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Fibromyalgia-Related fatigue and the quality of life, depression, anxiety, self-esteem, life satisfaction and physical activity in patients with Fibromyalgia

Marcos de Carvalho Alvarez

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Universidade da Beira Interior, Covilhã 05/08/2024

Marcos de Carvalho Alvarez

Dedicatory

I dedicate this to my grandmothers, Clara and Maria, who have always been and always will be my examples of overcoming adversity. always taught me a lot about life and about always persisting in what you dream of. And after many events, I have come to this moment looking up to you.

If I didn't give up in the midst of difficulties, it was to honor everything you taught me. Thank you for being my great examples of life and overcoming. I love you today and always.

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Resumo

A fibromialgia (FM) é uma doença crónica e persistente que provoca alterações físicas e sensoriais. Sua fisiopatologia ainda é debatida, mas acredita-se que o aumento dos sintomas esteja relacionado a um desequilíbrio de neurotransmissores ou hiperexcitabilidade do sistema nervoso central. Atualmente, 2% a 6% da população mundial tem FM, sendo que Portugal tem 3% e o Brasil 2,5%. A FM apresenta uma variedade de sintomas, incluindo dor muscular generalizada, fadiga excessiva, ansiedade e depressão, componentes psicológicos reduzidos e problemas de sono. Devido à sua complexidade, os pacientes com FM frequentemente apresentam uma diminuição significativa dos componentes psicológicos, levando ao isolamento social e à evitação das responsabilidades do trabalho e das atividades físicas. Portanto, este estudo teve como objetivo analisar a relação entre a Fadiga Relacionada à FM e a qualidade de vida, ansiedade, depressão, autoestima e satisfação com a vida e atividade física. A tese foi dividida em três estudos científicos, onde o primeiro investigou o potencial papel da atividade física como mediador na relação entre Fadiga e qualidade de vida, o segundo analisou as relações directas e indirectas entre Fadiga, ansiedade, depressão, autoestima e satisfação com a vida e níveis de atividade física e possíveis diferenças nestas associações entre duas culturas diferentes entre os pacientes, e o terceiro foi uma comparação das percepções dos sintomas entre duas culturas diferentes. Os resultados dos três estudos científicos incluídos nesta tese de doutoramento demonstram que: i) A atividade física, apesar de ter um papel extremamente importante, não actua como mediadora da relação entre a fadiga relacionada com a FM e a qualidade de vida dos seus doentes; ii) Todas as associações se revelaram significativamente relevantes, onde também se verificou a ausência de diferenças em termos de associações entre estas variáveis propostas em ambas as culturas estudadas; iii) Não se verificaram diferenças significativas na perceção da Fadiga, depressão, ansiedade, qualidade de vida, autoestima, satisfação com a vida e atividade física entre os doentes brasileiros e portugueses. A conjugação destes três estudos permite constatar que a fadiga relacionada com a FM é um sintoma extremamente relevante que afecta diretamente a componente psicológica dos seus doentes, em que a atividade física pode desempenhar um papel importante na redução e controlo dos sintomas negativos e no aumento das componentes positivas (qualidade de vida, autoestima e satisfação com a vida).

Palavras-chave: Fibromialgia; fadiga; componentes psicológicas; atividade física; comparação transcultural.

Abstract

Fibromyalgia (FM) is a chronic and persistent condition that causes physical and sensory changes. Its pathophysiology is still debated, but it is believed that the increase in symptoms is related to an imbalance of neurotransmitters or hyperexcitability of the central nervous system. Currently, 2% to 6% of the world's population has FM, with Portugal having 3% and Brazil having 2.5%. FM presents a variety of symptoms, including generalized muscle pain, excessive fatigue, anxiety and depression, reduced psychological components, and sleep problems. Due to its complexity, patients with FM often present a significant decrease in psychological components, leading to social isolation and avoidance of work responsibilities and physical activities. Therefore, this study aimed to analyze the relationship between FM-related fatigue and quality of life, anxiety, depression, self-esteem, and satisfaction with life and physical activity. The thesis was divided into three scientific studies, where the first investigated the potential role of physical activity as a mediator in the relationship between Fatigue and quality of life, and the second analyzed the direct and indirect relationships between Fatigue, anxiety, depression, self-esteem, and satisfaction with life. life and levels of physical activity and possible differences in these associations between two different cultures among patients, and the third was a comparison of symptom perceptions between two different cultures. The results of the three scientific studies included in this doctoral thesis show that: i) Although physical activity plays an extremely important role, it does not act as a mediator of the relationship between FM-related fatigue and the quality of life of its patients; ii) All associations proved to be significantly relevant, where there was also an absence of differences in terms of associations between these proposed variables in both cultures studied; iii) There were no significant differences in the perception of Fatigue, depression, anxiety, quality of life, self-esteem, satisfaction with life and physical activity between Brazilian and Portuguese patients. Combining these three studies, FM-related fatigue is an extremely relevant symptom that directly affects the psychological component of its patients, in which physical activity can have an important role in reducing and controlling negative symptoms and in increasing positive components (quality of life, self-esteem and satisfaction with life).

Keywords: Fibromyalgia; fatigue; psychological components; physical activity; cross-cultural comparison.

Resumo alargado

A fibromialgia (FM) é uma condição neurológica, musculoesquelética e crônica persistente que causa alterações físicas e sensoriais, onde sua fisiopatologia ainda é debatida por especialistas. Hoje acredita-se que os primeiros sinais de fibromialgia possuam relação com um desequilíbrio a nível dos neurotransmissores através de uma hiperexcitabilidade do sistema nervoso central. Hoje estima-se que 2% a 6% da população mundial tenha o diagnostico positivo para esta condição de saúde. Em Portugal, estima-se que até 3% da população adulta tenha esse diagnostico positivo para FM, enquanto no Brasil a estimativa é de até 2,5% de pacientes positivos para FM.

A nível de sua sintomatologia, a FM é ampla e variada, podendo cada paciente apresentar certos tipos de sintomas, contudo os sintomas mais relatados pelos pacientes são as dores musculares generalizadas e em pontos específicos (também chamados de tender points), fadiga excessiva, quadros de ansiedade e depressão, diminuição de componentes psicológicas (baixo valores reportados de qualidade de vida, autoestima, bem-estar e satisfação com a vida), irritabilidade e problemas no sono. Devido a essa heterogeneidade sintomatológica, o seu diagnostico tende a ser complexo e demorado, por falta de instrumentos, exames e ferramentas especificas para FM. Hoje, caso haja uma suspeita de FM por parte dos profissionais saúde, o paciente é submetido a uma série de exames laboratoriais e físicos com o intuito de descartar outras condições de saúde que pudessem explicar tais sintomas. Após isso, os pacientes são avaliados através de dois questionários, um com o objetivo de verificar o índice de dor generalizada e o outro em quantificar a gravidade dos sintomas apresentados por aquele paciente. Depois da conclusão e interpretação dos resultados obtidos nesses dois questionários, os mesmos exames para exclusão de outras doenças bem como os questionários são repetidos em um período posterior. Após isso, os resultados encontrados nessa segunda etapa do diagnóstico são comparados aos encontrados na primeira etapa, verificando se houve um aumento ou manutenção dos valores registrados na primeira etapa, o profissional de saúde pode diagnosticar aquele paciente como portador de FM.

Devido a toda a sua complexidade, estudos anteriores demonstram que pacientes com FM sofrem de uma considerável diminuição das componentes psicológicas, ainda mais quando esses são comparados a outros indivíduos saudáveis ou com outras condições crônicas de saúde, onde a dor e, principalmente, a fadiga relacionada a FM são relatadas com os principais sintomas que afetam diretamente a qualidade de vida, bem-estar, os níveis de autoestima e satisfação com a vida. Por muitas vezes, pacientes com FM devido

a suas limitações físicas e emocionais, tendem a adotar comportamentos reclusos, evitando socializações, responsabilidades laborais e até mesmo em realizar atividades físicas, o que acaba por auxiliar em um aumento do seu quadro depressivo e/ou ansioso. Neste seguimento, a literatura tem demonstrado que a atividade física é um importante fator no âmbito terapêutico da FM, pois além dos benefícios físicos advindos da sua prática, também auxilia na componente psicológica, promovendo uma sensação de bemestar geral e autoeficácia.

Almejando auxiliar a esse tipo de população em especial, torna-se necessário compreender e analisar a relação entre a fadiga relacionada a FM, as componentes psicológicas e a atividade física. No entanto essa temática ainda é limitada, ainda mais no âmbito de comparação entre pacientes com FM de culturas distintas. Assim, o presente estudo consistiu em analisar a relação da Fadiga relacionada a FM e os níveis de qualidade de vida, ansiedade, depressão, autoestima, satisfação com a vida e atividade física. Para alcançar este objetivo, verificamos o potencial papel mediador da atividade física na relação entre fadiga e qualidade de vida, analisamos as relações diretas e indiretas entre a fadiga e os níveis de ansiedade, depressão, autoestima, satisfação com a vida e atividade física e comparamos os níveis de perceções entre duas culturas distintas. Para isso, realizamos a divisão dessa tese em três grandes estudos científicos.

O primeiro estudo teve como objetivo analisar o potencial papel de mediação da atividade física na relação entre fadiga relacionada a FM com a qualidade de vida. Participaram neste estudo pacientes do sexo feminino com diagnóstico positivo para FM, onde foram submetidas a aplicação de três instrumentos psicométricos validados para quantificar os seus valores de fadiga, qualidade de vida e níveis de atividade física. Após a análise dos resultados obtidos, foi possível verificar que de ambas as amostras apresentam valores acima do ponto médio em todas as dimensões da fadiga relacionada a FM e escores abaixo da média para qualidade de vida e atividade física. Contudo, a atividade física demonstrou-se não possuir um papel mediador entre a fadiga relacionada a FM e a qualidade de vida. Porém, um outro resultado interessante deste estudo, foi que os resultados demonstraram que os domínios da fadiga apresentaram uma associação significante e negativa com os indicadores de qualidade de vida física e mental, demonstrando assim que paciente com FM com maiores valores de fadiga tendem a ter menores valores de qualidade de vida.

Por sua vez, nosso segundo estudo teve como objetivo compreender e analisar as associações entre a fadiga relacionada a FM e os níveis de ansiedade, depressão, autoestima, satisfação com a vida e atividade física se verificar se haveria diferenças entre

essas associações entre duas culturas distintas. Para isso, 473 pacientes do gênero feminino com diagnostico positivo para FM, responderam quatro instrumentos validados para mensurar os níveis das componentes desse estudo. Após a análise dos resultados, foi possível verificar que todas as associações foram significantes, onde a fadiga relacionada com à FM teve uma associação positiva com os níveis de ansiedade e depressão; a depressão e ansiedade foram negativamente associadas à autoestima; os níveis de autoestima apresentaram uma associação positiva com à satisfação com a vida; e a satisfação com a vida demonstrou um associação positiva com os níveis de atividade vida, onde não houveram diferenças de perceção das associações das variáveis entre as culturas analisadas. Com esses resultados, foi possível verificar a relevância que a fadiga relacionada a FM tem nas componentes psicológicas de seus pacientes, independente da sua localização geográfica ou cultural.

Já no terceiro estudo científico, que complementa esta tese, realizamos uma comparação transcultural para verificarmos possíveis diferenciações entre a perceção da fadiga e os níveis de qualidade de vida, ansiedade, depressão, autoestima, satisfação com a vida e atividade física. Participaram deste estudo apenas pacientes brasileiras e portuguesas do gênero feminino com diagnostico positivo para FM, onde completaram seis questionários validados e traduzidos para sua cultura. Depois de analisado os resultados, foi verificado que os pacientes demonstram valores acima do ponto médio para os sintomas negativos (fadiga, depressão e ansiedade) e valores mais baixos para satisfação com a vida, autoestima, qualidade de vida e níveis de atividade física, onde as pacientes brasileiras apresentaram maiores valores em todos os domínios da fadiga, na qualidade de vida psicológica e nos níveis de depressão, enquanto as pacientes portuguesas demonstraram ter maiores valores de qualidade de vida física, ansiedade, satisfação com a vida, autoestima e atividade física. Contudo, não foram encontradas diferenças significativas da perceção entre essas duas culturas estudadas. Com isso os resultados podem indicar que, embora se trate de duas culturas distintas, com grandes diferenças climáticas, socioeconómicas e geográficas, os sintomas relacionados com a FM são extremamente importantes e afetam diretamente a vida e o bem-estar dos seus portadores.

Após a conjunção destes três estudos, foi possível verificar que a fadiga relacionada a FM é um sintoma de extrema relevância que afeta diretamente as componentes psicológicas de seus portadores, onde a atividade física demonstra ter um papel de suma importância na atenuação e controlo dos sintomas negativos e aumento nas componentes psicológicas positivas (qualidade de vida, autoestima e satisfação com a vida).

Palavras-chave: Fibromialgia; Fadiga; qualidade de vida; ansiedade; depressão; autoestima; satisfação com a vida; atividade física; comparação transcultural.

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Acronym List

AVE – Average variance extracted

CF – Cognitive Fatigue

CI – Confidence Intervals

CFA – Confirmatory Factor

Analysis CFI – Comparative Fit

Index df - Degrees of Freedom

FM - Fibromyalgia

GFE – Global Fatigue Experience

IF – Impact on Funciton

IPAQ - International Physical Activity Questionnaire

M - Mean

MDF - Multidimensional Diary of Fatigue-Fibromyalgia-17

MH – Mental Health

MR – Measurement Residuals MW

– Measurement Weights

p – level of significance PA

– Physical Activity

PH – Physical Health

PF – Physical Fatigue

RMSEA – Root Mean Square Error of approximation

SD – Standard Deviation

SEM – Structural Equation Modeling

SR – Structural Residuals

SRMR – Standard Root Mean Residual

SW – Structural Weights

SWL – Satisfaction with Life

t – Test statistic

TLI – Tucker-Lewis Index

UM – Unconstrained Model

Chapter 1. General Introduction

Fibromyalgia (FM) can be defined as a neurological, physical, and chronic disorder that can cause sensory changes and muscle pain (Neumeister & Neumeister, 2020). Its pathogenesis is still debated by experts, and the hyperexcitability of the central nervous system and the imbalance of neurotransmitters are considered the main causes of fibromyalgia (Demirbag & Bulut, 2018; Shipley, 2018). It is estimated that FM affects between 2% and 6% of the world's population, with middle-aged women (30 to 50 years old) being the most affected (Assumpção et al., 2018; Saral et al., 2016). One of the main characteristics of FM is its symptomatological diversity, namely generalized muscle pain at specific points (called tender points), excessive fatigue (which is not relieved even with many hours of rest), loss of muscle strength, and psychological problems (i.e., sleep problems, anxiety, depression, and reduced levels of life satisfaction and self-esteem) (Busch et al., 2011; Chang et al., 2020).

As for the complexity of their symptoms, FM patients show difficulties in reporting their symptoms to health professionals, who often do not associate these clinical and somatic manifestations with FM or do not believe the patient's report (Qureshi et al., 2021). Diagnosis is complex and time-consuming, as there is still a lack of tools to diagnose FM (Häuser, 2018). Although widely used in the past, the tender point test is no longer accepted as a finding indicative of FM, which is why it has been excluded as a diagnostic criterion (Häuser, 2018). To confirm a positive diagnosis of FM, doctors carry out a series of laboratory tests to rule out any other disease that could cause symptoms similar to those of FM (Häuser, 2018). Patients are then assessed using the generalized pain index and a symptom severity score. With the combination of the values obtained in both questionnaires and no change in symptoms for three months, the patient is diagnosed with FM (Bernard et al., 2018; Häuser, 2018). It is very important in FM to receive a diagnosis of FM as soon as possible because a diagnosis helps healthcare professionals prepare therapies to relieve patients' symptoms (Clauw, 2014; White et al., 2002).

As some studies indicate, FM-related fatigue is the main symptom that affects overall perception of general health status and levels of quality of life and well-being (Hauser et al., 2015; Sallinen et al., 2011). Fatigue can be defined as the body's natural response to physical exertion or stress, but it can also be a symptom of a possible physical or mental dysfunction. In individuals without any adverse health conditions, fatigue is summarized as the physiological response to an activity carried out intensely and for a prolonged

period of time, in which the individual recovers easily after resting and which does not intend to affect their performance of daily activities (Hauser et al., 2015; Suhr, 2003; Guymer and Clauw, 2002). In the case of individuals with adverse health conditions or physical limitations (i.e., FM, anemia, hypothyroidism, respiratory diseases), fatigue behaves differently and is characterized by excessive physical tiredness that is usually not alleviated after several hours of rest (Suhr, 2003; Guymer and Clauw, 2002). FM patients, on the other hand, report that their fatigue is characterized by exhausting physical, mental, and cognitive tiredness, which doesn't improve even with many hours of rest, and which directly affects their work performance or even their daily tasks (Suhr, 2003; Guymer and Clauw, 2002). Because it is such an aggressive type of fatigue, some studies suggest that a specific name be created for this FM-related fatigue (Vincent et al., 2013; Jahan et al., 2012).

