the quality of life of these patients (Campbell et al., 2020; Vehmanen et al., 2022; Zimmer et al., 2016). Exercise interventions can also effectively address fatigue, a significant factor linked to CRCI (Koevoets et al., 2022). Research in breast cancer survivors has shown that an improvement in processing speed and self-reported cognition was associated with consistent physical activity (Koevoets et al., 2022; Cheng et al., 2022). Physical exercise was also linked to hippocampal neurogenesis contributing to a reduction in cognitive deficits in rodents (Andrade-Guerrero et al., 2023).

The link between physical activity and cognition has led numerous studies to explore its potential benefits in managing CRCI in cancer survivors. A large prospective cohort study examined the impact of high-intensity exercise on cognitive function in cancer patients. The results showed that engaging in physical activity before and during chemotherapy was associated with improved cognitive function immediately after completing treatment and that these improvements were still present six months later (Salerno et al., 2021). Another research study reported that moderate physical exercise improved recall of story memory among individuals using the extended *Mini Mental State Examination* (MMSE) measure (Cooke et al., 2016).

In 2015, Marinac and collaborators found a positive association between moderate to vigorous physical activity and information processing speed in breast cancer survivors. Similarly, a randomised controlled trial conducted by Hartman and colleagues (2018) demonstrated that a twelve-week exercise program for sedentary breast cancer survivors resulted in an improved processing speed for those with a cancer diagnosis within the previous two years, as well as a reduction in cognitive symptoms, supporting preliminary evidence of physical activity benefits on cognition in cancer survivors.

In a systematic review conducted by Campbell and colleagues (2020), aerobic exercise, ranging from 10 to 60 minutes, showed benefits for both self-reported and objectively measured cognitive function. Combining aerobic exercise with whole-body resistance training also had positive effects. Moderate to vigorous intensity levels may be necessary for cognitive benefits, but cautious interpretation is needed due to limited trials reporting significant effects.

A recent Physical Activity and Memory (PAM) study showed that a 6-month exercise intervention improved self-reported cognitive functioning, physical fitness, fatigue, quality of life, and depression in breast cancer patients with cognitive deficits. Although the overall tested cognitive functioning did not change significantly, subgroup analysis revealed a positive effect of exercise on cognitive performance, particularly in highly fatigued patients (Koevets et al., 2022).

On the other hand, a study conducted by Gokal and collaborators (2018) showed that self-managed walking had positive effects on perceived cognition but did not demonstrate such effects using objective neuropsychological measures. Other studies using only self-report measures, such as the Functional Assessment of Cancer Therapy-Cognitive Function-Version 3 (FACT-Cog-v3), produced contrasting results. One showed no significant changes in cognitive outcomes (Rogers et al., 2009), while the other, involving survivors randomised to eight sessions of yoga, demonstrated an improvement in cognitive symptoms within the yoga group ($d = -0.24$, $p < 0.05$), although presenting a small effect size (Janelsins et al., 2016).

Although significant effort has been made in research to find ways to manage CRCI in cancer survivors, there is still a gap regarding the effects of physical activity on cognitive performance in this population. Limited studies have been dedicated to fully explore this topic as a main objective, many of them lacking sufficient power and reproducing inconsistent results (Campbell et al., 2019; Koevoets et al., 2022). In these studies, the main outcome is usually quality of life or fatigue, cognition being only a secondary outcome. Moreover, most studies primarily rely on self-report questionnaires to assess subjective cognitive complaints, lacking objective standardised measures. Due to significant variations in the results and methods of the studies, it is crucial to use both subjective and objective cognitive measures to harmonise outcome measures across trials, as proposed by The International Cancer Cognition Task Force (Wefel et al., 2011) guidelines.

Additionally, many studies fail to account for confounding factors such as depression, anxiety, age, and cognitive reserve (Zimmer et al., 2016). These factors are crucial as they can significantly influence cognitive performance and subjective cognitive complaints, which are closely linked to affective symptoms, coping strategies, and adjustment (Wefel et al., 2011). Given their potential influence on cognitive outcomes, it is essential that these factors be considered in any comprehensive assessment of cognitive function (Campbell et al., 2020; Lange et al., 2019; Odynets et al., 2019). Moreover, it is also important to explore the association of physical activity and cognitive reserve, which provides a more comprehensive approach on the relationship between PA and short-term cognitive outcomes (e.g. attention, executive functions) while also examining its potential association to long-term adaptability to age-related or pathological changes (Chieffi et al., 2017; Erickson et al., 2013).

Despite these challenges, exercise guidelines for cancer survivors (Campbell et al., 2019; WHO, 2020) highlight the need for more robust evidence regarding the relationship between exercise and cognition in cancer patients and survivors. Intervention studies have provided compelling evidence of the benefits of structured physical activity on cognition and mood. However, these studies are often focused on implementing physical activity structured programmes, which differ from the real-world contexts in where physical activity behaviours are subject to individual variability.

Therefore, this study aims to better explore the relationship between regular ongoing physical activity and cognitive performance in cancer survivors. Given the gaps in the literature, this research will use both objective neuropsychological assessments and subjective self-report questionnaires on cognitive complaints and quality of life. Additionally, it will explore the connection between regular ongoing physical activity, as reported by participants during the initial clinical interview, and its impact on cognitive impairment, cognitive reserve, and mood.

3. Research Questions and Aims

The current study had as primary objective to answer to the following question: *What is the relationship between regular ongoing physical activity and cognitive performance in cancer survivors?* More specifically, *does cognitive performance in cancer survivors vary according to different levels of ongoing physical activity intensity?*

Furthermore, the secondary aims were to: *evaluate the potential contribution of ongoing physical activity on cognitive reserve* and *assess the role of physical exercise in reducing depression symptoms in cancer survivors*.

3.1 - Hypothesis

The present study proposes the following hypotheses:

Hypothesis 1: Cancer survivors who engage in higher levels of ongoing physical activity intensity have better scores in objective cognitive performance and less subjective cognitive complaints.

Hypothesis 2: Cancer survivors who practice ongoing physical activity have higher levels of cognitive reserve.

Hypothesis 3: Cancer survivors who engage in ongoing physical activity have lower depressive symptoms.

4. Methods

4.1 - Participants and Design

The sample for this study was recruited as a part of an ongoing multi-centre longitudinal prospective observational cohort study - FAITH (*Federated Artificial Intelligence solution for moniToring mental Health status after cancer treatment*) (Lemos et al., 2022) conducted at the Champalimaud Foundation Research and Clinical Centre. The participants were referred to the study by their oncologists or contacted directly by a research team member and agreed to participate in the FAITH study and in a sub study that aims at evaluating the cognitive performance of cancer survivors and its relationship with depression. Recruitment occurred within one to five years after the end of their cancer treatment, and the patients had to meet the inclusion and exclusion criteria defined by the FAITH protocol (see Lemos et al., 2022).

We only included the data of participants who had completed the baseline clinical and cognitive assessments. The total number of participants comprised 154 survivors of lung or breast cancer (the sample characterisation can be found in the results section, **Table 1**). The definition of cancer survivors in this study followed the proposal of Little and collaborators (2000), further designated as cancer survivors, who, after cancer treatment, are living without any recurrence or persisting oncological symptoms.

4.2 – Measures

4.2.1 - Physical Activity Measures

Type, intensity and duration of physical exercise were measured using the baseline clinical interview (M0) of the FAITH project. During the clinical interview, the clinician asks: "Do you practice physical activity?". This question specifically refers to the individual's current engagement in regular physical exercise, aiming to assess ongoing habits rather than past activities. If the response is positive, the clinician further explores the type of exercise and its frequency. After that, the answers are categorised based on the World Health Organization (WHO) guidelines on physical activity and sedentary behaviour (WHO, 2020). These guidelines provide a way to categorise different types of exercise according to their metabolic equivalent task (MET) threshold (i.e. standardised measure of the energy cost of various physical activities, with 1 MET representing the energy expenditure of an individual at rest, such as sitting quietly. Higher MET values indicate activities that require more energy). In that sense, according to the type of physical activity and frequency, the answers are then categorised as (WHO, 2020) following:

1) **Sedentary -** activities with an energy expenditure of 1.5 METs or less, such as sitting, lying down, or other behaviours that involve minimal movement. These activities align with definitions of sedentary behaviour and do not noticeably increase heart or breathing rates.

2) **Lightly active -** 1 to 2 times a week of light exercise (i.e. activities that require an energy expenditure between 1. 5 and 3.0 METs, including tasks such as slow walking or light household chores. These involve low physical effort, with minimal increases in heart or breathing rates).

3) **Moderately active -** 3 to 5 times a week of moderate exercise/sports (i.e. activities requiring

energy expenditure between 3.0 and less than 6.0 METs, such as brisk walking or recreational sports. These activities result in moderate increases in heart and breathing rates.

4) **Very active -** 6 to 7 week a week of hard exercise/sports (i.e. activities with energy expenditures of 6.0 METs or more, such as running or high-intensity aerobic exercises. These activities lead to significant increases in heart and breathing rates.

Furthermore, for this specific study, a participant who engages in physical activity at point M0, regardless of the level of intensity, will always be considered in the active group. On the contrary, if a participant does not exercise will be included in the sedentary group.

4.2.2 - Questionnaires

The *Functional Assessment of Cancer Therapy-Cognitive (Fact-Cog-v3)* (Oliveira et al., 2022) is a 37-item self-response measure designed to assess cognitive concerns in cancer patients. It consists of four subscales, including perceived cognitive impairments (CogPCI), comments from others (CogOth), perceived cognitive abilities (CogPCA), and impact on quality of life (CogQoL). Higher scores on this measure are associated with better perceived cognitive functioning (PCF), which is considered an important outcome in research and clinical practice within the cancer survivor population (Oliveira et al., 2022).

The *Cognitive Reserve Index Questionnaire (CRIq)* estimates an individual's cognitive reserve by gathering information about their life experiences. The questionnaire comprises three sections: CRI-Education, CRI-WorkingActivity and CRI-LeisureTime. CRI-Education evaluates years of education alongside possible training courses which last at least six months. CRI-WorkingActivity accounts for five different levels of working activities related to adulthood professions: unskilled; manual work; skilled manual work; skilled non-manual or technical work; professional occupation; and highly intellectual occupation. Finally, CRI-LeisureTime includes sixteen items referring to intellectual, social, and physical activities (Nucci et al., 2012).