FM-related fatigue is a symptom that directly affects the quality of life, well-being, levels of life satisfaction, and self-esteem and can also influence levels of depression and anxiety, causing patients to avoid socializing, work responsibilities, and any type of physical activity (Bernard et al., 2000; Lorente et al., 2014). Depression is a mental disorder characterized by a persistent feeling of sadness and a loss of interest or pleasure in activities that were once enjoyable (American Psychiatric Association, 2013). Other symptoms associated with depression include changes in sleep, appetite, energy, and concentration, as well as feelings of guilt or worthlessness (American Psychiatric Association, 2013). Depression can be classified into different types, such as major depression, dysthymia (persistent depressive disorder), and seasonal depression (Kupfer, 2015; Nestler et al., 2002). Patients with fibromyalgia (FM) have a high prevalence of depression (Cohen et al., 2002). Depression can exacerbate FM symptoms, including pain perception, fatigue, and sleep difficulties, creating a vicious cycle that intensifies the negative experience of the disease (Arnold et al., 2008). Changes in neurotransmitter levels, such as serotonin and norepinephrine, as well as dysfunctions in the hypothalamic-pituitary-adrenal (HPA) axis, are commonly observed in both depression and FM, suggesting a significant neurobiological overlap between the two conditions (Kupfer, 2015; Nestler et al., 2002; Goldenberg, 1999).

Anxiety is an emotional response to stress or a perceived threat, but when it is disproportionate to the situation or persists for long periods, it can be characterized as an anxiety disorder (American Psychiatric Association, 2013). Anxiety disorders include generalized anxiety disorder (GAD), panic disorder, social anxiety disorder, and specific phobias (Bandelow et al., 2017; Craske et al., 2009). These disorders are characterized

by intense and persistent feelings of fear and worry, accompanied by physical symptoms such as increased heart rate, sweating, trembling, and a sense of breathlessness (Craske et al., 2009). Similar to depression, anxiety is highly prevalent in patients with FM (Goldenberg, 2004). Anxiety can contribute to the amplification of fatigue and other physical symptoms, as well as negatively affect quality of life and daily functioning (Cohen et al., 2002). Neuroimaging studies indicate that amygdala hyperactivity and prefrontal cortex dysfunctions, which are characteristic of anxiety, are also observed in FM patients, suggesting that shared neurobiological mechanisms may underlie both conditions (Schweinhardt et al., 2008; Etkin & Wagner, 2007).

The interaction between depression, anxiety, and FM is complex and bidirectional. The presence of depression and anxiety can intensify the perception of fatigue and FM symptoms, while the challenges and limitations imposed by FM can lead to the development or worsening of depressive and anxiety disorders. This comorbidity can result in a significant impact on quality of life, functionality, and the ability to cope with the disease (Santos et al., 2012; Malt et al., 2002; Thieme et al., 2004).

Somes studies show that fibromyalgia patients have a higher prevalence of anxiety and depression symptoms when compared to patients with inflammatory and non-inflammatory rheumatic diseases (Cetingok et al., 2022; Yepez et al., 2022). In addition, the symptoms of anxiety and depression in fibromyalgia can be so intense that they interfere with professional and social activities, negatively affecting not only the patient's professional performance but also making it difficult to perform motor and cognitive tasks, destabilizing family relationships, and restricting social contact, strongly influencing daily life and making routine difficult, thus compromising their quality of life, self-esteem, sense of well-being, and satisfaction with life. Its consequences tend to last over time due to the chronic nature of the disease, favoring the emergence of progressive feelings of hopelessness, helplessness, and despair (Santos et al., 2012). This process can lead to worsening depression and anxiety, thus creating a vicious cycle that eventually culminates in a worsening of the FM patient's general condition (Cetingok et al., 2022; Yepes et al., 2022).

The association between fibromyalgia-related symptoms and psychological aspects remains unclear. Still, it is known that it is an extremely important relationship, as some studies have shown that FM patients tend to have worse levels of quality of life, self-esteem, and life satisfaction and higher levels of fatigue when compared to other patients

with different chronic conditions (i.e., rheumatoid arthritis, spondylarthritis, and Sjogren's syndrome) (Sechi et al., 2020; Bucourt et al., 2021).

Self-esteem is a component of self-concept defined as an individual's thoughts and feelings about their own value and importance, resulting in an overall positive or negative attitude towards themselves (Galvez-Sanchez et al., 2018). Satisfaction with life is one of the dimensions associated with quality of life, which is part of the cognitive component of subjective well-being, being physical, mental, and social, and is increasingly recognized as an important health parameter (Çeliker and Borman, 2001). In the current literature, there is ample evidence of reductions in self-esteem and satisfaction with life in patients with FM (Peñacoba-Puente et al., 2015; Garaigordobil, 2013; Michielsen et al., 2006). An increase in these components is related to greater self-control and self-confidence which contributes to the individual's intrinsic motivation, facilitating success in cognitive tasks (Zafra-Polo et al., 2014). However, some studies suggest that there is a relationship between lower life satisfaction, self-esteem, and quality of life scores, and an increased risk of developing or worsening chronic diseases (Diener and Chang, 2011; Boonstra et al., 2013). Patients who have higher levels of the components of quality of life, satisfaction with life, and self-esteem are associated with an improvement in adaptation to FM, causing a decrease in the perception of symptoms of pain, fatigue, anxiety, and depression and an improvement in their general perception of health (Luque-Reca et al., 2021, 2022).

To date, FM does not have a cure or any kind of treatment that is effective, but some interventions help to alleviate the symptoms. There are various types of pharmacological and non-pharmacological therapies to try to alleviate the symptoms of FM, but physical activity is highly recommended and used as a way of mitigating these symptoms (Macfarlane et al. 2017). As well as being a low-cost intervention, physical activity is associated with a reduction in symptoms, namely a reduction in tender points, the impact of the disease on daily activities, improved sleep, and functional capacity (Andrade, Dominski and Sieczkowska, 2020; Andrade, Vilarino and Bevilacqua, 2017; SchmidtWilcke and Clauw, 2011). In addition to the aforementioned physical factors, physical activity, carried out effectively and accompanied by professionals, can improve the perception and modulation of pain (Hakkinen et al. 2001) and also provides improvements in the psychological sphere, promoting a sense of satisfaction and selfefficacy, thus improving their vitality and quality of life, and in turn, reducing levels of depression and anxiety (Luque-Reca et al., 2022; Redondo et al., 2004; Salvat et al., 2016). However, health professionals should always consider the limitations of each

patient and always check physical fitness and fatigue levels so that patients can differentiate between the normal pain generated by performing physical activity and their FM-related pain, ensuring that the activity generates a feeling of well-being for the FM sufferer and not a worsening of their normal symptoms (McMorris et al., 2017).

Couto et al. (2022) conducted a meta-analysis study examining different types of physical activity prescriptions for patients with fibromyalgia (FM), which indicated that aerobic, resistance, and stretching exercises are beneficial for this population when the principle of individualization is considered. This approach leads to a reduction in FM-associated symptoms and thereby improves the quality of life for patients. Therefore, it is recommended that when the physical condition of these patients does not permit physical activity at levels recommended by generalized international guidelines for FM, professionals should adjust the exercise prescription, taking into account the limitations and capacities of each patient (Hauser et al., 2010, Couto et al., 2022, Busch).

In addition to this complexity, another factor that can influence the levels and perception of symptoms related to FM is related to socio-cultural factors (Ruiz-Montero et al. 2019). Although it affects people universally, cultural differences play a significant role in their perception and can influence the diagnosis, treatment, and experiences of individuals living with fibromyalgia (Wolfe and Wallit, 2013; Winfield, 2000). Some studies (Clark et al. 2013, Ruiz-Montero et al., 2019; Ruiz-Montero et al., 2015, Kuppens et al., 2016) have demonstrated that FM patients from different cultures may present with higher or lower levels of the same symptoms, thus causing an attenuation or worsening of their condition, where cultural, geographic, socioeconomic and climatic factors may be responsible for this difference in perceptions. However, this topic requires more in-depth studies on these relationships, as there is still a limited number of studies, which makes it difficult to accurately understand these different perceptions of FM symptoms in different cultures. However, despite being an extremely important symptom, there is still a lack of studies to better understand the effects and relationships of fatigue with the other symptoms and adverse conditions caused by FM.

Therefore, due to all this context and gaps about FM, the main purpose of this thesis is to analyze the relationship between fibromyalgia-related fatigue and quality of life, depression, anxiety, self-esteem, life satisfaction, and physical activity, and possible differentiations between these associations among patients from two culturally and geographically different countries. Considering the previous literature regarding the fibromyalgia fatigue, the proposed variables, and cross-cultural comparisons of patients with a positive diagnosis of FM, the thesis was divided into three scientific studies that

aimed to: 1) analyze the relation between fibromyalgia-related fatigue and quality of life and if physical activity can act as a mediator of this relationship; 2) verify the associations between fibromyalgia-related fatigue and psychological components (self-esteem, life satisfaction, anxiety, depression) and physical activity; 3) analyze whether there are significant differences in the perception of these symptoms between two different cultures.

Chapter 2. Cross-sectional Studies Study 1: Exploring the Relationship between Fibromyalgia-Related Fatigue, Physical Activity, and Quality of Life

Abstract

The symptoms of fibromyalgia are varied, including general muscle pain and pain at specific points (also called tender points), excessive fatigue, anxiety, depression, and some psychological problems that can have a negative impact on quality of life. Physical activity is a widely used option by health professionals to alleviate the effects of this syndrome. However, there is no clear information on the possible mediating role of physical activity in the relationship between fibromyalgia-related fatigue and quality of life. Therefore, this study aims to evaluate the relationship between fibromyalgia-related fatigue and quality of life and to investigate the mediating role of physical activity in patients with this syndrome. Methods: In a cross-sectional study, 237 Portuguese women aged 28 to 75 years (M = 49.12; SD ± 8.87) and 117 Brazilian women aged 20 to 69 years (M = 46.72; SD ± 8.38) were recruited to participate in this study. These patients completed three valid and reliable questionnaires related to the assessment of fibromyalgia-related fatigue (MDF-Fibro-17), physical activity (IPAQ), and quality of life (SF-36). Results: Both samples had scores above the midpoint for all dimensions of fibromyalgia-related fatigue and scores below the midpoint for quality of life. Physical activity had no mediating effect in either sample, as the total indirect effect was not significant. Conclusions: Physical activity does not mediate the relationship between fatigue and quality of life. However, the results also show that the fatigue dimensions associated with fibromyalgia had a negative and significant association with physical and mental health indicators in both samples. Thus, patients with FM with higher scores on fatigue-related symptoms might suffer more from physical and mental health, both of which are related to quality of life.

fibromyalgia; quality of life; fatigue; physical activity

Introduction

Fatigue is widely known and understood, as it is a natural response of the body to some type of physical and mental stress, but it can also be a sign of some possible physical and/or mental disorder (Finsterer & Mahjoub, 2014; Ulus et al., 2019). In healthy individuals, fatigue is a physiological reaction to a prolonged activity, from which the body tends to recover easily with rest, and which usually does not end up interfering with daily activities. However, in individuals affected by some pathology (e.g., FM, anemia, hypothyroidism, chronic obstructive pulmonary disease) or with physical limitations, fatigue symptoms are more pronounced when compared to healthy individuals (Finsterer & Mahjoub, 2014). Specifically, patients with FM report that their fatigue is characterized by excessive physical, mental, and cognitive tiredness and that it is usually not alleviated after hours of sleep or rest, which may end up hindering the performance of work or daily tasks, and thus may contribute to the adoption of sedentary behavior (Arnold et al., 2011; Finsterer & Mahjoub, 2014; Hudson et al., 2009).

Several studies (e.g., Arnold et al. (2011); Hudson et al. (2009)) have shown that fatigue is one of the main symptoms reported by patients with FM when asked about the determining factor impacting their overall health, quality of life, and overall perception of this syndrome. While fibromyalgia-related fatigue has a negative relationship with several health-related indicators such as quality of life, it is not always measured in clinical practice and scientific research (Mease et al., 2009; Morris et al., 2017).

Because of its complexity, FM leaves patients more vulnerable to stigmatization and psychological conditions (e.g., poor quality of life, higher levels of anxiety and depression, and low self-esteem) as evidenced by Garcia-Martinez et al. (2012). Patients with FM have significantly worse levels of quality of life when compared to healthy individuals (Garcia-Martinez et al., 2012). These patients see their syndrome as a serious condition that entails major consequences for their daily lives, affecting their socialization, making it difficult for them to work and perform their daily tasks (Verbunt et al., 2008).

The Mediation Role of Physical Activity

There is still no cure or fully effective treatment for FM, and the most recommended intervention for this type of population is the implementation of approaches that can

reduce fibromyalgia-related symptoms (Carville et al., 2008; Wolfe et al., 2011). In this sense, physical activity has been pointed out by health professionals as a means to alleviate the effects of this syndrome (Carville et al., 2008; Wolfe et al., 2011). Physical activity is recommended since it is considered a low-cost intervention, aimed at improving physical and psychological components, through the increase of some neurotransmitters (i.e., endorphins and serotonin) capable of producing a sense of selfefficacy and satisfaction, promoting thus a better quality of life (Larsson et al., 2020; Sawatzky et al., 2007).

Health professionals are advised to consider the physical limitations of each patient and measure the levels of physical fitness and fibromyalgia-related fatigue to understand possible pain caused by the training program (Larsson et al., 2020; Rooks, 2008). Therefore, research recommends a frequency of 2–3 times a week of low- to moderateintensity physical activity for patients with FM (Larsson et al., 2020; Rooks, 2008). Some studies have shown that aerobic and strength exercises have moderate effects on physical functioning, can reduce fibromyalgia-related pain (by increasing muscle strength) and increase flexibility, as well as improve quality of life (Busch et al., 2011; SorianoMaldonado et al., 2016).

Present Study

As previously described, FM is a chronic and complex biopsychosocial disorder that deteriorates and compromises the quality of life, and several studies (Amir et al., 2000; Lopez-Roig et al., 2016; Sechi et al., 2020) demonstrate that those patients may have these lower levels, which are influenced by several psychological aspects, such as depression and fatigue. Some studies (Bucourt et al., 2021; Lee et al., 2017) demonstrated that patients with FM tend to have worse health status and quality of life when compared to other patients with other chronic diseases (e.g., osteoarthritis, rheumatoid arthritis, lupus, hypertension, spondylarthritis, and Sjogren's Syndrome). Bernard et al. (2000) and Lorente et al. (2014) found that women with FM, when compared to healthy women, present significant differences in quality of life values, especially in the domains of functional capacity, vitality, emotional role, pain, and general health perception.

However, to the best of our knowledge, the association between fibromyalgia-related fatigue and quality of life is still under-researched. As demonstrated by Offenbaecher et al. (2021), more than 50% of FM patients reported that their quality of life levels is not related to pain, but to other aspects of FM.

Daily physical activity is an important behavioural mechanism that can influence fatigue directly or indirectly, through changes in neuroendocrine activities (increased levels of serotonin and other neurotransmitters, regulation of the hypothalamic-pituitary-adrenal axis, and the autonomic nervous system) and, consequently, it can help improve quality of life levels due to its role in promoting well-being, increasing levels of general health status, and improving some psychological aspects in cases where there is social interaction during physical exercise (Doerr et al., 2017; Junior et al., 2012). However, when the literature on the mediating role of physical activity in this relationship between fatigue and quality of life was consulted, a scarcity of specific literature was observed. Therefore, this study aims to evaluate the relationship between fatigue and quality of life in patients, as well as investigate how physical activity can act as a mediator of this relationship.

Materials and Methods

Study Design and Participants

A cross-sectional study considering two independent samples was collected for the present study. Sample 1 consisted of a total of 237 Portuguese women aged between 28 and 75 (M = 49.12; SD ± 8.87) years was conducted. The Portuguese subjects were diagnosed with FM on average 8.62 ± 7.14 years ago. Sample 2 consisted of data from 117 Brazilian women aged between 20 and 69 years (M = 46.72; SD = ± 8.38). The Brazilian subjects were diagnosed with FM on average 8.91 ± 6.92 years ago. According to Fritz and Mackinnon (2007), the present sample size is in line with simulations for mediation purposes with this number of variables, thus, ensuring proper statistical power.

Procedure: Data Collection

Prior to data collection, ethical approval was obtained from the Ethics and Scientific Committee of the University of Beira Interior (UBI), under reference number CE-UBIPj2021-038. The present study was conducted in accordance with the Declaration of Helsinki (Association, 2013) and its subsequent amendments.

Regarding data collection procedures, the National Association against Fibromyalgia and Chronic Fatigue Syndrome (MYOS) and the Brazilian Association of Fibromyalgia (ABRAFIBRO) were contacted, and the objectives were explained. After approval, FM specialists contacted potential participants to participate voluntarily in this study.

Afterward, the authors contacted patients with FM and explained the purpose of this study, along with providing detailed information regarding data collection procedures. After contact and clarification of the study objectives, informed consent was obtained from each individual participant. All individuals voluntarily participated in this study, and the time to complete the questionnaire was approximately 25 min.

Instrument

Fibromyalgia-Related Fatigue

The Multidimensional Daily Diary of Fatigue-Fibromyalgia-17 - MDF-Fibro-17 Portuguese and Brazilian versions (Alvarez et al., 2020) were used to measure the levels of different fatigue components in patients with FM. The 17 items assess different dimensions of fatigue: Global Fatigue Experience (4 items, for example, “How severe is your fatigue today?”); Physical Fatigue (3 items, for example, “How weak your muscles felt today?”); Cognitive Fatigue (4 items, e.g., “How hard was it to concentrate because you were tired today?”); Motivation (3 items, for example, “How much effort was it doing today?”), and Role Impact (3 items, for example, “Did you slow things down because you were tired today?”). Participants responded to each item using a 10-point scale ranging from 0 (“not at all”) to 10 (“extremely”). Higher scores indicated greater severity of fatigue. Previous studies have supported the validity and reliability of these questionnaires (Alvarez et al., 2020; Li et al., 2017).

Physical Activity

The International Physical Activity Questionnaire short form (IPAQ) was used to assess the levels of physical activity (Craig et al., 2003). The questionnaire comprises a total of seven questions, related to activities carried out in the last seven days before the application of the questionnaire (Benitez-Porres et al., 2013).