4.2.2 - Neuropsychological Measures

To assess objective cognitive performance, the study included a comprehensive neuropsychological battery according to the recommendations of the International Cognition and Cancer Task Force (ICCTF) (Wefel et al., 2011). This selection was made by a panel of experts and was based on the cognitive functions highly associated with cancer treatments and depression, using instruments that are already adapted and validated to European Portuguese:

1. *Montreal Cognitive Assessment (MoCA) - global cognitive function* (Freitas et al., 2011)
2. *Auditory Verbal Learning Test (AVLT) A and B* (Cavaco et al., 2015)
3. *Trail Making Test A and B (TMT-A, TMT-B)* (Cavaco et al., 2013a)
4. *Stroop Colour Word Test* (Fernandes, 2013)
5. *Verbal Fluency Tests* (Cavaco et al., 2013b)
6. *Letter-Number Sequencing subtest of the Wechsler Adult Intelligence Scale-III* (Wechsler, 2008)
7. *Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale-III* (Wechsler, 2008)
8. *Teste de Leitura de Palavras Irregulares (TeLPI)* (Alves, Simões, & Martins, 2017)

The *Montreal Cognitive Assessment (MoCA)* (Freitas et al., 2011) is a brief cognitive screening instrument that assesses milder forms of cognitive impairment through the administration of tasks associated with the following dimensions: visuospatial abilities, attention, concentration, working memory, language, executive functions, and temporal and spatial orientation. The MoCA is a powerful and popular tool for screening cognitive impairment, as it has multiple alternative versions that can be used to minimise learning biases; moreover, it assesses executive functions. This, alongside its high sensitivity for MCI, represents an advantage compared to other screening tools (Freitas et al., 2011).

The *Auditory Verbal Learning Test (AVLT)* (Cavaco et al., 2015) evaluates various aspects of learning and verbal memory in adults through immediate recall trials. A list of 15 unrelated high-frequent words is used. The examiner reads the words aloud and then asks the participant to recall every recalled word, with no specific order required. This process is repeated five times. A delayed recall trial is done 30 minutes after learning, followed by a recognition trial (Cavaco et al., 2015).

The *Trail Making Test A and B (TMT-A, TMT-B)* (Cavaco et al., 2013a) evaluates attention, processing speed, and cognitive flexibility through two parts. In TMT-A, the participant is asked to connect 25 encircled numbers in numeric order, assessing attention, and processing speed, while being urged to complete the task as quickly as possible. In TMT-B participants connect numbers and letters in ascending order, progressively alternating between them until the number 13. This is an important measure of divided attention and cognitive flexibility (Cavaco et al., 2013a).

The *Stroop Colour Word Test* (Fernandes, 2013) is comprised of three tasks related to word congruence: (1) the Word “W" condition, in which a word reading task is performed, and (2) the Colour “C" condition, a colour naming task, assess selective attention, being crucial for the interpretation of the last condition; (3) The Colour-Word “CW” condition involves a task where the participant must name the colour in which the word is written, regardless of its meaning. This condition is an indicator of the ability to inhibit interference from external stimuli (Fernandes, 2013).

The *Verbal Fluency Tests* (Cavaco et al., 2013b) evaluate cognitive flexibility, response inhibition, response speed, and search strategies. Additionally, these tests assess vocabulary, naming ability, and memory, specifically semantic memory. In the semantic fluency test, participants are required to name as many animal species as possible in 60 seconds without repetition. In the phonemic fluency test, participants need to produce words starting with specific letters (i.e., “M”, “R” and “P”). They are instructed not to name words of places or people and to avoid using the same word with different endings, such as "transport," "transportation," or "transporting.” Similarly to the semantic fluency test, repeated words (perseverations) are only considered once and words not related to the instructions (intrusions) are not considered (Cavaco et al., 2013b).

Letter-Number Sequencing is a *subtest of the Wechsler Adult Intelligence Scale-III* (Wechsler, 2008) and serves as a critical measure of verbal working memory capacity. During this task, the examiner reads a sequence comprising both letters and digits. Subsequently, the patients are required to reorder and recall the stimuli, arranging first the digits in ascending numerical order and secondly the letters in alphabetical order. This task offers important insights into an individual's ability to manipulate and retain information (Wechsler, 2008).

The *Digit Symbol-Coding* is a *subtest of the Wechsler Adult Intelligence Scale-III* (Wechsler, 2008) that evaluates attention, processing speed, working memory, and visual perception. Participants are provided with a symbol key paired with numbers from 1 to 9. In the task, they are presented with a number sequence and instructed to draw the symbols corresponding to each number for 120 seconds (Wechsler, 2008).

The *Teste de Leitura de Palavras Irregulares (TeLPI)* (Alves, Simões, & Martins, 2017) is a Portuguese test used to measure premorbid intellectual abilities. This test requires the participant to read aloud 46 irregular words. The total of accurately pronounced words contributes to a TeLPI raw score. From this raw score and considering the individual's educational background, the verbal IQ can be estimated (Alves, Simões, & Martins, 2017).

4.2.4 - Psychological Measures

The psychological measures used in this study were those outlined in the FAITH protocol and that were administered during the initial clinical interview (M0).