The questions measure principles of physical activity, such as walking, moderate intensity and vigorous-intensity activities, frequency, and duration (Benitez-Porres et al., 2013; Santos, 2009). The estimation of energy expenditure is processed according to the levels of physical activity (IPAQ, 2005). Specifically, the data obtained are converted to MET min/week (i.e., metabolic equivalent task) by calculating the scored minutes per week in each activity category by the specific metabolic equivalent, according to previous research (Benitez-Porres et al., 2013).

Quality of Life

The SF-36 survey (Ware and Sherbourne, 1992) was used to measure the quality of life dimensions. This survey consists of 11 questions and 36 items that encompass 8 components (domains or dimensions) on the quality of life state, represented by: physical functioning (10 items, for example, "Does your health limit you to performing violent activities, such as running, lifting weights, participating in strenuous sports? If yes, how much?"); Difficulties in Role Performance Caused by Physical Problems (4 items, for example, "During the past 4 weeks have you, in your work or daily activities, had decreased time spent working or in other activities as a result of your physical health status?"); Pain (2 items, for example, "During the past 4 weeks, how much has pain interfered with your normal work? (both outside work and housework)"); General Health (5 items, for example, "In general, I would say your health is"); Vitality (4 items, for example, "During the last 4 weeks, have you felt full of vitality?"); Social Functioning (2 items, for example, "During the past four weeks, how much has your physical health or emotional problems limited your social activity? (such as visiting friends or close family)"); Difficulties in Role Performance Caused by Emotional Problems (3 items, for example, "During the past 4 weeks, have you had, with your work or daily activities, a decrease in time spent at work or in other activities due to any emotional problems? (such as feeling depressed or anxious)"); Mental Health (5 items, for example, "During the past 4 weeks, have you felt so depressed that nothing cheered you up?") (Hoffman & Dukes, 2008). To verify the physical health status of the patient, a calculation is made of the following domains: Physical Functioning, Difficulties in Role Performance Caused by Physical Problems, Pain, and General Health. As for the psychological health status, the calculation is made from the domains: Vitality, Social Functioning, Difficulties in Role Performance Caused by Emotional Problems, and Mental Health. Values range from 0 to 100, where higher scores suggest better levels in each domain of the patient's quality of life, and mental and physical health (da Costa et al., 2000).

Statistical Analysis

Descriptive statistics (mean and standard deviation), as well as bivariate correlations, were calculated for all variables under analysis. The IBM SPSS Statistics version 22.0 (IBM Corp. Armonk, New York, NY, USA) was used for data analysis. Possible missing values and outliers were also searched in the data. To test the proposed interactions, simple mediation (model 4) analysis according to Hayes' (2018) recommendations was conducted using SPSS PROCESS v.3.5 (IBM Corp. Armonk, New York, NY, USA). In total, twenty models were tested, considering five fatigue dimensions as independent variables and two dependent variables in two independent samples. Specifically, the

levels of Global Fatigue Experience (GFE); Physical Fatigue (PF); Motivation (MOT), and Impact on Function (IF) were selected as independent variables in this model. The levels of physical activity (PA) were used as a mediator, and the levels of Physical Health (PH) and Mental Health (MH) were selected as dependent variables. This procedure allows the estimation of the direct and indirect effects in the proposed models while controlling for k mediators' influence between variables (Hayes, 2018). A 5000 samples bootstrap was used according to several recommendations (Hayes, 2018; Williams and Mackinnon, 2008) and significant indirect effects were considered if the confidence interval did not include zero. For all tests, the level of significance was set at $p < 0.05$.

Results

Descriptive Statistics and Bivariate Correlations

Data inspection did not show missing values and outliers. Descriptive statistics showed that both samples had scores above the midpoint for the experience of Global Fatigue, Physical Fatigue, Cognitive Fatigue, Motivation, and Impact on Function. The observed values of fibromyalgia-related fatigue dimensions are similar in both samples as can be seen in Table 1. Furthermore, the Portuguese sample seems to be physically more active than the Brazilian patients (MET = 2573.54 vs. MET = 1734.15). In terms of quality of life (physical and mental health), both the Portuguese and Brazilian patients showed scores below average. Fibromyalgia-related fatigue dimensions displayed a negative and significant association with physical and mental health indicators 5000 samples bootstrap was used according to several recommendations (Hayes, 2018; Williams & Mackinnon, 2008) and significant indirect effects were considered if the confidence interval did not include zero. For all tests, the level of significance was set at $p < 0.05$.

The Mediation Role of Physical Activity in the Relationship between Fibromyalgia-Related Fatigue and Quality of Life

Fibromyalgia-related fatigue dimensions displayed a negative and significant association with physical and mental health indicators in both samples, since direct regression coefficients were negative and significant ($p < 0.05$). However, fibromyalgia-related fatigue dimensions did not display any significant association with levels of physical activity. The levels of physical activity did not display any significant association with physical and mental health in both samples. Overall, no mediation effect of physical

activity was identified, since the total indirect effect was not significant in both samples (see Table 2).

Table 1. Descriptive statistics and bivariate correlations across study variables.

Portuguese sample										
Variables	**M**	**SD**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1.GFE	7.93	1.52	1	-	-	-	-	-	-	-
2.PF	8.13	1.52	.81**	1	-	-	-	-	-	-
3.CF	7.78	1.71	.66**	.67**	1	-	-	-	-	-
4.MOT	8.13	1.54	.75**	.75**	.77**	1	-	-	-	-
5.IF	8.20	1.52	.73**	.74**	.76**	.86**	1	-	-	-
6.PA	2573.54	675.04	-.05	-.003	-.04	.03	.020	1	-	-
7.PH	32.78	9.31	-.24**	-.27**	-.31**	-.32**	-.28**	.03	1	-
8.MH	27.41	15.48	-.15**	-.14*	-.30**	-.33**	-.29**	-.01	.50**	-
Brazilian sample										
Variables	**M**	**SD**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1.GFE	8.06	1.44	1	-	-	-	-	-	-	-
2.PF	8.33	1.46	.68**	1	-	-	-	-	-	-
3.CF	7.95	1.50	.66**	.51**	1	-	-	-	-	-
4.MOT	8.49	1.48	.60**	.54**	.76**	1	-	-	-	-
5.IF	8.42	1.59	.65**	.59**	.70**	.83**	1	-	-	-
6.PA	1734.15	368.12	.03	-.05	-.10	-.06	-.05	1	-	-
7.PH	33.81	8.85	-.16**	-.12*	-.17*	-.17*	-.14*	-.13*	1	-
8.MH	26.90	15.83	-.023**	-.21**	-.22**	-.16*	-.16*	-.18*	.23**	-

Notes: M = Mean; SD = Standard deviation; GFE = Global Fatigue Experience; PF = Physical Fatigue; CF = Cognitive Fatigue; MOT = Motivation; IF = Impact on Function; PH = Physical Health; MH = Mental Health; PA = Physical Activity; * $p < 0.05$; ** $p < 0.01$.

Table 2. Mediation analysis between fibromyalgia-related fatigue, physical activity, and quality of life.

Portuguese sample						
Path 1	**Effect**	**Path 2**	**Effect**	**Path 3**	**Effect**	**Total indirect effect**
GFE→PH	-0.17 [-.251,-.078]	GFE→PA	0.03 [-.057, .120]	PA→PH	0.04 [-.088, .161]	0.001 [-.004, .010]
GFE→MH	-.11 [-.191, -.015]	GFE→PA	0.03 [-.057, .120]	PA→MH	-0.006 [-.133, .120]	-0.001 [-.006, .004]
PF→PH	-0.18 [-.255, -.093]	PF→PA	-0.001 [-.086, .823]	PA→PH	0.02 [-.098, .148]	<0.001 [-.007, .005]
PF→MH	-0.09 [-.174, -.007]	PF→PA	-0.001 [-.086, .823]	PA→MH	-0.01 [-.140, .113]	<0.001 [-.005, .003]
CF→PH	-0.18 [-.253, -.110]	CF→PA	-0.02 [-.097, .052]	PA→PH	0.01 [-.108, .135]	-0.001 [-.016, .028]
CF→MH	-0.17 [-.245, -.102]	CF→PA	-0.02 [-.097, .052]	PA→MH	-0.02 [-.146, .098]	0.01 [-.017, .010]
MOT→PH	-0.20 [-.283, -.126]	MOT→PA	0.02 [-.062, .102]	PA→PH	0.04 [-.086, .157]	0.001 [-.005, .010]
MOT→MH	-0.22 [-.704, -.329]	MOT→PA	0.02 [-.062, .102]	PA→MH	-0.003 [-.123, .118]	-0.001 [-.006, .003]
IF→PH	-0.18 [-.263, -.101]	IF→PA	0.01 [-.070, .097]	PA→PH	0.03 [-.091, .154]	<0.001 [-.004, .008]
IF→MH	-0.19 [-.270, -.109]	MOT→PA	0.02 [-.062, .102]	PA→MH	-0.007 [-.129, .115]	-0.001 [-.005, .002]
Brazilian sample						
Path 1	**Effect**	**Path 2**	**Effect**	**Path 3**	**Effect**	**Total indirect effect**
GFE→PH	-0.19 [-.259,-.103]	GFE→PA	0.02 [-.088, .129]	PA→PH	0.03 [-.128, .188]	0.001 [-.003, .011]
GFE→MH	-0.16 [-.266, -.053]	GFE→PA	0.02 [-.088, .129]	PA→MH	0.05 [-.109, .198]	0.001 [-.004, .012]
PF→PH	-0.17 [-.245, -.112]	PF→PA	-0.03 [-.140, .075]	PA→PH	0.03 [-.127, .189]	-0.001 [-.018, .003]
PF→MH	-0.14 [-.243, -.030]	PF→PA	-0.03 [-.140, .075]	PA→MH	0.03 [-.127, .183]	-0.001 [-.022, .003]
CF→PH	-0.15 [-.241, -.098]	CF→PA	-0.07 [-.172, .036]	PA→PH	0.05 [-.054, .156]	-0.002 [-.022, .007]
CF→MH	-0.14 [-.244, -.037]	CF→PA	-0.07 [-.172, .036]	PA→MH	0.02 [-.139, .171]	-0.001 [-.022, .011]
MOT→PH	-0.08 [-.167, -.005]	MOT→PA	0.06 [-.127, .248]	PA→PH	0.04 [-.122, .194]	-0.001 [-.014, .007]
MOT→MH	-0.11 [-.210, -.013]	MOT→PA	0.06 [-.127, .248]	PA→MH	0.03 [-.128, .185]	-0.001 [-.057, .155]
IF→PH	-0.12 [-.201, -.023]	IF→PA	-0.04 [-.135, .063]	PA→PH	0.03 [-.129, .188]	-0.001 [-.008, .007]
IF→MH	-0.10 [-.190, -.009]	IF→PA	-0.04 [-.135, .063]	PA→MH	0.03 [-.127, .186]	-0.001 [-.010, .009]

Notes: Path 1 = Path between independent and dependent variables; Path 2 = Path between independent variable and mediator; Path 3 = Path between mediator and dependent variable; GFE = Global Fatigue Experience; PF = Physical Fatigue; CF = Cognitive Fatigue; MOT = Motivation; IF = Impact on Function; PH = Physical Health; MH = Mental Health; PA = Physical Activity. For exploratory purposes and since results were similar between samples, the authors examined the model with both samples (total sample). However, the results did not differ significantly from those reported in the manuscript. Thus, we maintained current results from each sample for clarity.

Discussion

The present study aimed to evaluate the influence of fatigue on the quality of life of patients with FM, and to verify whether the level of physical activity can mediate the association between fatigue and quality of life. First, the results of this study showed that women with FM scored above the midpoint on all components of fatigue in both samples. This has been observed in previous studies that showed that patients with FM have higher levels of fatigue and its components, especially at the muscular, cognitive, and emotional levels (Humphrey et al., 2010; Ofluoglu et al., 2005; Zautra et al., 2007). The studies conducted by Humphrey et al. (2010) and Öncü et al. (2013) have shown that fatigue at FM affects patients not only at the physical level but also at the cognitive and psychosocial levels. These patients reported reduced mental resilience and slow thinking, which directly affects their quality of life (Öncü et al., 2013).

Other studies show that patients with FM tend to be more aware of fatigue and its components compared to other pathologies (Offenbaecher et al., 2021; Park et al., 2001; Suhr, 2003; Wolfe et al., 2000). For example, the study by Humphrey et al. (2010) showed that patients described their fatigue as excessive, affecting their motivation to perform desired activities and even interfering with their ability to concentrate, think clearly, and remember certain things or themselves. This was confirmed by the patients in the study by Offenbaecher et al. (2021), where they reported that fatigue is an important symptom of the disease and that it has several important consequences that affect their functioning and well-being.

In terms of quality of life (physical and mental health), the results of the present study indicated that, both in the Brazilian and Portuguese samples, the scores were below the midpoint. This finding is supported by the existing literature (da Costa et al., 2000; Garcia-Martinez et al., 2012; Wolfe et al., 2000), which demonstrates that patients with FM have a low perception of their quality of life. Garcia-Martinez et al. (2012) found in their study that patients with FM had significantly worse levels of quality of life when compared to healthy people, which is understandable given the number of symptoms that patients with FM face. In addition, a study conducted by Wolfe et al. (2000) verified that patients with FM have lower levels of quality of life when compared to patients with other systemic disorders (namely chronic obstructive pulmonary disease and insulindependent diabetes mellitus). Concomitantly, the study carried out by da Costa et al. (2000) verified that women with FM had a lower perception of their quality of life values when compared to women with systemic lupus erythematosus.

The studies conducted by Tander et al. (2008) and Walker et al. (1997) compared patients with FM and rheumatoid arthritis and found that patients with FM had higher values in fatigue and social isolation, and lower values in sleep quality and all parameters of the SF36 in terms of quality of life. The study by Borman & Çeliker (1999) also found that patients with FM had lower levels of quality of life when compared to patients with rheumatoid arthritis. Another important finding was that patients with FM had lower levels of perceived ability to cope with their disease when compared with patients with rheumatoid arthritis. The study by Burckhardt et al. (1993) corroborates these findings, as their study compared the quality of life among patients with FM, rheumatoid arthritis, and osteoarthritis, and found that patients with FM had much lower values in all domains of quality of life.

Neumann et al. (2000) carried out a study comparing the quality of life between patients with FM, patients with generalized chronic pain syndrome, and healthy people, and demonstrated that patients with FM had the lowest values of quality of life. Picavet & Hoeymans (2004) compared 12 different pathologies of the musculoskeletal system (i.e., herniated disc, gout, repetitive strain injury, epicondylitis, knee osteoarthritis, hip osteoarthritis, osteoporosis, whiplash, rheumatoid arthritis, fibromyalgia, tendonitis, and capsulitis), and found that all patients had low scores of quality of life. However, patients with rheumatoid arthritis and FM had the lowest values compared to other pathologies under analysis (Picavet & Hoeymans, 2004).

Yilmaz et al. (2008) carried out a comparative study among four diseases (i.e., knee osteoarthritis, shoulder impingement syndrome, fibromyalgia, and osteoporosis), and found that patients with FM had low values in all quality-of-life scores. The study by Ataoğlu et al. (2018) compared the quality of life of patients with FM, knee osteoarthritis, and rheumatoid arthritis, and found that patients with FM had lower values in all quality of life parameters compared to other diseases (Yilmaz et al., 2008).

The Mediation Role of Physical Activity

In our study, it was possible to verify that physical activity does not play a mediating role in the relationship between fibromyalgia-related fatigue and quality of life. The study developed by Doerr et al. (2017) corroborates our findings, where no association was found between the mediating role of physical activity concerning fatigue and other symptoms associated with FM. However, Sawatzky et al. (2007) verified in their study that physical activity partially mediates the relationship between chronic diseases and

quality of life. Another study with contradictory findings compared to ours was by Molinari et al. (2019) who found that physical activity acted as a possible mediator between FM symptoms and patients' quality of life. These results demonstrated the need for further studies to verify if physical activity can act as a mediator between fibromyalgia-related fatigue and quality of life in patients with FM (Molinari et al., 2019).

Indeed, physical activity is considered an effective tool of controlling the symptoms of FM. It could reduce fatigue, pain, depression, and anxiety, and could promote improvement in quality of life (Busch & Overend, 2009; Busch et al., 2011; Fontaine et al., 2011; Segura-Jiménez et al., 2015).

However, research still differs on what intensity of physical activity is best for FM patients. For instance, the studies conducted by Gavilán-Carrera et al. (2019) and Buman et al. (2010) have shown that patients with FM have better control of fibromyalgiarelated symptoms when they engage in low-intensity physical activity. Further, the studies developed by Fanning et al. (2016) and Kaleth et al. (2013) demonstrated that patients with FM showed improvement in quality of life and relieved symptoms of the syndrome when they participated in a high-intensity physical activity program. However, Clauw (2014) argued that moderate-intensity physical activity is the most effective treatment for the management of fibromyalgia-related symptoms. Therefore, da Cunha Ribeiro et al. (2018) suggested that exercise programs should be individualized. That is, the intensity should be considered based on the patient's limitations, level of physical fitness, and fatigue. In this regard, Rooks (2008) found that the health benefits of physical activity in patients with FM are increased and/or maintained compared to those patients who are physically inactive. Some studies (Larsson et al., 2020; Rooks, 2008) have shown that FM patients undergoing group exercises improved their physical, emotional, and social capacities. Therefore, it is reasonable to assume that the physical activity intensity could act as a possible mediator, however, the type of intensity of physical activity should be further investigated in the future.

Despite all the benefits of physical activity for this type of population, training programs must be supervised by a qualified professional (Ramsay et al., 2000). For example, King et al. (2003) and Ayan et al. (2009) found that patients with FM who adhered to the supervised physical exercise protocol showed an improvement in their ability to manage the FM symptoms. In addition, Sevimli et al. (2015) found that patients who exercise under supervision had a significant reduction in pain and FM impact when compared to other patients who performed physical activity without supervision. One of the factors

that may explain the difference between our results and the existing literature by Ramsay et al. (2000), is that the patients had difficulties in remembering and performing exercise programs without supervision, thus generating a fear that these exercises performed incorrectly could increase pain levels. The study by Kayo et al. (2011) found that after the end of the supervised exercise program, there was low adherence to physical activity by patients, leading to a detraining effect. Thus, it seems that, for physical activity to influence FM symptoms and other related health indicators (e.g., quality of life), exercise programs should be supervised. Hence, we suspect that in our study, physical activity did not mediate the relationship between FM fatigue and both mental and physical health since physical activity was subjectively measured and not determined as supervised exercise.

For instance, the study by Tomas-Carus et al. (2019) demonstrated that in 3 months of exercise, patients demonstrate great relief from pain, and emotional problems, an improvement in quality of life, physical functional capacity, and balance. This same study found that 12 weeks after the end of the experimental intervention, there was a decrease in physical fitness, as well as in some components of quality of life. This demonstrates that the monitoring of physical activity can help to improve the quality of life and attenuate the symptoms of patients with FM.

The study by Salvat et al. (2016) showed that patients who underwent a multidisciplinary treatment, involving supervised physical activity, showed an improvement in their functional status, and an increase in the level of physical activity. However, the study by Ramsay et al. (2000) compared a supervised and unsupervised aerobic exercise program and found that the group that underwent the supervised training program had an improvement in measures of psychological well-being when compared to the other group. Another interesting finding of the study by Ramsay et al. (2000) was that exercise adherence by the unsupervised group was very low when compared to the supervised exercise group.

The study conducted by Burckhardt et al. (1994) compared the effects of an education program (where patients were instructed and performed the activity independently) with exercise monitoring and found that both groups showed improvements in quality of life and self-efficacy. However, only in the group that performed supervised physical activity was there also improvement in pain, fatigue, and muscle stiffness. King et al. (2003) also suggested that for this type of population, it may be better to emphasize the adoption of

a physically active lifestyle, with appropriate professional supervision, rather than just promoting exercise per se.

Practical Implications and Limitations

In recent years, scientific publications on FM have increased considerably, which can be explained by a greater awareness and shared interest from various stakeholders, including patients with FM, specific organizations for these groups, researchers, and professionals in the field of health and physical activity. Although our results show that there does not have a connection between the quality of life and fatigue, some studies (Larsson et al., 2020; Rooks, 2008; Tomas-Carus et al., 2019) show that physical activity is an important tool in reducing fatigue levels and improving quality of life levels in patients with FM.

However, the physical activity prescribed for this population should be supervised and performed in an observational manner. Thus, the professional can adjust and adapt the intensity and volume, so that the patient can better adapt to this type of activity and prevent poor performance, avoiding any worsening of FM symptoms resulting from incorrect or exaggerated physical activity.

Firstly, this study had a cross-sectional design. Therefore, longitudinal/experimental studies may be useful in measuring fatigue symptoms and quality of life in FM patients. Another limitation of this study was the specificity of the sample, where only Portuguese and Brazilian patients took part in the research, meaning that the data obtained could not be generalized and compared to other countries and cultures. In addition, the physical activity was evaluated through a self-reported way (i.e., a questionnaire). It means that no definition of intensity was considered, nor whether there was any type of professional supervising the activity. Therefore, future studies should try to address this limitation to confirm the importance of professional supervision in performing physical activities for these groups.

The age group presented between patients in both samples should be considered as another limitation, since some studies (Jiao et al., 2014; Keskindag, 2018) suggest that patients with younger ages tend to have higher levels of fatigue and lower levels of quality of life when compared to older patients. As a suggestion for future research, studies could be carried out on how age can influence the quality of life, fatigue, and levels of physical activity in patients with FM.

Finally, one more limitation is the participation of male patients, since in the current study, only female participants were included. This decision was made considering the

existing literature which demonstrates that FM has a greater impact in women compared with men, so we opted for a more conservative approach, solely with female patients with FM (Yunus, 2001; Yunus et al., 2000). Nevertheless, future studies should try to collect some data on male FM patients to analyze these associations between genders and explore their impact across cultures.

Conclusion

Overall, the results suggest that physical activity does not mediate the association between quality of life and fatigue in patients with FM. However, the results also show that fatigue dimensions associated with fibromyalgia have negative and significant associations with physical and mental health indicators in both samples. Thus, FM patients with higher scores on fatigue-related symptoms might suffer more from physical and mental health, both of which are related to quality of life.

Study 2: Understanding the Associations across Fibromyalgia-Related Fatigue, Depression, Anxiety, Self-Esteem Satisfaction with Life and Physical Activity in Portuguese and Brazilian Patients: A Structural Equation Modeling Analysis

Abstract

Fibromyalgia is heterogeneous and differ from patient to patient; however, the most reported are general myalgia and at specific points associated with fatigue and certain psychological adversities. Physical activity can mitigate the effects of the symptoms. However, the associations between fibromyalgia-related fatigue, self-esteem, anxiety, depression, satisfaction with life and physical activity are unclear. Therefore, the aim of the present study was to understand the associations between these symptoms and whether there are differences between these associations across two distinct cultures. A total of 473 women aged between 28 and 75 years (M = 49.27; SD ± 8.28) completed five questionnaires about fibromyalgia related fatigue, physical activity, anxiety, depression, self-esteem, and satisfaction with life. Fibromyalgia-related fatigue was positively associated with depression and anxiety, depression and anxiety were negatively associated with self-esteem, self-esteem was positively associated with satisfaction with life, satisfaction with life was positively associated with physical activity and there were no differences in terms of the perceptions and associations of these variables between Portuguese and Brazilian patients. Our results showed the significant role of associations between these variables and a similarity in the perception and relationship of the variables between the two cultures. fibromyalgia; depression; anxiety; self-esteem; satisfaction with life; physical activity

Introduction

Due to its complexity, patients with FM tends to be more vulnerable to psychological conditions (e.g., higher levels of anxiety and depression, low self-esteem and lower levels of life satisfaction) (Garcia-Martinez et al., 2012). Some studies (Oliveira et al., 2009; Walker et al., 1997) have shown that when compared, FM patients demonstrated higher levels of anxiety and depression than patients with other chronic diseases (i.e., rheumatoid arthritis and osteoarthritis). This increase in depressive and anxious conditions affects the social and emotional functioning of FM patients, causing them to avoid socializing, work responsibilities and any type of physical activity, causing a cycle of events that culminates in worsening of the depressive and anxious symptoms and thus reporting lower levels of self-esteem and satisfaction with life, generating a vicious circle (Pizzorno & Murray, 1999; Rudy & Harris, 2001).

Self-esteem is related to self-confidence and expectation of self-efficacy; some studies (Garaigordobil, 2015; Michielsen et al., 2006; Miró et al., 2012; Penacoba Puente et al., 2015) have demonstrated that patients with FM have considerably lower levels of selfesteem in comparison to healthy individuals or those with other chronic diseases. This decrease in self-esteem levels causes a cognitive decline, directly affecting the levels of satisfaction with life, physical activity and fatigue in patients with FM (Galvez-Sanchez et al., 2019).

Satisfaction with life is one of the dimensions associated with quality of life, which is part of the cognitive component of subjective wellbeing, which is increasingly recognized as an important health parameter; lower levels of satisfaction with life may be related to the development or worsening of chronic diseases (Boonstra et al., 2013; Diener & Chan, 2011; Feller et al., 2013) In patients with FM, previous studies (Luque-Reca et al. 2021; Raak et al., 2003; Luque-Reca et al., 2022) have concluded that higher levels of life satisfaction are associated with improved adaptation to FM (i.e., reduced levels of fatigue, anxiety, depression and disease severity).

Therefore, therapies and interventions in patients with FM should act to improve psychological components, as some studies (Arrayás-Grajera et al., 2021; Sin & Lyubomirsky, 2009) revealed that such interventions significantly improve the levels of psychological components, causing an improvement in patients coping with FM.

Physical Activity and Psychological Aspects in FM

Physical activity as a therapy for FM is highly recommended because in addition to being a low-cost intervention, it can improve physical and psychological components (increasing the activity of certain neurotransmitters, such as endorphins and serotonin) and promote a sense of satisfaction and self-efficacy (Larsson et al., 2020; Sawatzky et al., 2007).

Health professionals should always take into account the limitations of each patient and thus evaluate those of physical fitness and fatigue related to fibromyalgia so that it is possible to understand and plan the activities to be performed by patients, minimizing any adversities arising from the training program (Larsson et al., 2020; Rooks, 2008). Patients with FM are recommended to perform physical activities of low to moderate intensity at a frequency of two to three times per week (Larsson et al., 2020; Rooks, 2008).

Patients with FM demonstrate a behavior of rejection to perform physical activities in order to preserve stressor effects, whether physical and/or psychological, which can negatively affect their physical and psychological symptomatology (Russell et al., 2018). Some studies (Cordoba-Torrecilla et al., 2016; McDowell et al., 2017; Munguia-Izquierdo et al., 2021; Sener, 2016; Soriano-Maldonado et al., 2016) have demonstrated that FM patients with higher levels of activity and physical fitness demonstrated lower levels of depression and anxiety.

Differences between Portugal and Brazil in Fibromyalgia

Despite sharing a certain similarity in their language, Portuguese and Brazilian patients have some differences in their FM-related symptoms. In Portugal, it is estimated that 2.1% of the population has a positive diagnosis for FM, with a ratio of six women for every man with a positive diagnosis (EpiReuma, 2013; Gomes, 2010). Branco et al. (2010) that Portugal, when compared with other Western European countries (i.e., Germany, Spain, Italy and France) has the highest number of patients with a positive diagnosis of FM. In Brazil, 2.5% of the population has a positive diagnosis of FM, with a ratio of 1:5 between men and women, respectively (Souza & Perissinotti, 2018). A study by Duenas et al. (2016) showed that one of the leading problems faced by Brazilian patients is difficulty in accessing treatment, care and even a diagnosis due to social disparity and the difficulty in finding health centers due to distance (Duenas et al., 2016).

There is still a lack of studies analyzing and exploring these cross-cultural differences at the symptomatologic level of FM, as some studies (Clark, 2013; Kuppens et al., 2016; Ruiz-Montero, 2019) have shown that socioeconomic, demographic, climatic and even cultural reasons can alter the perception of symptoms by FM patients, causing an improvement or worsening of FM symptom levels.

Therefore, the aim of the present study is to analyze the associations between fibromyalgia related fatigue, depression, anxiety, self-esteem, satisfaction with life and physical activity and to analyze the invariance of these relationships between Brazilian and Portuguese patients. Specifically, we explore the relationships between these psychological components. We hypothesized that (a) fibromyalgia-related fatigue is positively associated with levels of depression and anxiety and negatively related to levels of self-esteem, satisfaction with life and physical activity (Galvez-Sanchez et al., 2018); (b) levels of depression and anxiety are negatively associated with levels of self-esteem (Luque-Reca et al., 2022); (c) self-esteem is positively associated with life satisfaction (Garcia-Martinez et al., 2012); (d) levels of life satisfaction are positively associated with levels of physical activity (Raak et al., 2003); and (e) there are possible differences between Portuguese and Brazilian patients in terms of the associations between the study variables, which is supported by previous studies (Kuppens et al., 2016; Ruiz-Montero, 2019) showing differences between cultures.

Materials and Methods

Study Design and Participants

Two independent samples of Portuguese (sample 1) and Brazilian (sample 2) women with a positive diagnosis of FM participated in present cross-sectional study. First, the participants were asked about their age; nationality; time since diagnosis; and levels of fatigue, depression, anxiety, self-esteem, life satisfaction and physical activity. Sample 1 comprised 222 Portuguese patients aged between 28 and 75 years (M = 49.53; SD ± 8.80). Portuguese patients were diagnosed with FM at a mean age of 9.29 ± 7.71 years. Sample 2 comprised 251 Brazilian patients with FM, aged between 27 and 75 years (M = 49.03; SD ± 8.86). These Brazilian patients had a mean time of diagnosis of 10.05 ± 7.69 years. The required sample size was determined using the Daniel Sopper online calculator [59], and the following input parameters were considered: anticipated effect size (0.3), statistical power level (0.80), number of latent variables (7) and number of observed variables (37) (Westland, 2010). Therefore, the minimum sample size to detect

an effect was 170, the minimum sample size for the model structure was 119 and the recommended minimum sample size was 170, which was respected in the present study for each sample.

We contacted the doctors responsible for the specific FM groups on Facebook, so that they could forward and administer the questionnaires to members with FM. All individuals participated voluntarily in this study, receiving no monetary reward for their contribution. Before data collection, ethical approval was obtained from the ethical and scientific director of the Center for Research in Sport, Health and Human Development (CIDESD) under the reference UID04045 / 2020, Portugal. The current study was conducted in accordance with the Helsinki declaration and its latest amendments.

Procedure: Data Collection

The Ethics and Science Committee of the University of Beira Interior, Covilhã, Portugal (UBI) granted approval for this study (reference number CE-UBIPj- 2021-038). The present study was conducted according to the standards defined by the Declaration of Helsinki (Association, 2013).

For data collection, two institutions related to FM (National Association Against Fibromyalgia and Chronic Fatigue Syndrome, Lisbon, Portugal (MYOS) and the National Association of Fibromyalgia, São Paulo, Brazil (ABRAFIBRO)) were contacted, and the objectives of the study were explained. With the approval, these institutes referred some patients who voluntarily chose to participate in the study. These patients were contacted by the authors, and the purpose and objectives of the study were explained, and information was provided, with details about the data collection process. After contact and clarification, each participant filled out the informed consent, where it was explained that the individuals would participate in this study voluntarily and anonymously. The time to answer the questionnaires was approximately 35 min. MYOS is a Portuguese institution that helps people with FM and chronic fatigue syndrome and is composed of about 7000 patients with a positive diagnosis of FM, 500 of whom were contacted by the researchers, resulting in 227 participants who answered the questionnaires. Evaluation of the completed questionnaires revealed that five patients did not answer correctly, resulting in their exclusion, for a total of 222 Portuguese patient participants. ABRAFIBRO is a Brazilian institution that helps patients with FM, with a total of more than 6000 people diagnosed with the disease. With the help of this institution, 580 FM patients were contacted, and 253 patients answered the proposed questionnaires. Of

these, only two participants did not fill out the questionnaire correctly, resulting in the exclusion of these patients from the study, for a total of 251 Brazilian participants.

Instruments

Fibromyalgia-Related Fatigue

The questionnaire used to measure fibromyalgia-related fatigue levels was the Multidimensional Diary of Fatigue-Fibromyalgia-17 (MDF-Fibro-17), using the validated and translated version for the Portuguese and Brazilian populations (Alvarez et al., 2020). The MDF-Fibro-17 includes 17 questions evaluating the various dimensions of fatigue. The questionnaire comprises five sections: global fatigue experience, consisting of 4 questions, for example, “How severe was your fatigue today?”; physical fatigue, consisting of 3 questions, for example, “How heavy did your body feel today?”; cognitive fatigue, consisting of 4 questions, for example, “How difficult was it to think clearly due to tiredness today?”; motivation, measured by 3 questions, such as, ”How difficult was it to motivate yourself to do something today?”; and the role impact, composed of 3 questions, for example, “Did you do something slower because you were feeling tired today?”. Participants evaluated fatigue components using a scale ranging from 0 (“not at all”) to 10 (“extremely”). Higher values indicate a higher level of fatigue. Previous studies support the validity, reliability and use of this questionnaire (Alvarez et al., 2020; Li et al., 2017). However, in the present study, only global fatigue experience, and physical and cognitive fatigue were used, as several previous studies (Galvez-Sanchez et al., 2019; Munguia-Izquierdo et al., 2021) showed that these factors affect more of the psychological components in FM patients.

Hospital Anxiety and Depression Scale (HADS)

To measure anxiety and depression levels, the Portuguese version of the Hospital Anxiety and Depression Scale was used (Pais-Ribeiro et al., 2007). This instrument consists of 14 questions, seven of which assess all aspects of anxiety and the other seven of which measure depression levels. This questionnaire employs a 4-point Likert scale (from 0 to 3); higher values represent higher levels of anxiety and depression. A study by Bjelland et al., 2002 demonstrated that the HADS Portuguese version is well-structured and is reliable and precise in terms of measuring depressive and anxious conditions, as well as symptoms of anxiety and depression disorders.

Self-Esteem

The Portuguese version of the Rosenberg Self-Esteem Scale (Faria & Silva, 2000) was used to assess selfesteem. Although the original version contains 10 items, for present study, we considered the 5 positively coded items (e.g., "On the whole, I am satisfied with myself"), as the negatively coded items can contaminate results (van Sonderen et al., 2013). The participants answered on a four-point Likert scale, with possible responses varying between 1 ("strongly agree") and 4 ("strongly disagree"). The Rosenberg SelfEsteem Scale is widely used, and previous studies support its validity and reliability (Baumeister et al., 2003).

Satisfaction with Life

The Portuguese version of the Satisfaction with Life Scale (Neto, 1993) was used to measure global cognitive judgement the subjects' life satisfaction. This scale has five questions (for example, "I'm happy with my life."), and participants responded using a 5-point Likert scale, where 1 represents strongly disagree and 5 represents strongly agree. A study by (Teixeira et al., 2021) demonstrated the reliability and validity of this instrument.