The *Hamilton Depression Rating Scale* (Ham-D) (Hamilton, 1960) is used to measure the severity of depressive symptoms. The version used in this study includes 17 items which are measured either on five-point or three-point scales with higher scores indicating greater symptom severity. The total score categorizes depression into levels of severity: mild, moderate, severe, and very severe. According to Hamilton (1960) the scale is subdivided on ten main variables: Depressed Mood; Suicide; Work and Loss of Interest; Retardation; Agitation; Gastro-intestinal Symptoms; General Somatic Symptoms; Hypochondriasis; Insight; Loss of Weight. The total score ranges between 0 and 52, with a higher score indicating higher depressive symptom severity. Whereas a score between 0 and 7 indicates normal health status, scores between 8 and 16 indicate mild depressive symptomatology, between 17 and 23 moderate, and scores equal or greater than 24 indicate severe depressive symptomatology (Hamilton, 1960).

5. Statistical Analyses

The data was collected and processed using Microsoft Excel (Microsoft Corporation, 2021) and analysed using the software JASP version 0.19.1 (JASP Team, 2024). The sample size for this study was considerable (n = 154), therefore, the Kolmogorov-Smirnov test was conducted to assess normality. The results showed that most variables were normally distributed. Although four variables (Years of Education, MoCA, TeLPI and CogQoL) did not meet the normality assumption, parametric methods were still applied due to the large sample size, and because such methods (e.g., t-test, ANOVA) are robust to moderate violations of normality and for all those variables the assumption of equality of variances was met, shown by the Levene's test.

Z-score composites were calculated for each cognitive domain, specifically Attention and Processing Speed (APS), Executive Functions (EF), and Learning and Memory (LM). The composites were created by standardizing the data for each task and then averaging the standardized scores for the cognitive tasks within each domain. This approach enables the combination of performances across tasks, reducing the potential influence of task-specific variability and providing a more stable estimate of cognitive ability in each domain (Gibbons et al., 2012).

To test the first hypothesis, an ANOVA was initially conducted to examine the relationship between varying levels of physical activity intensity and several cognitive domains, including global cognitive functioning (as measured by MoCA scores), attention and processing speed, executive functions, and learning and memory (using the z-score composites of these cognitive domains), as well as subjective cognitive complaints (assessed via the CogPCI and CogPCA subscales of the FACT-Cog-v3). However, as these analyses did not reveal statistically significant results, a supplementary approach was adopted to explore potential differences between sedentary and active participants specifically. For this purpose, an independent samples t-test was performed to compare the two groups in terms of objective cognitive performance and subjective cognitive complaints. To test the second hypothesis whether cancer survivors who practice regular ongoing PA possess a higher cognitive reserve, measured by TeLPI and CRIq, a multiple linear regression analysis was used. Finally, to test the third hypothesis a linear regression was conducted to explore the impact of different levels of PA intensity on depression scores.

Statistical significance was set at $\mathbf{p < 0.05}$.

6. Results

6.1 - Sample Characterization

The study included a total sample of 154 participants. The characteristics of the sample are summarised in **Table 1**. Participants had an average age of 53.7 years (SD = 8.6), and the average number of years of education was 15.9 (SD = 3.8), ranging from 4 to 30 years. The sample consisted of 87% of participants with breast cancer and 13% with lung cancer. The majority of participants were female (92.9%), with only 7.1% male participants (they are all included in the lung cancer group).

In terms of psychological measures, the total score mean of the HAM-D was 5.1 (SD = 3.6), suggesting a lower average of depressive symptoms. The global cognitive performance, as measured by the Montreal Cognitive Assessment (MoCA), had a mean score of 25.6 (SD = 2.3). Of the 154 participants, 88 (57.1%) presented a score within the normal range, and 64 (41.6%) scored below at least 1 SD and 2 were missing.

Table 1

Participant Characteristics (n = 154)

Variable	Mean (SD)	Range
Age, years	53.7 (8.6)	25 – 70
Years of Education	15.9 (3.8)	4 – 30
BMI, kg/m2	25.4 (4.7)	17.7 – 41.7
HAM-D total score	5.1 (3.6)	0 – 15
MoCA total score	25.6 (2.3)	18 – 30

Cancer Type	N	%
Breast	134	87
Lung	20	13
Gender		
Female	143	92.9
Male	11	7.1

BMI = Body Mass Index, HAM-D = Hamilton Depression Rating Scale, MoCA = Montreal Cognitive Assessment

Regarding physical activity, 30.5% of participants were classified as sedentary, 30.5% as lightly active, 25.3% as moderately active, and 11% as very active. **Table 2** presents the sociodemographic variables according to the different intensity levels of PA. The sedentary, lightly, moderately and very active groups had mean ages of 52.5 (SD = 8.7), 52.2 (SD = 8.5) 56.0 (SD = 8.1), and 55.5 (SD = 9.2) years, respectively. The years of education were similar across groups. The BMI was highest in the sedentary group (M = 26.3, SD = 4.9) and lowest in the very active group (M = 24.2, SD = 5.1), with all groups falling within the normal BMI range. In terms of sex distribution, the sedentary group consisted of 93.6% females and 6.4% males, the lightly active of 97.9% females and 2.1% males, the moderately active group of 92.3% females and 7.7% males, and the very active group of 82.4% females and 17.6% males. Additionally, global cognitive performance was relatively consistent across groups.