Physical Activity

To measure physical activity levels, we used the International Physical Activity Questionnaire (IPAQ) short form (Craig et al., 2003). This questionnaire has seven questions, which are related to intense, moderate and walking activities performed in the last seven days before the completion of the questionnaire (Benitez-Porres et al., 2013).

Another value obtained through the IPAQ is an estimate of energy expenditure derived from levels of physical activity (Benitez-Porres et al., 2013). In other words, the data are converted into MET min/week by calculating the minutes per week in each type of activity performed by the patient according to the specific metabolic equivalent (Benitez-Porres et al., 2013; IPAQ, 2005).

Statistical Analysis

Descriptive statistics and bivariate correlation were calculated for variables under analysis. The hypothesized model was test with AMOS v.27 based on a two-step maxi mum likelihood approach, as suggested by Kline (2016). The first step was a confirmatory factor analysis (CFA) to analyze the psychometric properties of the model. In particular, internal consistency was determined via composite reliability according to Raykov (2016), with 0.70 as a cutoff value (Hair et al., 2019); convergent validity was assessed

through average variance extracted (AVE) (Hair et al., 2019), considering values higher than or equal to 0.50 as an adequate value; and discriminant validity via square correlations between factors, considering correlation coefficients lower than the AVE for each construct adequate (Fornell & Larcker, 1981). Then, a second step was performed based on structural equation modeling (SEM) to analyze the purposed associations. Standardized direct and indirect effects on the outcome variable were analyzed, considering coefficients significant if the 95% confidence intervals (CIs) were greater than zero (Williams & Mackinnon, 2008). Bootstrap resampling (1000 samples) considering a bias-corrected 95% CI was used to assess the significance of the direct and indirect effects. The adequacy of the models was evaluated using the following traditional incremental and absolute indices: comparative fit index (CFI), Tucker–Lewis index (TLI), standard root mean residual (SRMR) and root mean square error of approximation (RMSEA) with its confidence interval (CI: 90%); the following cutoff values were adopted: CFI and TLI ≥ 0.90, SRMR and RMSEA ≤ 0.8 [76,79,80].

Multigroup Analysis

An SEM multigroup analysis was performed according to the suggestion of Byrne (2016) to test whether the proposed SEM model can be replicated in groups with different characteristics. Hence, the procedures recommended by Byrne (2016) and Cheung & Rensvold (2002), were followed. First, the SEM model should be adjusted to each group under analysis, and the following invariance types should be respected: unconstrained model, measurement weights, structural weights, structural covariances, structural residuals and measurement residuals. Invariance assumptions were verified through the differences in CFI (ΔCFI), using <0.01 a cutoff value (Byrne, 2016).

Full information robust maximum likelihood (FIML) was used to handle the small amount of missing data at the item level (missing at random = 2%), as proposed by Enders (2010). Then, we analyzed descriptive statistics and bivariate correlations. The values of skewness and kurtosis (between −2 and +2 and −7 and +7, respectively) revealed no deviations from univariate normality (Hair, 2019). However, the normalized estimate of Mardia's coefficient of multivariate kurtosis was greater than 5.0 in all samples under analysis. Consequently, Bollen–Stine bootstrap (2000 samples) was employed for subsequent analysis (Nevitt & Hancock, 2001).

Results

Preliminary analysis

The measurement model, including the factors of global fatigue experience, physical fatigue, cognitive fatigue, depression, anxiety, self-esteem, satisfaction with life and physical activity exhibited adequate fit to the data in all samples under analysis: general sample: $\chi 2 = 979.83$ (364), BS-p < 0.001, CFI = 0.939, TLI = 0.929, RMSEA = 0.062 90% (0.057, 0.066) and SRMR = 0.043; Brazilian Sample: $\chi 2 = 895.83$ (364), BS-p < 0.001, CFI = 0.922, TLI = 0.919, RMSEA = 0.073 90% (0.063, 0.078) and SRMR = 0.052; Portuguese Sample: $\chi 2 = 921.64$ (364), BS-p < 0.001, CFI = 0.932, TLI = 0.921, RMSEA = 0.061 90% (0.055, 0.067) and SRMR = 0.045. CFI and TLI were above and SRMR and RMSEA were below to the previously reported cutoff values.

Descriptive Statistics and Bivariate Correlations

Descriptive statistics showed that the participants presented scores above the midpoint for fibromyalgia-related fatigue, depression, anxiety and self-esteem and scores below the midpoint for satisfaction with life. The participants also showed a total amount of physical activity above 1000 Metz in the general sample. The same tendency was observed across the Portuguese and Brazilian samples, except for depression, for which the obtained values were below midpoint, and in terms of physical activity; the Portuguese sample seemed to be physically more active than the Brazilian patients (MET = 1721 vs. MET = 1334). With respect to correlation patterns in all samples analyzed, fibromyalgia-related fatigue was positively associated with depression and anxiety and negatively associated with self-esteem and satisfaction with life. In addition, fibromyalgia-related fatigue, particularly cognitive fatigue, showed a negative and significant association with physical activity, whereas global fatigue experience and physical fatigue did not present any association with physical activity. Depression and anxiety showed a negative and significant association with self-esteem, satisfaction with life and physical activity, whereas self-esteem and satisfaction with life were positively and significantly associated, as well as with physical activity, as shown in Tables 3–5.

Table 3. Descriptive statistics, bivariate correlations, average variance extracted values, and composite reliability coefficients in general sample.

Variables	M	SD	1	2	3	4	5	6	7	8	AVE	CR
1. GFE	7.66	1.71	1	-	-	-	-	-	-	-	0.83	0.95
2. PF	7.98	1.69	0.87**	1	-	-	-	-	-	-	0.87	0.95
3. CF	7.44	1.88	0.78**	0.77**	1	-	-	-	-	-	0.79	0.92
4. Depression	1.52	0.67	0.36**	0.36**	0.39**	1	-	-	-	-	0.51	0.80
5. Anxiety	2.01	0.68	0.35**	0.37**	0.38**	0.67**	1	-	-	-	0.50	0.79
6. Self-Esteem	3.01	0.92	-0.14*	-0.10**	-0.12**	-0.55**	-0.36**	1	-	-	0.53	0.82
7. SWL	2.40	0.87	-0.34**	-0.29**	-0.38**	-0.69**	-0.56**	0.45**	1	-	0.87	0.87
8. PA	1527	401.83	0.02	0.01	-0.24**	-0.10**	-0.17**	-0.16**	-0.18**	1	-	-

Note. M = Mean; SD = Standard Deviation; GFE= global fatigue experience; PF= physical fatigue; CF= cognitive fatigue; SWL= Satisfaction with life; PA= physical activity in METS per week; AVE= average variance extracted; CR= composite reliability * p<0.05; ** p<0.01.

Table 4. Descriptive statistics, bivariate correlations, average variance extracted values, and composite reliability coefficients in Brazilian sample.

Variables	M	SD	1	2	3	4	5	6	7	8	AVE	CR
1. GFE	7.67	1.74	1	-	-	-	-	-	-	-	0.83	0.94
2. PF	7.98	1.73	0.88**	1	-	-	-	-	-	-	0.86	0.95
3. CF	7.45	1.91	0.79**	0.77**	1	-	-	-	-	-	0.79	0.93
4. Depression	1.41	0.68	0.36**	0.37**	0.41**	1	-	-	-	-	0.50	0.79
5. Anxiety	2.02	0.69	0.35**	-0.11**	0.39**	0.69**	1	-	-	-	0.50	0.79
6. Self-Esteem	3.02	0.91	-0.16*	-0.31**	-0.13**	-0.56**	-0.38**	1	-	-	0.54	0.81
7. SWL	2.41	0.87	-0.33**	-0.32**	-0.39**	-0.71**	-0.55**	0.48**	1	-	0.88	0.87
8. PA	1334	368.12	0.04	0.03	-0.26**	-0.11**	-0.18**	-0.18**	-0.21**	1	-	-

Note. M = Mean; SD = Standard Deviation; GFE= global fatigue experience; PF= physical fatigue; CF= cognitive fatigue; SWL= Satisfaction with life; PA= physical activity in METS per week; AVE= average variance extracted; CR= composite reliability * p<0.05; ** p<0.01.

Table 5. Descriptive statistics, bivariate correlations, average variance extracted values, and composite reliability coefficients in Portuguese sample.

Variables	M	SD	1	2	3	4	5	6	7	8	AVE	CR
1. GFE	7.67	1.68	1	-	-	-	-	-	-	-	0.84	0.95
2. PF	7.98	1.66	0.89**	1	-	-	-	-	-	-	0.86	0.95
3. CF	7.42	1.85	0.79**	0.78**	1	-	-	-	-	-	0.80	0.94
4. Depression	1.39	0.67	0.37**	0.38**	0.42**	1	-	-	-	-	0.51	0.80
5. Anxiety	2.10	0.67	0.35**	-0.13**	0.40**	0.70**	1	-	-	-	0.51	0.79
6. Self-Esteem	3.00	0.93	-0.17*	-0.32**	-0.14**	-0.57**	-0.39**	1	-	-	0.54	0.81
7. SWL	2.40	0.85	-0.34**	-0.34**	-0.41**	-0.70**	-0.56**	0.49**	1	-	0.89	0.88
8. PA	1721	575.04	0.06	0.04	-0.27**	-0.12**	-0.19**	-0.18**	-0.23**	1	-	-

Note. M = Mean; SD = Standard Deviation; GFE= global fatigue experience; PF= physical fatigue; CF= cognitive fatigue; SWL= Satisfaction with life; PA= physical activity in METS per week; AVE= average variance extracted; CR= composite reliability * p<0.05; ** p<0.01.

Direct and Indirect Regression Paths

The results from the SEM analysis showed that the structural model provided an acceptable fit to the data in all samples: General sample: χ 2 = 2254. 95 (382), BS-p < 0.001, CFI = 0.949, TLI = 0.938, RMSEA = 0.071 90% (0.053, 0.087) and SRMR = 0.072; Brazilian sample: χ 2 = 1993.27 (382), BS-p < 0.001, CFI = 0.942, TLI = 0.929, RMSEA = 0.074 90% (0.057, 0.091) and SRMR = 0.071; and Portuguese sample: χ 2 = 1883.37 (382), SRMR = 0.073, BS-p < 0.001, CFI = 0.9446, TLI = 0.932, RMSEA = 0.071 90% (0.052, 0.083) and SRMR = 0.070.

Table 6 shows the direct regression paths among studied variables in all samples. Specifically, the following associations were observed: (i) fibromyalgia-related fatigue showed a positive and significant association with anxiety and depression, (ii) depression and anxiety displayed a negative and significant association with self-esteem, (iii) selfesteem demonstrated a positive and significant association with satisfaction with life and (iv) satisfaction with life displayed a positive and significant association with physical activity.

Table 6. Direct regression paths

Path	Effect	CI 95%	p
GFE→Depression	0.14	[0.073, 0.318]	0.003
GFE→Anxiety	0.18	[0.133, 0.287]	0.002
PF→Depression	0.19	[0.132, 0.325]	0.004
PF→Anxiety	0.16	[0.142, 0.268]	0.003
CF→Depression	0.25	[0.066, 0.409]	0.001
CF→Anxiety	0.23	[0.035, 0.387]	0.001
Anxiety →Self-Esteem	-0.29	[-0.661, -0.376]	0.001
Depression→Self-Esteem	-0.53	[-0.656, -0.386]	0.001
Self-Esteem→SWL	0.51	[0.395, 0.612]	0.001
SWL→PA	0.27	[0.315, 0.566]	0.001
Brazilian Sample			
GFE→Depression	0.16	[0.071, 0.388]	0.025
GFE→Anxiety	0.20	[0.022, 0.298]	0.002
PF→Depression	0.18	[0.135, 0.329]	0.003
PF→Anxiety	0.19	[0.157, 0.279]	0.002
CF→Depression	0.28	[0.086, 0.433]	0.001
CF→Anxiety	0.25	[0.045, 0.3418]	0.001
Anxiety →Self-Esteem	-0.31	[-0.768, -0.299]	0.001
Depression→Self-Esteem	-0.55	[-0.686, -0.359]	0.001
Self-Esteem→SWL	0.52	[0.399, 0.652]	0.001
SWL→PA	0.29	[0.352, 0.598]	0.001
Portuguese Sample			
GFE→Depression	0.17	[0.079, 0.396]	0.003
GFE→Anxiety	0.21	[0.196, 0.315]	0.002
PF→Depression	0.18	[0.128, 0.314]	0.003
PF→Anxiety	0.19	[0.192, 0.303]	0.002
CF→Depression	0.28	[0.101, 0.514]	0.001
CF→Anxiety	0.27	[0.034, 0.413]	0.001
Anxiety →Self-Esteem	-0.28	[-0.651, -0.356]	0.001
Depression→Self-Esteem	-0.54	[-0.676, -0.317]	0.001
Self-Esteem→SWL	0.50	[0.399, 0.599]	0.001
SWL→PA	0.30	[0.403, 0.678]	0.001

Note. GFE= global fatigue experience; PF= physical fatigue; CF= cognitive fatigue; SWL= satisfaction with life; PA=physical activity; CI 95%= confidence interval at 95%; p = level of significance

The indirect regression paths, in all samples, showed that neither global fatigue experience nor physical fibromyalgia-related fatigue are indirectly associated with selfesteem, satisfaction with life and physical activity through depression and anxiety, selfesteem and satisfaction with life, respectively. However, fibromyalgia-related fatigue in terms of cognitive fatigue showed a positive indirect association with self-esteem and

satisfaction with life and a positive indirect association with physical activity, with depression and anxiety, self-esteem and satisfaction with life as a possible mediator, respectively. In addition, depression and anxiety displayed a negative indirect association with satisfaction with life via self-esteem. Nevertheless, depression and anxiety showed a positive and negative indirect association with physical activity, with satisfaction with life as a mediator. Furthermore, self-esteem displayed a negative association with physical activity via satisfaction with life as possible mediator, as shown in Table 7.

Table 7. Indirect regression paths

Path	Effect	CI 95%	p
	General Sample		
GFE→Self-Esteem	-0.07	[-0.203, 0.047]	0.230
GFE→SWL	-0.04	[-0.111, 0.024]	0.221
GFE→PA	0.004	[-0.001, 0.018]	0.148
PF→Self-Esteem	-0.06	[-0.201, 0.072]	0.340
PF→SWL	-0.03	[-0.111, 0.038]	0.323
PF→PA	0.005	[-0.003, 0.017]	0.216
CF→Self-Esteem	-0.15	[-0.271, -0.044]	0.005
CF→SWL	-0.08	[-0.151, -0.002]	0.005
CF→PA	0.12	[0.056, 0.189]	0.011
Anxiety →SWL	-0.05	[-0.115, -0.012]	0.032
Depression→SWL	-0.27	[-0.386, -0.165]	0.005
Anxiety →PA	-0.006	[-0.001, 0.019]	0.099
Depression→PA	0.03	[0.009, 0.061]	0.015
Self-Esteem→PA	-0.06	[-0.110, -0.013]	0.020
	Brazilian Sample		
GFE→Self-Esteem	-0.06	[-0.193, 0.042]	0.267
GFE→SWL	-0.03	[-0.012, 0.018]	0.334
GFE→PA	0.006	[-0.003, 0.021]	0.251
PF→Self-Esteem	-0.06	[-0.201, 0.072]	0.340
PF→SWL	-0.05	[-0.211, 0.048]	0.381
PF→PA	0.004	[-0.002, 0.012]	0.316
CF→Self-Esteem	-0.18	[-0.381, -0.074]	0.004
CF→SWL	-0.09	[-0.162, -0.005]	0.005
CF→PA	0.12	[0.077, 0.201]	0.009
Anxiety →SWL	-0.07	[-0.134, -0.034]	0.029
Depression→SWL	-0.28	[-0.401, -0.179]	0.004
Anxiety →PA	-0.004	[-0.001, 0.014]	0.114
Depression→PA	0.06	[0.010, 0.091]	0.012
Self-Esteem→PA	-0.08	[-0.123, -0.015]	0.019
	Portuguese Sample		
GFE→Seld-Esteem	-0.09	[-0.214, 0.057]	0.211
GFE→SWL	-0.05	[-0.124, 0.057]	0.221
GFE→PA	0.002	[-0.001, 0.010]	0.377
PF→Self-Esteem	-0.08	[-0.390, 0.096]	0.290
PF→SWL	-0.04	[-0.123, 0.047]	0.297
PF→PA	0.004	[-0.002, 0.012]	0.236
CF→Self-Esteem	-0.17	[-0.292, -0.057]	0.005
CF→SWL	-0.10	[-0.167, -0.006]	0.004
CF→PA	0.14	[0.066, 0.212]	0.008
Anxiety →SWL	-0.07	[-0.127, -0.023]	0.028
Depression→SWL	-0.29	[-0.395, -0.178]	0.004
Anxiety →PA	-0.004	[-0.001, 0.014]	0.100
Depression→PA	0.05	[0.091, 0.067]	0.020
Self-Esteem→PA	-0.07	[-0.1117, -0.012]	0.023

Note. GFE= Global fatigue experience; PF= physical fatigue; CF= cognitive fatigue; SWL= satisfaction with life; PA=physical activity; CI 95%= confidence interval at 95%; p = level of significance.

Multigroup Analysis

The results of multigroup analysis (see Table 8) evidenced that the hypothesized SEM model was invariant between countries, as all the invariance criteria were attained,

meaning that all factor loadings, structural paths, factor covariances, factor residual variances and measurement error variances were equivalent between countries (ΔCFI < 0.01).