Table 2

Sociodemographic variables according to different levels of Physical Active Intensity (n = 154)

Variable	Sedentary (n = 47)	Active (n = 103)		
		Lightly (n = 47)	Moderately (n = 39)	Very (n = 17)
Age, years	M = 52.5 (SD = 8.7)	M = 56.0 (SD = 8.1)	M = 52.2 (SD = 8.5)	M = 55.5 (SD = 9.2)
Years of Education	16.0 (4.7)	16.3 (3.0)	16.2 (3.7)	14.4 (3.1)
BMI, kg/m2	26.3 (4.9)	25.2 (4.6)	25.3 (4.5)	24.2 (5.1)
HAM-D total score	4.8 (3.2)	4.9 (4.0)	6.0 (3.7)	5.1 (3.5)
Cancer Type	N (%)	-	-	-
Breast	39 (83)	45 (95.7)	33 (84.6)	14 (82.4)
Lung	8 (17)	2 (4.3)	6 (15.4)	3 (17.6)
Gender				
Female	44 (93.6)	46 (97.9)	36 (92.3)	14 (82.4)
Male	3 (6.4)	1 (2.1)	3 (7.7)	3 (17.6)

BMI = Body Mass Index, HAM-D = Hamilton Depression Rating Scale

6.2 – Physical Activity and Cognitive Performance

The primary aim of this study was to investigate whether different levels of PA intensity have a significant impact on cognitive performance. As such, an analysis of variance (one-way ANOVA) was performed, to assess the presence of significant differences in cognitive performance among the groups under study, across four cognitive domains: global cognitive performance (MoCA scores), Attention and Processing Speed (APS), Executive Functions (EF), and Learning and Memory (LM). The analysis also included subjective cognitive complaints, using the FACT-Cog-v3 sub-scores for Perceived Cognitive Impairment (CogPCI) and Perceived Cognitive Abilities (CogPCA). The results of this analysis are presented in **Table 3**. For global cognitive functioning, as measured by the MoCA, the relationship with physical activity intensity levels was not statistically significant. Similarly, no significant associations were found for any cognitive composite measures and perceived cognitive performance.

Given the high number of participants who had at least 1 SD below the normal mean for their age and years of education on the MoCA scores, a subgroup analyses was also conducted based on participant's MoCA classification as either below cut-off (scores at least one standard deviation below the mean) or within the normal range. For the within the normal range group, there were no significant differences in subjective cognitive complaints (**FACT-cog PCI -** $F(3, 83) = 0.57$, $p = 0.63$; **FACT-cog PCA** - $F(3, 83) = 0.47$, $p = 0.70$) and any cognitive domains (**APS** - $F(3, 83) = 1.19$, $p = 0.32$; **EF** - $F(3, 83) = 0.97$, $p = 0.41$; **LM** - $F(3, 83) = 0.76$, $p = 0.52$). For the bellow cut-off group, there were also no significant differences for subjective cognitive complaints (**FACT-cog PCI -** $F(3, 56) = 0.57$, $p = 0.64$; **FACT-cog PCA -** $F(3, 56) = 0.11$, $p = 0.95$) or the cognitive domains (**APS** - $F(3, 57) = 2.06$, $p = 0.12$; **EF -** $F(3, 57) = 0.33$, $p = 0.81$; **LM** - $F(3, 57) = 0.85$, $p = 0.47$).

Table 3

Comparison of cognitive performance between levels of physical activity intensity

Variable	Sd		LA		MA		VA		F	*p*-value	η^2
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*			
MoCA	25.4	2.1	25.6	2.4	26.0	2.1	24.3	2.8	2.18	0.09	0.04

APS	0.4	0.6	0.5	0.5	0.4	0.6	0.7	0.5	1.60	0.19	0.03
EF	0.2	0.6	0.1	0.6	0.3	0.6	0.2	0.6	0.78	0.51	0.02
LM	0.1	0.5	-0.1	0.7	0.0	0.6	-0.0	0.8	0.90	0.45	0.02
CogPCI	53.1	11.8	54.0	12.6	55.5	13.1	58.4	2.5	0.87	0.46	0.02
CogPCA	15.7	6.0	16.6	5.5	16.9	6.5	18.1	5.0	0.83	0.48	0.02

F = one-way ANOVA, MoCA = Montreal Cognitive Assessment, APS = Attention and Processing Speed, EF = Executive Functioning, LM = Learning and Memory, CogPCI = Perceived Cognitive Impairment subscale of the FACT-Cog-v3, CogPCA = Perceived Cognitive Abilities subscale of the FACT-Cog-v3, Sd = Sedentary, LA = Lightly Active, MA = Moderately Active, VA = Very Active.

Considering the lack of statistically significant findings when comparing cognitive performance across PA intensity groups, an alternative approach was adopted to explore the data further. Specifically, participants were reclassified into two broader groups: sedentary and active. This dichotomization aimed to investigate whether grouping participants by overall activity level, rather than specific intensity levels, might yield clearer patterns of association with cognitive outcomes. Therefore, to explore if there are differences in cognitive performance between physically active participants and those who are less active (sedentary group), an independent samples t-test was conducted. The results of this analysis are presented in **Table 4**.

The analysis revealed no statistically significant differences in global cognitive performance, as measured by the MoCA, between the sedentary group (M = 25.4, SD = 2.1) and the physically active group (M = 25.6, SD = 2.4), $t(146) = -0.35$, p = 0.73, $d = -0.06$. Furthermore, the results show that there are no significant differences in cognitive performance between individuals who engage in PA and those who do not. Moreover, there were no significant differences between the two groups on subjective cognitive complaints.