Table 8. Goodness-of-fit indexes for the invariance of the structural model between countries

Model	χ^2	df	Δ χ^2	Δdf	p	CFI	ΔCFI
Brazilian vs Portuguese							
UM	2978.084	1170	-	-	-	0.933	-
MW	2980.674	1199	2.580	29	0.026	0.931	0.002
SW	2981.360	1208	3.276	38	0.054	0.930	0.003
SR	2983.118	1215	5.030	45	<.001	0.929	0.004
MR	2989.010	1251	10.926	81	<.001	0.921	0.008

Note. χ^2= Chi-square; Δχ^2= differences in value of chi-square; Δdf = differences in degrees of freedom; p= level of significance; CFI= comparative fit index; ΔCFI= differences in the value of the comparative fit index; UM: unconstrained model; MW: measurement weights; SW: structural weights; SR: structural residuals; MR: measurement residuals.

Discussion

Descriptive Statistics and Bivariate Correlations

The aim of this study was to analyse the associations across fibromyalgia-related fatigue, depression, anxiety, self-esteem, satisfaction with life and physical activity. We obtained interesting findings that may add to the scarce literature on fibromyalgia-related fatigue. In addition, the stability of the proposed model was tested by means of cross-country (Brazil and Portugal) multigroup analyses. Initially, five hypotheses were proposed, which will be discussed according to the current literature.

With respect to the values of descriptive statistics, the composite reliability of each factor showed an adequate internal consistency for all studied variables in all samples under analysis, as the obtained values were higher than to 0.70. In addition, convergent validity was found to be acceptable (AVE ≥ 0.50), and discriminant validity was also adequate due to the square correlations between factors and AVE of each factor, as shown in Tables 3–5. In summary, these results support the preliminary conditions necessary to perform SEM analysis, as well as to analyze the direct and indirect effects among the studied variables.

The participants in this study presented scores above the midpoint for fatigue, depression, anxiety and self-esteem related to fibromyalgia and values below the midpoint for satisfaction with life; this scenario was verified both in the global sample

and in the samples separated between Brazilian and Portuguese populations. These results were expected according to the current literature; however a factor of difference was that our patients demonstrated above-average values for self-esteem, in contrast to the results of other studies (Galvez-Sanchez et al., 2018; Garaigordobil, 2015), which demonstrated that patients tend to have lower levels of self-esteem due to the adversity caused by FM.

Direct and Indirect Regression Paths

Regarding the first hypothesis, our results showed that fibromyalgia-related fatigue is positively associated with depression and anxiety and negatively associated with levels of self-esteem, life satisfaction and physical activity, confirming our expectations, thus demonstrating how fibromyalgia-related fatigue may be an important aspect of psychological aspects. Owing to these associations, it is likely that patients with higher levels of fatigue tend to have higher levels of depression and lower levels of self-esteem, satisfaction and physical activity. A study carried out by Kurtze & Svebak (2001) corroborates these findings, revealing that when fatigue levels in patients with FM increased, anxiety and depression levels also increased, demonstrating a positive association between these components.

Our findings are in line with the results of several previous studies (Luque-Reca et al., 2022; Raak et al., 2003), which demonstrated that fatigue is negatively associated with life satisfaction and self-esteem. In their study, Galvez-Sanchez et al. (2018) explained that this negative association might occur because patients with FM require an increased effort, with above-normal pain, to perform e tasks (such as daily activities and work tasks) due to their fatigue, thus causing a feeling of frustration and decreased expectation of self-efficacy, directly affecting the levels of self-esteem and satisfaction with life. This assumption seems to be confirmed by Johnson et al. (1997), who it demonstrated that chronicity of Fibromyalgia-related fatigue ends up exposing the patient to extreme situations, which causes long-term psychological damage, thus affecting his/her selfconfidence, self-esteem and satisfaction with life.

Another interesting finding of the present study is the negative and significant association between cognitive fatigue and physical activity levels, whereas the overall experience of fatigue and physical fatigue showed no association. Van As et al. (2021) defined cognitive fatigue as a psychobiological state characterized by cognitive wasting, causing a series of negative feelings and leading to low levels of energy and positive affect

in patients, resulting in decreased performance of physical activities. However, studies by Lukkahatai et al. (2016) and Vicent et al. (2013) showed that fatigue and all its domains are negatively and significantly associated with physical activity, demonstrating that there is a need for further in-depth studies to verify these associations between the domains of fatigue and physical activity.

In the case of the second hypothesis, we confirmed the negative association between the levels of depression and anxiety with self-esteem, thus confirming our expectations, suggesting that patients who present with higher levels of anxiety and depression tend to have lower levels of self-esteem. A study by (Michalak et al., 2011) corroborates the findings of this study, demonstrating a negative association between depression and anxiety with self-esteem.

This negative association between depression and anxiety with self-esteem can be explained by the fact that anxious and depressive conditions directly affect the lifestyle of FM patients, leading them to opt for social isolation and fostering a feeling of frustration and sadness, thus causing a decrease in self-esteem in these patients (Pizzorno & Murray, 1999; Rudy & Harris, 2001). Sowislo & Orth (2013) performed a review of the associations between depression, anxiety and self-esteem and observed that low self-esteem is a consequence and not a causative factor because depressive episodes leave permanent scars on the self-concept, as in the anxiety state, it can generate a feeling of constant threat in patients and can reduce self-concept, thereby reducing self-esteem, demonstrating that depression and anxiety share high negative affectivity, i.e., stable disposition to non-specific distress and unpleasant mood, affecting levels of self-esteem.

In the present study, we also observed a positive association between the levels of selfesteem and life satisfaction. This shows that patients with higher levels of self-esteem tend to experience improved life satisfaction. Some studies (Asbring, 2001; GalvezSanchez et al., 2019) have shown that FM patients with low levels of self-esteem have reduced cognitive performance, especially in terms of attention, memory and planning skills, thus affecting their self-identity and their life satisfaction. Some studies (Diener & Diener, 1995; Hong & Giannakopoulos, 1994) have shown that self-esteem acts as a strong predictor of life satisfaction because self-esteem is considered an important subjective construct based on personal perception and evaluation, involving not only the emotional aspect but also the performative aspect of functioning, which, once decreased, affects the levels of satisfaction in various areas of life (i.e., interpersonal relationships, cognitive and health changes, success and failure to perform tasks).

Our results further confirmed another hypothesis; levels of life satisfaction are positively associated with physical activity, which can demonstrate the need for health professionals seek ways for FM patients to feel more satisfied with life by increasing levels of physical activity. Previous studies (Soriano-Maldonado et al., 2016; Wiese et al., 2017) have shown that people with higher levels of life satisfaction have higher levels of physical activity and physical fitness. A possible explanation for this positive association is that physical activity, besides having a physiological impact, also affects the subjective wellbeing of the patient, thus improving psychological components, especially the levels of life satisfaction (Cordoba-Torrecilla et al., 2016; Munguia-Izquierdo et al., 2021; Soriano-Maldonado et al., 2016).

With respect to indirect effects, the overall experience of fatigue and physical fatigue showed no association with self-esteem, life satisfaction and physical activity, but cognitive fatigue showed an indirect positive association with self-esteem, life satisfaction and physical activity, with the amount of depression and anxiety, self-esteem and life satisfaction as possible mediators, respectively. In addition, depression and anxiety showed a negative indirect association with life satisfaction through self-esteem. However, depression and anxiety showed an indirect positive and negative association with physical activity, respectively, with life satisfaction as a mediator. It was also possible to verify that self-esteem showed a negative association with physical activity, with life satisfaction as a possible mediator. These analyses of the indirect regression pathway provided additional information supporting our hypotheses and identified some important new perceptions related FM and how fatigue relates to psychological components and physical activity levels.

The results of this study support the significant role FM as a complex health condition, whereby therapies, especially physical activity, should focus on improving subjective wellbeing because a according to some cross-sectional studies (Gowans et al., 2001; Redondo et al., 2004; Wiese et al., 2017), FM patients with better physical fitness and higher levels of physical activity are associated with lower levels of depression, fatigue, anxiety and higher quality of life, life satisfaction and self-esteem.

Multigroup Analysis

The results of multigroup analysis showed that the model was structurally invariant across countries, confirming the similarity of the model across two investigated cultures. More specifically, the results demonstrate that the variables underlying the structural

model were perceived in the same way by Brazilian and Portuguese FM patients and that the hypothesized relationships in the model could be interpreted in a similar way and with equivalent associations for all groups. Furthermore, these results are not only important because they support the relationships between fibromyalgia-related fatigue, including the experience of global fatigue, physical and cognitive fatigue, depression, anxiety, self-esteem, life satisfaction and physical activity, but also support the notion that the expected relationships between constructs may be generalizable to both Portugal and Brazil. Furthermore, this exposes the importance of these associations in PA of FM patients, reinforcing the suitability of this model for FM patients to increase their PA.

To the best of our knowledge, this is the first study to simultaneously examine the crosscultural invariance between Portuguese and Brazilian populations considering all of these variables; however, our results disproved our hypothesis that there were cultural differences in terms of the associations between these variables, as suggested by previous literature (Clark, 2013; Kuppens et al., 2016; Ruiz-Montero et al., 2015; Ruiz-Montero, 2019; Sallinen et al., 2011) reporting differences in associations and perceptions of FM symptoms between cultures. Kuppens et al. (2016) conducted a comparative study of FM patients from different cultures and found that Belgian patients demonstrated higher levels of fatigue and increased severity in psychological symptoms when compared to Dutch patients. This scenario was verified by Ruiz-Montero et al. (2015), who found that Spanish patients showed higher values of associations between fatigue, anxiety and depression when compared to patients from Sweden, Belgium and the Netherlands. Our findings are in line with the results of a study by Clark et al. (2013), who compared the perception and association of fatigue, anxiety, depression, difficulty in concentrating and pain symptoms of FM between European and Latin American patients and found that Latin American patients reported higher levels of these symptoms. Therefore, the results of this study reinforce the need for more in-depth studies to verify the influence of cultural aspects on the associations between fibromyalgia-related fatigue, anxiety, depression, self-esteem, satisfaction with life and physical activity.

Practical Implications and Limitations

The number of scientific publications on FM, especially in the area of therapies for symptom control, has increased in recent years, as it has been verified that interventions, among which physical activity stands out, have achieved positive results in treating the symptoms of FM patients. The results of this study offer a significant contribution to the literature with respect to the association between fibromyalgia-related fatigue,

psychological components and physical activity, helping to fill a gap in the literature, as it is the first study to verify the association of all these variables simultaneously, which demonstrates how FM is a delicate and complex health condition that must be further studied and explored to ensure a better quality of life for FM patients. The uniqueness of this study further reinforces the importance of assessing fatigue in patients with FM, as it is one of the main barriers to physical activity and directly affects the levels of anxiety, depression, life satisfaction and self-esteem, independent of culture.

Although the present study contributes new knowledge and data on the associations between fibromyalgia-related fatigue, depression, anxiety, self-esteem, life satisfaction, and physical activity, it is subject to some limitations that should be addressed. The present study was conducted with a cross-sectional design; further studies should be conducted using different approaches (i.e., longitudinal or experimental) to verify the associations between the variables investigated in this study. In addition, physical activity was evaluated through a subjective questionnaire, so the actual intensity of each activity reported by the patients was not necessarily considered due to a lack of supervisors to verify the conditions under which such activities were performed. In the present study, only female patients answered the proposed questionnaires, preventing generalization of the findings to male patients with FM. Future studies should include male patients for comparison with the results presented herein. A further limitation of this study is that we did not verify whether the patients used any type of medication to control FM symptoms. Therefore, futures studies should make an effort to collect data on this indicator for use as a possible moderator across studied variables.

Conclusion

One of the main strengths of the current study is the considerable sample size of patients with FM, from which it was possible to verify the relationships between the studied variables. Another positive aspect of our study is the use of psychometrically valid and reliable measures to evaluate of the proposed variables. The use of these instruments allowed us to make more reliable comparisons between studies. Another strong point is the uniqueness of this study, as it is the first study to analyze and compare the proposed variables simultaneously, in addition to a comparison between two distinct cultures.

In general, our results showed significant associations between fibromyalgia-related fatigue, depression, anxiety, self-esteem, life satisfaction and physical activity, with no difference in perception and association between two distinct cultures. Thus, patients

with FM who have higher levels of fatigue, especially in the domain of cognitive fatigue, tend to have higher levels of anxiety and depression, causing a possible decrease in levels of self-esteem, life satisfaction and physical activity. In addition, it seems that fibromyalgia related fatigue, depression and anxiety, self-esteem, satisfaction of with life and physical activity follow a similar trend, independent of the patient's culture.

Study 3: Exploring the Difference Across Fibromyalgia-Related Fatigue, Quality of Life, Depression, Anxiety, Self-Esteem, Satisfaction with Life and Physical Activity in Brazilian and Portuguese Patients.

Abstract

Fibromyalgia (FM) is a chronic, persistent neurological, musculoskeletal condition that causes sensory changes and muscle pain, and its pathophysiology is still debated by experts. The aim of this study was to analyse the differences between FM-related fatigue, quality of life, depression, anxiety, self-esteem, life satisfaction and physical activity between Brazilian and Portuguese patients. Two independent samples of Portuguese and Brazilian women with a positive diagnosis of FM took part in this cross-sectional study. 222 Portuguese patients aged between 28 and 75 years (M = 49.53; SD 8.80) and 251 Brazilian patients with FM, aged between 27 and 75 years, answered the six proposed questionnaires measuring levels of fatigue, quality of life, anxiety and depression, selfesteem, satisfaction with life and physical activity. The results show that both samples had above-average scores for fatigue, depression and anxiety, and below-average scores for quality of life, self-esteem, life satisfaction and physical activity levels. The Brazilian patients had higher scores in all the domains of fatigue, physical quality of life and depression, while the Portuguese patients had higher scores in terms of mental quality of life, self-esteem, satisfaction with life and physical activities, but no significant differences were found between the two cultures studied. Our results showed that Brazilian patients had levels above the midpoint for negative symptoms (fatigue, depression and anxiety) and lower values for satisfaction with life. However, there are significant differences in the perception of these symptoms.

Fibromyalgia, quality of life, depression, anxiety, self-esteem, satisfaction with life, physical activity, Cross-cultural comparison.

Introduction

FM is a chronic illness with serious consequences for patients' psychological well-being and quality of life (Denche-Zamorano et al., 2023; Sechi et al., 2020). Some studies

(Bucourt et al., 2021; Catala et al., 2023; Wolfe et al., 2023) discovered that FM patients had higher levels of depression and anxiety, as well as lower levels of self-esteem, life satisfaction, and quality of life, when compared to patients with other chronic conditions evidenced by fatigue (e.g., rheumatoid arthritis and spondylarthritis).

Fatigue is recognized as the body's natural response to stress, whether physical or mental; however, it can also serve as an indicator of changes in physical and mental health (McMorris, 2020; Ulus et al., 2019). Fatigue is a physiological response to prolonged activity in people without health problems and is easily relieved after rest. FM patients, on the other hand, describe their fatigue as excessively affecting their physical, mental, and cognitive levels, typically not improving despite many hours of sleep or rest, directly interfering with their performance at work or daily tasks, and possibly contributing to the acceptance of less active behavior (Finsterer & Mahjoub, 2014). FM patients report that fatigue is the most significant symptom affecting their overall quality of life, as well as anxiety, depression, life satisfaction and self-esteem (Mascarenhas et al., 2021; Pagano, 2004). Although fatigue is negatively associated with several aspects of health and psychological components, there is still a paucity of information regarding the measurement of fatigue in scientific studies and clinical practice (Dailey et al., 2015; Morris et al., 2017).

Patients with FM are more vulnerable to psychological conditions due to their complexity (e.g., higher levels of anxiety and depression). According to some studies, FM patients have higher levels of anxiety and depression than patients with other chronic diseases (i.e., rheumatoid arthritis and osteoarthritis) (Bucourt et al., 2021). This increase in depressive and anxious pictures affects the social and emotional functioning of FM patients, causing them to avoid social interaction, work responsibilities and any kind of physical activity, resulting in a cycle of events that culminates in worsening depressive and anxious symptoms and thus directly affecting their level of quality of life, self-esteem and satisfaction with life generating a vicious circle (Arrayás-Grajera et al., 2021; LuqueReca et al., 2022).

Quality of life can be defined as a subjective perception of well-being and general satisfaction with several aspects of life, being encompassed by several individual, social and cultural factors that vary from person to person (Sechi et al., 2020). Self-esteem, on the other hand, is a subjective evaluation of oneself, taking into consideration one's entire psychological well-being (Garaigordobil, 2015) . Satisfaction with life can be defined as a subjective evaluation of the degree of contentment and general happiness, involving an assessment of your life circumstances (Boonstra et al., 2013). These components may

vary over time and are influenced by several factors such as professional and personal achievements, level of overall health and emotional well-being, where FM patients report lower levels in this component because of all the symptoms and limitations arising from their health condition (Penacoba Puente et al., 2015).

Therefore, treatments and interventions in patients with FM should aim to improve the psychological components, since several research (Arrayás-Grajera et al., 2021; LuqueReca et al., 2021) have found that such interventions considerably increase the levels of psychological variables, resulting in an improvement in the way patients cope with FM.

Consequently, physical activity is highly recommended as a therapy for FM because, in addition to providing a low-cost intervention, it can improve both physical and psychological components (by enhancing the action of certain neurotransmitters such as endorphins and serotonin) and promote a sense of accomplishment and self-efficacy (Larsson et al., 2020; Sawatzky et al., 2007).