Table 4

Comparison of cognitive performance between Sedentary and Active groups

Variable	Sedentary		Active		*t*	*p*-value	Cohen's *d*
	M	*SD*	*M*	*SD*			
MoCA	25.4	2.1	25.6	2.4	-0.35	0.73	-0.06
APS	0.4	0.6	0.5	0.5	-0.57	0.57	-0.10
EF	0.2	0.6	0.2	0.6	0.47	0.64	0.08
LM	0.1	0.5	-0.0	0.7	1.57	0.12	0.26
CogPCI	53.1	11.8	55.3	12.4	-1.00	0.32	0.18
CogPCA	15.7	6.0	17.0	5.8	-1.30	0.20	0.18

t = Independent t-student sample test, MoCA = Montreal Cognitive Assessment, APS = Attention and Processing Speed, EF = Executive Functioning, LM = Learning and Memory, CogPCI = Perceived Cognitive Impairment subscale of the FACT-Cog-v3, CogPCA = Perceived Cognitive Abilities subscale of the FACT-Cog-v3

Building on the previous subgroup analysis based on MoCA impairment status, a subsequent comparison was conducted between sedentary and physically active participants. For the within the normal range group, there were no significant differences between physically active and sedentary participants across the subjective cognitive complaints measures (**FACT-cog PCI** - t(85) = -1.23, p = 0.22; FACT-cog PCA- t(85) = -1.07, p = 0.29) or any cognitive domain (**APS -** t(85) = 0.56, p = 0.58; **EF -** t(85) = 0.97, p = 0.34; **LM -** t(85) = 1.31, p = 0.19). However, for the bellow cut-off group a marginally statistically significant difference was observed in **APS**, with physically active participants having better MoCA scores than sedentary participants (t(59) = -2.02, *p* = 0.048).

6.3 - Physical Activity and Cognitive Reserve

For the second aim, to determine if there is an association between physical activity intensity levels and cognitive reserve measures (i.e. TeLPI, CRIq, and its Leisure-Time subscale), a Spearman's correlation was performed. The findings are presented in **Table 5** and demonstrated no statistically significant correlation between physical activity intensity levels and the TeLPI, indicating that the intensity of physical activity did not significantly relate to premorbid IQ as estimated by TeLPI. Similarly, PA intensity levels did not show a significant relationship with CRIq total scores. However, a small but significant positive correlation was observed.

Table 5

Spearman's Correlation between Physical Activity Intensity Levels and Cognitive Reserve Measures

Variable	*n*	M	SD	1		2		3	
				ρ	*p*-value	ρ	*p*-value	ρ	*p*-value
1. PA Intensity Levels	150	2.17	1.00	-	-	-	-	-	-
2. TeLPI	151	120.99	8.13	-0.093	0.868	-	-	-	-
3. CRIq Total Score	145	393.85	120.53	0.109	0.099	**0.186***	**0.013**	-	-
4. CRIq Leisure-Time	146	263.50	93.36	**0.152***	**0.035**	0.080	0.170	**0.927*****	**<0.001**

Note. All tests one-tailed, for positive correlation.
PA = Physical Activity, ρ = Spearman's ρ

Significant Correlation = * $p < .05$; *** $p < .001$

In order to analyse the strength of the association between the levels of physical activity intensity and cognitive reserve (i.e. CRIq Leisure-Time), a linear regression model was conducted with these two variables. Since variables like age and years of education are known to significantly influence cognitive reserve, they were added as covariates to the model. This adjustment helps control for their effects, providing a clearer understanding of the specific contribution of physical activity intensity to cognitive reserve. The results are shown in **Table 6**.

In the first model the association between PA intensity levels and CRIq Leisure-Time scores was assessed without controlling for age and years of education. The model only explained 1.5% of the variance in CRIq Leisure-Time scores ($R^2 = 0.015$) and was not statistically significant ($p = 0.170$), as indicated by the ANOVA result, suggesting that the combination of physical activity levels in this model did not significantly predict CRIq Leisure-Time scores.

The second model, which was adjusted for age and years of education, demonstrated an improvement in explanatory power, explaining 26.8% of the variance in CRIq Leisure-Time scores ($R^2 = 0.268$), and having a highly significance ($F = 11.25$, $p < 0.001$). The very active level of PA intensity showed a significant positive association with this factor in both Model 1 and Model 2. However, other variables were also identified that, together with this level of PA (increasing its statistical significance), help explain the variation in the CRIq Leisure-Time scores. Regarding physical activity, being moderately active was also a significant and positive factor associated with cognitive reserve ($B = 36.79$, $p = 0.042$). Additionally, age ($B = 36.79$, $p = 0.042$) and years of education ($B = 36.79$, $p = 0.042$) were also significantly and positively associated with CRIq Leisure-Time scores.

Table 6

Linear Regression Models of CRIq Leisure-Time and Physical Activity levels of Intensity, adjusted for age and years of education

Effect	*B*	SE	*t*	*p*	R²a
Model 1					0.015
PA (2)	28.64	19.97	1.43	0.154	
PA (3)	31.99	20.74	1.54	0.125	
PA (4)	55.65	27.34	2.04	**0.044***	
Model 2					0.268
PA (2)	11.08	17.39	0.64	0.525	
PA (3)	36.79	17.89	2.06	**0.042***	
PA (4)	50.15	23.80	2.11	**0.037***	
Years of Education	4.86	1.79	2.71	**0.008****	
Age	5.76	0.84	6.884	**<0.001*****	

Note. N = 139; *B* = unstandardized coefficient; SE = standard error of the unstandardized coefficient; *t* = t-statistic; R²a = adjusted R-squared.
* $p < .05$; ** $p < .01$; *** $p < .001$

6.4 - Physical Activity and Psychological Variables

To explore the third hypothesis, in which higher levels of physical exercise are associated with reduced depressive symptoms (lower scores in the HAM-D scale), a Spearman's correlation was initial conducted. The results were not statistically significant between the depression scores and physical activity levels of intensity ($\rho = 0.092$, $p = 0.134$). Given the absence of a significant correlation, a linear regression analysis was not pursued, as regression analyses are typically used to build predictive models when there is evidence of an association (Marôco, 2018), which was not the case in this instance.

Additionally, Spearman's correlation analyses were also conducted to examine the relationship between baseline depression scores and various cognitive measures. The results indicated a statistically significant negative correlation between the depression scores and both the CogPCI ($\rho = -0.430$, $p < 0.001$) and CogPCA ($\rho = -0.337$, $p < 0.001$), FACT-Cog-v3 sub-scales scores, suggesting that higher depression scores were associated with lower self-reported cognitive functioning and perceived cognitive abilities.

However, no significant correlations were observed in either objective cognitive measure, as showed by the MoCA ($\rho = 0.025$, $p = 0.761$), APS ($\rho = -0.062$, $p = 0.446$), EF ($\rho = -0.082$, $p = 0.317$), and LM ($\rho = -0.039$, $p = 0.636$) scores.

7. Discussion

The primary aim of this study was to examine the relationship between different levels of ongoing physical activity intensity and cognitive performance, as well to explore an association between cognitive reserve and depressive symptoms in cancer survivors. While various studies suggest that physical activity is beneficial for cognition and mood (Campbell et al., 2020; Koevoets et al., 2022), the findings from this study reveal a complex relationship between PA and cognitive performance, as well as their association with depressive symptoms in this specific population. Although a potential role for PA was identified in cognitive reserve, specifically in the CRIq Leisure-Time subscale, the results explained only a small proportion of the variance in cognitive reserve.

A key objective of this study was to explore the relationship between physical activity and cognitive performance. To address this, the study initially used a one-way ANOVA to compare the cognitive performance between groups of physical activity intensity. Contrary to expectations, no significant differences in cognitive performance were observed across different levels of physical activity intensity or between sedentary and active participants. These findings contrast from prior studies, such as those by Salerno et al. (2021) and Cooke et al. (2016), which identified cognitive benefits of practicing physical activity in cancer patients.

One possible explanation for the discrepancy between the findings of this study and those in the literature is the lack of detailed information regarding the types of PA performed by the participants. Studies that have shown cognitive benefits of PA often distinguish between structured aerobic activities, strength training, yoga, and other modalities (Campbell et al., 2020; Northey et al., 2018). Furthermore, when looking deeper into literature, the state of the art usually uses metabolic equivalents of task (MET) measured by accelerometers (Amagasa et al., 2018) a method which was not available to utilise in this thesis. Another limitation is that the present study did not specify different PA types, neither had an objective measure of physical activity, relying on self-reported answers from the initial clinical interview. This may have introduced bias within the participants (e.g. social desirability) and variations in the categorisation of the PA levels between clinicians.

Additionally, the context and type of physical activity may play a significant role in its effects on cognition. While this study did not find significant associations between physical activity levels and cognitive performance, the type of exercise performed, and its contextual factors might help explain these findings. For instance, studies on green exercise have suggested that nature may provide additional cognitive and emotional benefits beyond physical activity alone (Han, 2017). Han (2017) found that physical activity in natural environments enhanced attention and emotional regulation, particularly when combined with moderate levels of exercise. Similarly, yoga has been linked to improvements in cognitive function through its mindful and stress-reducing aspects (Gothe & McAuley, 2015). However, the current study relied on self-reported physical activity data without distinguishing between different modalities or settings, limiting the ability to explore how these factors may have influenced cognitive outcomes. Future studies on PA and cognitive performance should include data that precisely indicates and categorises different types of PA and perhaps explore a qualitative assessment of the contexts, intensity and meanings behind each participant’s physical activity practice, and an objective assessment of PA.

In this study, a subgroup analysis based on MoCA impairment status was also conducted to investigate whether PA differed between those with MoCA scores bellow cut-off versus within the normal range. While no significant differences were found in cognitive performance between PA intensity levels in the within the normal range group, a significant difference emerged in the APS domain for the bellow cut-off group, with physically active participants exhibiting better performance than their sedentary counterparts. This finding suggests that PA may have a positive effect on certain cognitive domains, such as attention, particularly in individuals that present cognitive impairments, but the overall lack of widespread associations points to the need for more targeted and nuanced research.

Another key factor may be the educational level of the sample. Participants in this study had an average of 15.9 years of education, a known protective factor for cognitive performance (Stern, 2002). This high educational attainment may have mitigated the impact of PA on cognition, as the cognitive reserve associated with education could serve as a "buffer" against potential deficits.