Since FM patients exhibit a rejection of physical activities to maintain the effects of stress, both physical and psychological, which may have a deleterious impact on their physical and psychological symptomatology (Denche-Zamorano et al., 2023; Russell et al., 2018). Some studies (Cordoba-Torrecilla et al., 2016; Sener, 2016; SorianoMaldonado et al., 2016) have concluded that FM patients who are more physically active have fewer symptoms of depression, anxiety, and quality of life. Thus, health professionals should always consider the limitations of each patient and thus analyze those of physical conditioning and fatigue related to fibromyalgia to understand and prepare the activities that patients will perform, minimizing the adversities that may arise from the training program (Rooks, 2008). Low to moderate intensity physical activities should be performed two to three times a week for patients with FM (Larsson et al., 2020; Rooks, 2008).

Self-esteem is related to self-confidence and expectation of self-efficacy; some studies (Russell et al., 2018; Sener, 2016; Soriano-Maldonado et al., 2016) have demonstrated that patients with FM have considerably lower levels of self-esteem in comparison to healthy individuals or those with other chronic diseases. This decrease in self-esteem levels causes a cognitive decline, directly affecting the levels of satisfaction with life, physical activity and fatigue in patients with FM (Rooks, 2008).

Satisfaction with life is one of the dimensions associated with quality of life, which is part of the cognitive component of subjective wellbeing, which is increasingly recognized as an important health parameter; lower levels of satisfaction with life may be related to the development or worsening of chronic diseases (Clark, 2013; Ruiz-Montero et al., 2015; Ruiz-Montero, 2019). In patients with FM, previous studies (Duenas et al., 2016; Henriksson, 1996; Kuppens et al., 2016) have concluded that higher levels of life satisfaction are associated with improved adaptation to FM (i.e., reduced levels of fatigue, anxiety, depression and disease severity).

Differences in Fibromyalgia perception between cultures

Due to its symptomatologic complexity, some studies (Clark, 2013; Kuppens et al., 2016; Ruiz-Montero et al., 2015; Ruiz-Montero, 2019) show that FM patients from different cultures may have higher or lower levels of their symptoms, leading to an attenuation or worsening of their condition. The study by Kuppens et al. (2016) found substantial variations in the perception of related symptoms between Belgium and Dutch FM patients, with Belgian patients reporting greater intensity severity in their symptom's levels than Dutch patients.

Clark (2013) investigated the perception of FM symptoms in patients from Europe and Latin America and discovered that Latin American patients perceived more the symptoms than the European patients. According to Duenas et al. (2016), Brazil has the highest number of FM patients in Latin America, with one of the primary challenges being the difficulty in accessing therapy, care, and even a diagnosis owing to socioeconomic inequalities and the difficulty in locating health centers due to distance.

Henriksson and Burckhardt (1996) carried out a comparative study between patients from Sweden and the United States with FM and showed that the American patients reported higher levels of stress, fatigue and lower values of satisfaction with life and quality of life when compared to the group of Swedish patients. In this study it was also possible to verify that this difference between the levels of the components verified can be explained by the fact that the Swedish patients had more free time to rest and did more physical activities than the patients from the United States.

Another factor that may influence the difference in the perception of FM symptoms is climate sensitivity, where FM patients report higher levels of fatigue and experiential distress from the disease when they faced colder climates than when they were in warmer

climates (Hayashi et al., 2021). However, some studies (Bossema et al., 2013; Fors, 2002) show that climate differences do not directly affect the severity of physical symptoms in FM patients but do affect them at the psychological level where higher levels of depression and anxiety and lower levels of quality of life and life satisfaction have been reported in FM patients in periods of colder climates. But there is still an absence of research analyzing and exploring these cross-cultural variations in FM symptomatology.

Present Study

Therefore, the objective of the present study is to analyze the differences between fatigue related to fibromyalgia, quality of life, depression, anxiety, self-esteem, life satisfaction and physical activity between Brazilian and Portuguese patients. Therefore, this study aims to assist the limited literature in the context of cross-cultural comparisons between patients with FM.

Based on this central objective, we hypothesize that: (a) Brazilian patients perceive the effects of FM fatigue more than Portuguese patients; (b) Portuguese patients have higher levels of quality of life compared to Brazilian patients; (c) Brazilian patients have higher levels of anxiety and depression compared to Portuguese patients; (d) Brazilian patients have lower self-esteem and life satisfaction scores; (e) Brazilian patients have lower values regarding physical activity when compared to Portuguese patients.

All these hypotheses arise after verifying several previous studies (Kuppens et al., 2016; Ruiz-Montero et al., 2015; Ruiz-Montero, 2019), where it was possible to verify that more underdeveloped countries present worse levels in relation to FM symptoms when compared to patients living in more developed countries, for governmental reasons, socioeconomic, geographic, and climatic

Materials and Methods

Participants

Two independent samples of Portuguese and Brazilian women with a positive diagnosis of FM participated in present cross-sectional study. First, the participants were asked about their age; nationality; time since diagnosis; and levels of fatigue, depression, anxiety, self-esteem, life satisfaction and physical activity. Sample 1 comprised 222 Portuguese patients aged between 28 and 75 years (M = 49.53; SD 8.80). Portuguese

patients were diagnosed with FM at a mean age of 9.29±7.71 years. Sample 2 comprised 251 Brazilian patients with FM, aged between 27 and 75 years (M = 49.03; SD 8.86). These Brazilian patients had a mean time of diagnosis of 10.05±7.69 years. The participants of this research were diagnosed with FM by licensed rheumatologists and their diagnosis was established by the recommended guidelines proposed by the American College of Rheumatology (Häuser, 2018).

The required sample size was determined using the G. Power 3.1.9.7 (Faul, 2009) and the following input parameters were considered: effect size (0.5), statistical power level (0.95), and probability level (0.05). The suggested effect size and remaining parameters were defined according with similar studies (e.g., (Alvarez et al., 2021; Alvarez, 2022)). The minimum required sample was 88 in each group, which was respected in present study.

Procedure: Data Collection

The University of Beira Interior, Covilhã, Portugal (UBI) Ethics and Science Committee approved this study (reference number CE-UBIPj- 2021-038). The current study was carried out in accordance with the Helsinki Declaration (Association, 2013).

Two FM-related organizations (National Association Against Fibromyalgia and Chronic Fatigue Syndrome, Lisbon, Portugal (MYOS) and the National Association of Fibromyalgia, So Paulo, Brazil (ABRAFIBRO)) were contacted for data collection, and the study's aims were described. These institutes recommended some individuals who freely volunteered to participate in the trial after receiving approval. The authors contacted these patients and described the goal and objectives of the study, as well as information on the data collection method. Following contact and explanation, each participant signed the informed consent form, which stated that they would be participating in this study willingly and anonymously. The questions took about 35 minutes to complete. MYOS is a Portuguese organization that assists persons with FM and chronic fatigue syndrome. It has over 7000 patients with a positive FM diagnosis, 500 of whom were contacted by the researchers, resulting in 227 volunteers who filled the questionnaires. For a total of 222 Portuguese patient participants, the evaluation of completed questionnaires found that five patients did not answer correctly, leading in their exclusion. ABRAFIBRO is a Brazilian organization that assists FM patients, with over 6000 persons diagnosed with the condition. This institution assisted in contacting 580 FM patients, and 253 patients completed the planned questionnaires. Only two

individuals did not correctly complete the questionnaire, resulting in their elimination from the research, for a total of 251 Brazilian participants.

Instruments

Fibromyalgia-Related Fatigue

The questionnaire used to measure fibromyalgia-related fatigue levels was the Multidimensional Diary of Fatigue-Fibromyalgia-17 (MDF-Fibro-17), using the validated and translated version for the Portuguese and Brazilian populations (Alvarez et al., 2020). The MDF-Fibro-17 includes 17 questions evaluating the various dimensions of fatigue. The questionnaire comprises five sections: global fatigue experience, consisting of 4 questions, for example, “How severe was your fatigue today?”; physical fatigue, consisting of 3 questions, for example, “How heavy did your body feel today?”; cognitive fatigue, consisting of 4 questions, for example, “How difficult was it to think clearly due to tiredness today?”; motivation, measured by 3 questions, such as, ”How difficult was it to motivate yourself to do something today?”; and the role impact, composed of 3 questions, for example, “Did you do something slower because you were feeling tired today?”. Participants evaluated fatigue components using a scale ranging from 0 (“not at all”) to 10 (“extremely”). Higher values indicate a higher level of fatigue. Previous studies support the validity, reliability, and use of this questionnaire (Alvarez et al., 2020; Li et al., 2017). However, just global fatigue experience, physical and cognitive fatigue were used, because other studies (Galvez-Sanchez et al., 2019; Munguia-Izquierdo et al., 2021) showed that these factors can affect more of the psychological components in FM patients.

Quality of Life

The quality-of-life components were assessed using the SF-36 scale (Ware, 1992). This survey has 11 questions and 36 items that cover 8 components (domains or dimensions) of the quality-of-life state, which are represented by: physical functioning (10 items, for example, "Does your health limit you to performing violent activities, such as running, lifting weights, or participating in strenuous sports?" If so, how much?" Difficulties in Role Performance Caused by Physical Issues (4 questions, for example, "During the past 4 weeks, have you, in your work or daily activities, had decreased time spent working or in other activities as a result of your physical health status?"); Pain (2 items, for example, "How much has pain interfered with your normal work over the last 4 weeks? (both outside work and housework)"); General Health (5 questions, such as "In general, I would say your health is"); vigor (4 items, for example, "Have you felt full of vitality in

the last 4 weeks?"); Social Functioning (2 questions, for example, "How much has your physical health or emotional problems limited your social activity in the last four weeks?" (for example, visiting friends or relatives)"); Difficulties in Role Performance Caused by Emotional Problems (3 items, for example, “During the past 4 weeks, have you had, with your work or daily activities, a decrease in time spent at work or in other activities due to any emotional problems? (such as feeling depressed or anxious)”); Mental Health (5 items, for example, “During the past 4 weeks, have you felt so depressed that nothing cheered you up?”) (Hoffman and Dukes , 2008). To verify the physical health status of the patient, a calculation is made of the following domains: Physical Functioning, Difficulties in Role Performance Caused by Physical Problems, Pain, and General Health. As for the psychological health status, the calculation is made from the domains: Vitality, Social Functioning, Difficulties in Role Performance Caused by Emotional Problems, and Mental Health. Values range from 0 to 100, where higher scores suggest better levels in each domain of the patient’s quality of life, and mental and physical health (Gomes, 2010).

Hospital Anxiety and Depression Scale (HADS)

The Portuguese version of the Hospital Anxiety and Depression Scale (Pais-Ribeiro et al., 2007) was used to assess anxiety and depression levels. The questionnaire has 14 items, seven of which examine all elements of anxiety and the remaining seven of which measure depression levels. This questionnaire uses a 4-point Likert scale (from 0 to 3); higher numbers indicate greater anxiety and depression. According to Bjelland et al., (2002), the HADS Portuguese version is well-structured and trustworthy in evaluating depressed and anxious situations, as well as symptoms of anxiety and depression disorders.

Self-Esteem

To measure self-esteem, the Portuguese version of the Rosenberg Self-Esteem Scale (Faria & Silva, 2000) was used. Although the original form comprises ten questions, we focused on the five positively coded items (e.g., "On the whole, I am satisfied with myself") for this study since negatively coded items might taint results (van Sonderen et al., 2013). Participants responded on a four-point Likert scale, with potential answers ranging from 1 ("strongly agree") to 4 ("strongly disagree"). Previous research supports the validity and reliability of the Rosenberg Self-Esteem Scale (Baumeister et al., 2003).

Satisfaction with Life

To evaluate the individuals' life satisfaction, the Portuguese version of the Satisfaction with Life Scale (Neto, 1993) was used. This questionnaire has five items (for example, "I'm happy with my life.") to which participants replied using a 5-point Likert scale, with 1 representing strongly disagree and 5 representing strongly agree. Teixeira et al., (2021) conducted research to establish the instrument's reliability and validity.

Physical Activity

We utilized the International Physical Activity Questionnaire (IPAQ) short form (Craig et al., 2003) for evaluating physical activity levels. This questionnaire has seven items on intensive, moderate, and walking activities undertaken in the seven days preceding the completion of the questionnaire (Benitez-Porres et al., 2013) .

Another number produced from the IPAQ is an estimate of energy expenditure based on physical activity levels (Benitez-Porres et al., 2013). In other words, the data are transformed into MET min/week by calculating the patient's minutes per week in each type of exercise based on the specific metabolic equivalent (Benitez-Porres et al., 2013; IPAQ, 2005).

Statistical Analysis

The IBM SPSS Statistics version 22.0 (IBM Corp. Armonk, New York, NY, USA) was used for preliminary analyses. Descriptive statistics, including mean, standard deviation was calculated for all studied variables in both samples. Inspection of missing values and outliers was also carried out.

Subsequently, an independent sample t-test was used to analyze differences between fatigue-related symptoms in Brazilian and Portuguese patients with FM, as well as between the values of quality of life, anxiety, depression, self-esteem, satisfaction with life, and physical activity. In accordance with Ho (2014) recommendations, we considered a p-value less than or equal to 0.05 as grounds for rejecting the null hypothesis. In cases of significant results, we also calculated the effect size using partial eta square, as proposed by Denis (2019). Following Cohen (1988) guidelines, we categorized the effect sizes as follows: trivial (0–0.19), small (0.20–0.49), medium (0.50–0.79), and large (0.80 and above).

Results

An examination of the data revealed no missing values or outliers. Table 9 summarizes the descriptive data for all fatigue-related symptoms. In terms of mean values, Brazilian women reported higher scores in all fatigue-related symptoms compared to Portuguese women.

Table 9. Descriptive statistics of each fatigue variables according to samples (Portugal and Brazil).

		N	M	SD	t	df
Global fatigue experience	Portugal	222	7,92	1,44	0,008	471
	Brazil	251	7,92	1,76		
Physical Fatigue	Portugal	222	8,13	1,52	-0,262	471
	Brazil	251	8,17	1,8		
Cognitive Fatigue	Portugal	222	7,78	1,71	-0,219	471
	Brazil	251	7,82	1,82		
Motivation	Portugal	222	8,13	1,55	-1,197	471
	Brazil	251	8,34	1,84		
Impact on function	Portugal	222	8,20	1,52	-0,369	471
	Brazil	251	8,27	1,94		

Note. N = sample size; M = mean; SD = standard deviation; t = test statistic; df = degrees of freedom.

The analysis of the t-test for independent samples showed that there were no significant differences in all fatigue-related symptoms as a function of country ($p < 0.50$). Effect sizes were trivial. For detailed information see Table 9.

Regarding the psychological components, the Brazilian population demonstrated a small positive difference in terms of physical quality of life and higher values of depression, while the Portuguese sample demonstrated higher values in terms of mental quality of life, anxiety, self-esteem, life satisfaction and physical activity, but no significant differences were found between the perception of these symptoms, as can be seen in table 10.

Table 10. Descriptive statistics of psychological components and physical activity between the two samples.

		N	M	SD	t	df
Fisical quality of life	Portugal	222	32,78	9,31	-1,603	471
	Brazil	251	34,32	9,63		
Mental quality of life	Portugal	222	27,41	15,48	.050	471
	Brazil	251	27,33	16,11		
Anxiety	Portugal	222	13,03	3,98	0,052	471
	Brazil	251	13,01	4,14		
Depression	Portugal	222	10,60	3,04	-0,207	471
	Brazil	251	10,66	3,08		
Self-Esteem	Portugal	222	30,57	3,07	0,093	471
	Brazil	251	30,55	3,07		
Life satisfaction	Portugal	222	12,04	4,24	0,022	471
	Brazil	251	12,03	4,35		
Physical Activity	Portugal	222	1673,16	4048,47	.746	471
	Brazil	251	1397,96	3963,72		

Note. N = sample size; M = mean; SD = standard deviation; t = test statistic; df = degrees of freedom.

Discussion

The objective of this study was to compare the levels of fatigue, depression, anxiety, satisfaction with life and physical activity related to fibromyalgia between Brazilian and Portuguese patients, where it was possible to obtain interesting findings that may contribute to the scarce literature on fatigue related to fibromyalgia. Initially, five hypotheses were proposed, which will be discussed based on current literature.

In this study, the two samples present values above the average for fatigue, depression, anxiety, and self-esteem associated to fibromyalgia, and values below the midpoint for life satisfaction, quality of life and physical activity values. According to the current literature, these results were expected; however, an unusual finding was that our patients demonstrated above-average self-esteem values, in contrast to the findings of other studies (Galvez-Sanchez et al., 2018; Garaigordobil, 2015), which demonstrated that patients tend to have lower levels of self-esteem due to adversities caused by FM.

In relation to the first hypothesis, Brazilian patients present higher median values of perception of the domains of fatigue in relation to the Portuguese population, however these differences were not significant, thus rejecting our first hypothesis. Our findings corroborate the study carried out by Humphrey et al. (2010) who also found no significant differences when comparing patients with FM from three different countries (Germany, France, and the United States). However, in a study prior to this one, Alvarez

et al. (2020) carried out a comparative study between Brazilian and Portuguese patients with FM and found that there were significant differences in the perception of fatigue domains between these two cultures. Thus, suggesting that more studies are needed regarding the analysis of fatigue perception among patients from different cultures.

Regarding our second hypothesis, in average values, Brazilian patients demonstrate a greater perception of values in terms of quality of life at a physical level, while Portuguese patients demonstrate greater values in quality of life at a mental level, however these differences were also not significant. The study carried out by Clark et al. (2013) demonstrated that patients from Latin America had a greater severity and perception of FM symptoms when compared to European patients, thus directly affecting the qualityof-life levels of FM patients.