The second aim of this study was to investigate whether PA intensity levels were associated with cognitive reserve (CR), measured by the TeLPI, CRIq, and its Leisure-Time subscale. The analysis revealed no significant correlation between PA intensity levels and the TeLPI, or the CRIq scores. However, a small but statistically significant positive correlation was observed between PA intensity levels and CRIq Leisure-Time scores. To further explore this relationship, a linear regression analysis was conducted, controlling for age and years of education, which are well-established predictors of cognitive reserve (Stern, 2002). The very active group showed a significant positive association with cognitive reserve in both models, suggesting that engaging in high levels of PA may contribute to a higher cognitive reserve. Older age and years of education also emerged as significant positive (and better) predictors of cognitive reserve. These findings suggest that while PA may have a role in enhancing cognitive reserve, factors such as education and age are more influential in shaping cognitive reserve, supporting the notion that cognitive reserve is shaped by a combination of early-life cognitive engagement and later-life experiences (Stern, 2002). In that sense, the participant's self-reported PA levels might not reflect long-term habits, and cognitive benefits may require a more consistent, lifelong engagement in exercise to become evident.

The hypothesis that higher levels of physical exercise are associated with reduced depressive symptoms was also not supported by the findings of this study. No significant correlation was found between depressive symptoms and PA intensity. One possible reason for this discrepancy could be the unique psychological and emotional challenges faced by cancer survivors, who may experience prolonged anxiety, depression, and post-treatment stress, all of which PA alone might not adequately address (Mitchell et al., 2013; Shapiro, 2018). Cancer survivorship, as noted by Shapiro (2018) and Jefford et al. (2022), is often associated with long-term psychological impacts, including anxiety and depression, which may require targeted psychosocial interventions beyond exercise. Interestingly, a Spearman's correlation analyses revealed a significant negative correlation between depression scores and both the CogPCI and CogPCA sub-scores of the FACT-Cog-v3, suggesting that higher depression levels were associated with lower self-reported cognitive abilities and greater perceived cognitive impairment. However, no significant correlations were observed between depression and objective cognitive performance measures, such as MoCA, APS, EF, or LM scores. This finding suggests that depressive symptoms may impact perceived cognitive impairments more than the actual cognitive performance, reflecting the tendency of subjective cognitive complaints to be more influenced by affect, a pattern observed in other studies (Hsu et al., 2021).

7.1 - Limitations

As been mentioned in the discussion of this study, there are several limitations that should be considered when interpreting the results. First, the reliance on self-reported physical activity data introduces potential biases, which may have led to inaccurate categorization of activity levels. Objective measures, such as accelerometers, could provide more accurate and reliable data. Second, the cross-sectional design limits the ability to draw causal inferences about the relationships between PA, cognition, and emotional well-being. Longitudinal studies are needed to explore how sustained PA impacts these outcomes over time.

Additionally, the study did not account for the type or context of physical activity, which may have differential effects on cognition. For example, structured aerobic exercise and yoga have been shown to enhance cognitive function through distinct mechanisms, including improved cardiovascular health and stress reduction (Campbell et al., 2020; Gothe & McAuley, 2015).

Potential confounding factors, including socioeconomic status and cancer treatment history, were not controlled for. Furthermore, the generally low baseline depression scores in this sample may have limited the ability to detect any significant effects of physical activity on depressive symptoms, suggesting that a more diverse sample with varying depression levels might reveal different associations.

7.2 - Future Directions

The findings of this study emphasize the complexity of the relationship between physical activity, cognitive performance, cognitive reserve, and depressive symptoms in cancer survivors. Future research should incorporate objective measures, such as accelerometers, to obtain more precise data on physical activity intensity and frequency, which may yield a clearer understanding of its relationship to cognitive and psychological outcomes. Additionally, adopting a longitudinal approach would be beneficial to capture the effects of physical activity over time rather than at a single time point. Tracking changes across multiple time points would allow researchers to examine how sustained or cumulative physical activity impacts cognitive performance and mental health, offering insights into potential long-term benefits or risks. An experimental design, where participants initially do not engage in physical activity but are later introduced to a structured exercise program, could further strengthen causal inferences by providing a "before-and-after" comparison that enhances internal validity.

This study's findings suggest that the effects of PA on cognitive outcomes may be more pronounced in individuals with existing cognitive impairments or lower cognitive reserve. Future research should focus on vulnerable subgroups, such as cancer survivors with MoCA-defined impairments or those with lower educational attainment, to better understand how PA might offer targeted benefits in these populations. For example, subgroup analyses could explore whether specific cognitive domains, such as attention and processing speed, are more sensitive to PA in these groups. Lastly, future research should also investigate how PA interacts with other modifiable lifestyle factors, such as diet, sleep, and social engagement, to provide a more holistic understanding of its role in cognitive health.

Ultimately, these future directions could deepen our understanding of the complex interplay between physical activity, cognitive performance, and psychological well-being, particularly for cancer survivors who may face unique cognitive and mental health challenges.

8. Conclusion

In this study of cancer survivors, no significant differences were observed in cognitive performance (APS, EF, LM) between various levels of physical activity intensity, and individuals who engage in physical activity and those who do not. also did not impact cognitive performance. However, the results suggest that very active physical activity was positively associated with cognitive reserve, particularly with the leisure-time subscale of the CRIq. Additionally, there was no significant link between PA and depression scores, but higher depression was associated with lower self-reported cognitive functioning, though not with objective cognitive measures.

While this study did not establish a clear relationship between physical activity and cognitive performance in cancer survivors, the results highlight the complexity of factors influencing cognitive outcomes in cancer survivors and that there’s still a lot of research to be done regarding the effects of physical activity in this population.

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