Mas et al., (2008) carried out a study that verified the prevalence and impact of FM on quality of life throughout Spain and found that within the same country there may be differences in the perception and impact of FM on the quality of life of its sufferers. These findings demonstrate a greater need for studies to verify the reason why these differentiations occur.

In our third hypothesis, we suggested that Brazilian patients would have higher levels of anxiety and depression compared to Portuguese patients, which did not end up happening, because when compared, Brazilian patients demonstrated higher levels of depression, while Portuguese patients showed higher levels of anxiety, but these differences were not significant. The study carried out by Kuppens et al. (2016) found that Belgian and Dutch patients tended to have different perceptions of the levels of anxiety and depression related to FM. While Belgian patients showed higher levels of depression due to FM, Dutch patients showed higher levels of anxiety due to their health condition. Henriksson and Burckhardt (1996) compared Swedish and North American patients with FM and found that there were differences in the levels of anxiety and depression between these two countries. These findings suggest that illness perceptions in FMS patients are prone to local influences, including possible differences in healthcare system, meteorological and socioeconomic conditions.

About our fourth hypothesis, we suggested that Brazilian patients would present lower values of life satisfaction and self-esteem when compared to Portuguese patients, which ended up happening, but without there being a significant difference. This finding corroborates with the study by Marr et al., (2020) where it was found that patients with FM from minority countries have worse levels of satisfaction with life, self-esteem and quality of life when compared to patients with FM from more developed countries. The difference reported by these patients from less developed countries was based on the

difficulty in treating FM, disbelief in their health status on the part of health professionals, greater workloads and consequently less time for rest (Marr et al., 2020).

Our fifth hypothesis suggested that Brazilian patients with FM would present lower levels of physical activity when compared to Portuguese patients. Our hypothesis was confirmed where Brazilian patients demonstrated mean values below those of Portuguese patients, however there was no significant difference between them. Our finding is consistent with the findings of Martinez et al., (2003) who found that Brazilian patients with FM present slight differences in the perception of their health condition when compared to patients from other more developed countries, and that this directly affected their level of functionality well with physical activity levels, thus favoring the adoption of less active behavior.

Practical Implications and Limitations

The results of this study support the significant role of FM as a complex health condition that can be perceived and experienced in different ways depending on your culture or country. Therefore, known therapies to alleviate symptoms, especially physical activity, should focus on improving subjective well-being because, according to some crosssectional studies (Redondo et al., 2004; Wiese et al., 2017), FM patients with better physical fitness and Higher levels of physical activity are associated with lower levels of depression, fatigue, anxiety and greater quality of life, life satisfaction, self-esteem and consequently an improvement in your general health status.

The current study adds to our understanding of the relationships between fibromyalgia and various cultural perspectives on fatigue, depression, anxiety, self-esteem, quality of life, life satisfaction, and physical activity. However, there are certain limitations that need to be addressed. The current study used a cross-sectional methodology; to confirm perceptions between the variables examined in this study, additional research utilizing various methodologies (e.g., longitudinal or experimental) should be conducted. Moreover, a subjective questionnaire was used to measure physical activity, therefore the actual intensity of each activity that patients claimed was not always taken into account because there were no supervisors present to confirm the circumstances in which these activities were performed. The results of this study cannot be applied to male FM patients because only female patients answered the suggested questionnaires. Male patients should be included in future research so that the outcomes reported here may be compared. The fact that we did not confirm if patients were using any kind of medication to manage FM symptoms is another limitation of this study. Consequently, to use this indicator as a potential mediator between the variables under study, future research should aim to gather data on it.

Conclusion

One of the important factors in this study is the considerable sample size of FM patients, from which it was possible to verify the perceptions between the variables studied in the two cultures. Another positive factor in our study was the use of psychometrically valid instruments to assess the proposed variables, thus enabling a more reliable analysis of the variables studied. In addition, the uniqueness of this study is an important factor, as it is the first study to analyze the proposed variables complemented by a verification between two different cultures.

The aim of this study was to compare fatigue, depression, anxiety, quality of life, life satisfaction and physical activity related to fibromyalgia between Brazilian and Portuguese patients.

With the results obtained from this comparative analysis, we found that both samples had below-average values for quality of life, life satisfaction and activity levels, and above-average values for fatigue, anxiety, depression and self-esteem. As far as differentiating perception between the two cultures is concerned, both samples showed no significant differences in the perception of symptoms related to FM.

Our findings may indicate that even though these are two distinct cultures, with major climatic, socio-economic and geographical differences, the symptoms related to FM are extremely important and directly affect the lives and well-being of its sufferers.

Chapter 3. General Discussion

The main objective of this thesis was to assess the associations between fatigue, quality of life, anxiety, depression, self-esteem, satisfaction with life, and levels of physical activity among Brazilian and Portuguese patients with FM.

As previously described, fibromyalgia (FM) is a chronic illness characterised by widespread musculoskeletal pain, fatigue, and tenderness (Buskila, 2009). Although the physical symptoms of FM are well known, the psychological impact of the disease is often put on the back burner (Vicente Martínez-Quiñones et al. 2020). FM-related fatigue is not the same as regular tiredness or sleepiness, but is characterised by a constant, overwhelming exhaustion that persists even after adequate rest or sleep (Michielsen et al. 2016). This debilitating fatigue can lead to emotional distress as patients struggle with the frustration of feeling exhausted and lacking the energy to carry out daily activities (Arnold et al. 2008)).

Fatigue has a significant impact on the psychological components of fibromyalgia patients, regardless of their cultural background (Galvez-Sanchez et al. 2019). The impact of fatigue on mental well-being is further exacerbated by the fact that FM patients often experience a decreased ability to cope with daily challenges (Hamama and Itzhaki, 2023). Persistent fatigue can interfere with motivation and desired activities, making it difficult for FM patients to engage in hobbies, work, social interactions, or physical activity (Velasco-Furlong et al. 2020). In addition, the cognitive symptoms associated with FM fatigue, such as difficulty concentrating, memory problems and "fibrofog", can further contribute to psychological distress (Galvez-Sanchez et al. 2018). Patients may struggle with mental tasks, have difficulty concentrating and suffer memory lapses (Ibraheem et al. 2021). These cognitive deficiencies can be frustrating and lead to feelings of inadequacy and loss of self-confidence, leading to an increase in depression and anxiety, directly influencing their levels of quality of life, satisfaction with life and selfesteem (Galvez-Sanchez et al., 2018).

The psychological impact of fatigue is not limited to any one cultural context in the context of FM (Kuppens et al., 2016, Clark et al., 2013). However, cultural factors can influence the way individuals perceive and express their psychological distress (Malin and Littlejogn 2012). Cultural beliefs and practices, as well as access to reliable diagnosis and symptom-relieving therapies, can shape the way FM patients understand and cope with their fatigue and psychological conditions (Brown, 2021). For example, in some

cultures, there can be stigmas associated with chronic illnesses, can lead to feelings of shame or guilt for not being able to fulfil society's expectations (Earnshaw and Quinn, 2012). Cultural norms and expectations can also influence the support and understanding that FM patients receive from their families, friends and communities (Ashe et al., 2017). In some cultures, there may be a lack of awareness or acceptance of FM as a legitimate medical condition, which can further contribute to the psychological burden felt by patients (Häuser and Fitzcharles, 2018).

All in all, this research could have an important impact on research into FM, since fatigue is a symptom of extreme relevance and impact on the psychological components of FM patients, regardless of their culture. To achieve this goal, three scientific investigations were carried out, each with its relevance to the final objective.

Our first study aimed to analyse the impact of fatigue on the quality of life of patients with FM and whether physical activity can play a role in mediating this association. This objective was based on previous studies which found that patients with FM have higher levels of fatigue and its components, especially at the muscular, cognitive and emotional levels, where these patients reported reduced mental resilience and decreased speed of thought and execution of daily or work tasks, directly affecting their quality of life (Offenbaecher et al. 2021; Öncü et al. 2013; Humphrey et al. 2010; Wolfe et al. 2000). In this sense, after analysing the descriptive analyses and bivariate correlations, we also checked the simple measurements, as suggested by the literature (Hayes 2018), where our results showed values below the midpoint for quality of life, both in the physical and mental components, and values above the midpoint for the fatigue components, which was initially expected and was corroborated by the existing literature, which shows that FM patients have a low perception of their quality of life and an increased perception of fatigue (Öncü et al. 2013; Humphrey et al. 2010; Park et al. 2001).

However, when we checked the possible mediating role, we found that physical activity did not have a mediating role in the relationship between fibromyalgia-related fatigue and quality of life. However, this finding contributes to the current literature, because there are few studies (Molinari et al. 2019; Doerr et al. 2017; Sawatzky et al. 2007) with contradictory findings, where there is a need for more in-depth studies to verify the possible mediating role of physical activity in the relationship between fatigue and quality of life.

Our second study aimed to analyze the associations between fatigue and levels of depression, anxiety, self-esteem, and life satisfaction between two different cultures, and came up with several interesting findings that could contribute to the literature on

FMrelated fatigue. Initially, five hypotheses were proposed and debated alongside the current literature. To conduct this study, a confirmatory factor analysis was carried out to analyze the psychometric properties of the model, taking into account the reference values as suggested by current literature (Kline, 2016). Structural equation modeling was then carried out to analyze the proposed associations and the standardized direct and indirect effects on the outcome variable were analyzed. To check whether the proposed model could be replicated in groups with different characteristics, a multi-group analysis was carried out according to Byrne's (2016) suggestion.

Our results showed values above the midpoint for the fatigue, anxiety, depression, and self-esteem components and values below the midpoint for life satisfaction and physical activity levels. About the relationships between the variables studied and the hypotheses proposed, the fatigue components proved to be significantly positively associated with levels of depression and anxiety and negatively associated with levels of self-esteem, life satisfaction, and physical activity, which means that patients with higher levels of the fatigue components tend to have higher levels of depression, anxiety and physical inactivity and worse levels of self-esteem and life satisfaction. In turn, levels of depression and anxiety were shown to have negative associations with self-esteem, life satisfaction, and physical activity levels, suggesting that patients with higher levels of anxiety and depression tend to have lower levels of the other proposed psychological components and physical activity. It was also possible to see a positive association between self-esteem and levels of life satisfaction, which in a way was to be expected, since as FM patients have higher levels of self-esteem there tends to be an increase in life satisfaction values. The results of our multi-group analysis showed that the proposed model was invariant across the countries studied, thus confirming the similarity of the perception of the two cultures about the proposed variables. Overall, this study found solid evidence of the relationship between the proposed variables, which demonstrates the significant role of FM as a health condition that requires maximum attention and a need to seek therapies to improve not only physical but also mental well-being.

Finally, study three aimed to compare the levels of fatigue, quality of life, depression, anxiety, self-esteem, life satisfaction, and physical activity between Brazilian and Portuguese patients with a positive diagnosis of FM. To achieve the objective set for this study, a descriptive statistical analysis was first carried out for all the variables studied in both samples. Subsequently, a t-test for independent samples was carried out to analyze possible differences between symptoms related to fatigue in Brazilian and Portuguese patients with FM, as well as between values for quality of life, anxiety, depression, self-esteem, satisfaction with life, and physical activity. The results obtained in this study showed that both samples showed values below the midpoint for the positive

components (quality of life, self-esteem, physical activity, and life satisfaction) and values above the midpoint for the negative components (fatigue, anxiety, and depression). While the Brazilian sample showed higher values for the fatigue, depression, and physical quality of life components, the Portuguese sample showed higher values for mental quality of life, anxiety, self-esteem, satisfaction with life, and physical activity. However, no significant differences were found between the two cultures studied. This finding may contribute to the scarce and contradictory literature on cross-cultural comparisons of FM patients, but there is still a need for more studies to understand this cultural influence.

The associations across fibromyalgia-related fatigue, quality of life, depression, anxiety, self-esteem, life satisfaction, and physical activity in patients with fibromyalgia disclose a complex interplay within this chronic pain condition (Adams et al., 2023). This interrelation highlights the multifaceted nature of fibromyalgia and its profound impact on various dimensions of individuals' lives, necessitating a comprehensive approach to patient care and management (Fernández-Feijoo et al., et al., 2022). Fibromyalgiarelated fatigue stands as a feature symptom, significantly influencing physical, cognitive, and emotional functioning. Its pervasive presence intertwines with other variables, exacerbating the burden experienced by individuals with fibromyalgia (Galvez-Sánchez et al., 2019). The quality of life for these individuals is notably affected, encompassing multiple domains such as physical health, social interactions, and psychological wellbeing. The intricate relationship between fatigue and quality of life underscores the profound challenges faced by patients and the need for interventions targeting symptom management and overall improvement of life aspects (Fernandez-Feijoo et al., 2022). Depression and anxiety, prevalent comorbidities in fibromyalgia, contribute significantly to the overall symptom burden. They represent not only psychological distress but also potential exacerbators of pain and fatigue, forming a cycle that further compromises the individual's well-being (de Heer et al., 2017; Aguglia et al., 2011). Self-esteem, closely intertwined with the limitations imposed by fibromyalgia, experiences fluctuations influenced by the perceived impact of symptoms on daily functioning. The ongoing management of self-esteem becomes an integral part of comprehensive care, necessitating tailored interventions addressing both physical and psychological dimensions (Davies et al., 2020). In addition, life satisfaction as a cognitive aspect of well-being, despite the challenges posed by fibromyalgia, could act as a buffer in terms patients' resilience in the form of adaptive coping mechanisms and social support systems (Hamama et al., 2023). Understanding and fostering these aspects become crucial in improving patient outcomes and overall adjustment to the chronic nature of the condition (Hamm (a et al., 2023). Physical activity, while often restricted due to symptoms, emerges as a modifiable factor that can positively impact various facets of

fibromyalgia management. Tailored exercise regimens, focusing on individual capacities, not only improve physical function but also contribute to psychological well-being (Albuquerque et al, 2022; Albuquerque et al., 2023; Bush et al., 2011; Larsson et al., 2020).

Overall, the associations among these variables underscore the intricate nature of fibromyalgia and its impact on the multifaceted dimensions of individuals' lives. Addressing fibromyalgia necessitates a multidisciplinary approach that integrates pharmacological, psychological, and lifestyle interventions (Gisuti et al., 2017). Therefore, adapted treatments targeting symptom management, promoting physical activity, and addressing psychological well-being are paramount in enhancing the overall quality of life for individuals affected by fibromyalgia (Albuquerque et al., 2022). In this regards, continued research and holistic approaches remain pivotal in advancing the understanding and management of this complex chronic pain condition.

Although this thesis has made progress in analyzing the association between fatigue and quality of life, anxiety, depression, self-esteem, satisfaction with life, and activity levels in patients with FM in Brazilian and Portuguese patients, it has its limitations that should be considered. Firstly, this study had a cross-sectional design. Therefore, longitudinal/experimental studies could be an asset in verifying the relationship and perception of fatigue symptoms, psychological components, and physical activity levels in FM patients. Another limitation of this thesis was the specificity of the sample, in which only female patients participated, which means that the data obtained cannot be generalized and compared to male patients, this decision was made considering the existing literature which indicates that FM has a greater impact on women compared to men. In addition, physical activity was assessed on a self-reported basis and there was no verification of whether this physical activity was accompanied by a professional to supervise the activity. Another limiting factor in this study was that it was not checked whether the patients were using any medication or other methods to control the symptoms of FM.

Chapter 4. General Conclusion

Following our analysis of fibromyalgia-related fatigue and the quality of life, depression, anxiety, self-esteem, life satisfaction, and physical activity between the two cultures, the results can be summarized as follows:

i) Several gaps in the literature could be observed, specifically regarding investigations into the effects of fatigue and its components in FM patients, especially in the realm of psychological conditions.

ii) There was also a great lack of studies on cross-cultural comparisons since this difference at a geographical level can affect the symptomatology of FM.

iii) Although the study showed that physical activity did not mediate the relationship between fatigue and quality of life, it proved to be an extremely valuable therapy for alleviating the symptoms of FM, but one that requires supervision by a sports professional.

iv) The results show that the dimensions of fatigue associated with fibromyalgia are negatively associated with quality of life (physical and mental).

v) It was also possible to verify significant associations between fatigue, depression, anxiety, self-esteem, satisfaction with life, and levels of physical activity related to fibromyalgia, with no difference in association or perception between two different cultures.

vi) Patients with higher levels of cognitive fatigue tended to have higher levels of anxiety and depression, which in turn can lead to lower levels of self-esteem, life satisfaction, and physical activity.

vii) Although Brazilian and Portuguese patients showed values above the midpoint for the negative components (fatigue, depression, and anxiety) and lower values for the positive components (satisfaction with life, self-esteem, quality of life, and physical activity), it was not possible to verify significant differences between the two cultures studied.

Chapter 5. Suggestions for Future Research

Upon completing this thesis, several ideas for future studies have emerged. One suggestion is to conduct experimental studies that include physical activity through a specific training program to examine the relationship between symptoms and components related to FM.

Another potential study would be to include male FM patients to see if there is any differentiation in the perception of these studied components between genders. It would also be beneficial to include patients from other cultures, therefore increasing the coverage of different regions and contributing to the limited literature on this subject.

Furthermore, it would be useful to measure more psychological symptoms or symptoms that affect the well-being of FM patients. For example, assessing the quality of sleep among these patients and examining whether physical activity can improve this aspect of their health.

Chapter 6. References

Chapter 1 – General Introduction

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Chapter 2 – Experimental Studies

Study 1 - Exploring the Relationship between Fibromyalgia-Related Fatigue, Physical Activity, and Quality of Life

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Chapter 3 – General Discussion

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