Evaluating the interaction between pain intensity and resilience on the impact of pain in the lives of people with fibromyalgia

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Structured abstract

Objective: Recent theoretical models posit that resilience acts as a resource/mechanism opposing pain catastrophizing and other vulnerability sources against pain adaptation. The aim of this study was to investigate the relationship between resilience, pain and functionality in people living with fibromyalgia. **Methods**: We conducted a cross-sectional online survey of people participating in Brazilian fibromyalgia virtual support groups on Facebook in May 2018. Resilience was evaluated by the Connor-Davidson Resilience Scale. Average pain and the degree of interference of pain in the lives of participants (DIPLP) were assessed using the Brief Pain Inventory. The association between these three variables was evaluated through multivariable robust linear regression with adjustment for 21 potential confounders. **Results**: We included 2176 participants with fibromyalgia. Resilience was associated with a decreased DIPLP (β: -0.38, 95%CI: -0.54 to -0.22, P<0.001) but not with average pain scores (β: -0.01, 95%CI: -0.18 to 0.16, P=0.93). A significant interaction between resilience and average levels of pain on the DIPLP was observed so that resilience showed a much stronger protective association among participants with average null-to-mild pain than among those with moderate and severe pain levels. **Discussion**: Our results provide evidence against beliefs that the pain of people with fibromyalgia is related to low psychological resilience and shed light on the complex interrelationships between resilience, pain, and functionality. This research signals both the relevance and limits of resilience in the management of fibromyalgia. Future studies evaluating behavioral interventions for fibromyalgia should consider how those interventions interact with baseline pain levels and resilience.

INTRODUCTION

Chronic pain exerts a heavy toll on modern societies. It is associated with a large burden of decreased quality of life and functional impairments. In the US alone, it has been estimated that 560 to 630 billion dollars are spent each year due to chronic pain [1], including health care expenses and lost productivity, configuring a major public health problem with few effective treatment options available and little improvement over time [2, 3]. Fibromyalgia is one of the world's most common chronic pain conditions, characterized by several symptoms that significantly affect the quality of life of people living with the condition [3-5].

Although the pathophysiology of fibromyalgia is not yet well established, there is strong evidence that it is a central nervous system disturbance with increased pain sensitivity even in the face of non-painful stimuli [6, 7]. The management of fibromyalgia involves patient education, physical exercise and an individualized treatment plan based on specific functional, physical, and psychosocial patients' needs [8, 9]. Catastrophizing is one of the major psychosocial issues that must be considered in the development of such individualized care plans and may represent a mechanism of chronic pain maintenance and exacerbation in fibromyalgia [7, 10]. Pain catastrophizing is a maladaptive coping strategy whereby individuals experience an exaggerated negative mental response to an expected or actual pain experience [11, 12].

Recent theoretical models concerning individual responses to chronic pain propose resilience as a resource/mechanism opposing pain catastrophizing and other sources of vulnerability against pain adaptation [13]. Resilience in chronic pain can be defined as the ability to recover and sustain a fulfilling life despite the presence of intense pain and is believed to play an important role in physical and mental health [8, 14]. It is a psychological and behavioral adaptation mechanism that is influenced by a variety of neurochemical, psychosocial, developmental, genetic, and epigenetic factors [7, 10].

Although it appears intuitive that resilience may play a role in decreasing pain and its impact on the lives of people with fibromyalgia, few studies have investigated the association of resilience with those outcomes in that population [15, 16]. A recent narrative review on resilience and fibromyalgia concluded that, despite resilience representing a possible therapeutic target, it is still an under-developed area of investigation [10]. Hence, in this study we aimed to assess the association between resilience, pain, and the degree of interference of pain in the lives of people living with fibromyalgia. We were especially interested in whether and how resilience and pain interact concerning the impact of pain in people living with fibromyalgia.

MATERIALS AND METHODS

We conducted an open cross-sectional online survey, which was advertised in eight Brazilian general fibromyalgia open virtual support groups on Facebook. Those Facebook

groups are very popular virtual communities of people who have received a diagnosis of fibromyalgia and try to help each other by sharing knowledge and experiences about living with that disease. They are run by people living with fibromyalgia, do not provide any kind of professional therapeutic clinical or psychological services, and do not have regular meetings. Invitations to participate in this research with information about survey purpose were posted on those groups on a single day in May/2018 and the survey remained open to voluntary participants for two weeks. Participants from those groups were also asked to share the invitation to participate in the research to other people from their personal network. The invitation post was a straightforward message featuring the headline "Fibromyalgia Study / Wellness with Fibro Project / Join in!" followed by four bullet points outlining the key details: 1) the study involved an online questionnaire; 2) it was open to anyone diagnosed with fibromyalgia; 3) participation incurred no costs; and 4) participants would receive a token of gratitude as a reward.

A participant information sheet/informed consent form was presented to anyone visiting the survey website, which explained the study's purpose, length of time required, privacy issues and provided information about the investigators. Only individuals who provided consent were able to start answering the survey. Participation in the survey was voluntary and access to the Facebook groups wherein the survey was advertised was not conditional on participation. No monetary incentives for participation were offered but participants received a short educational material about fibromyalgia that was developed by one of the authors (LAT) as a small token of gratitude for having participated in the research. Participants could quit the questionnaire at any time and contact the investigators in case of doubts or concerns. Participants's responses were captured automatically by the survey website and stored on a secure server accessible only to the corresponding author. The survey consisted of three pages, containing 34, 15 and 25 items, related to sociodemographic and clinical characteristics of participants, the Brief Pain Inventory (BPI), and the Connor-Davidson Resilience scale (CD-RISC), respectively. To complete the questionnaire, participants had to respond to all items, however among the existing responses there was the option "rather not say". We did not randomize the items of the survey questionnaire or the order that they were presented in. We also did not use cookies, collect data on the IP addresses of visitors, or record the time that participants took to complete the survey. The usability and technical functionality of the electronic survey questionnaire was pilot tested before fielding the questionnaire.

This study was approved by the local Ethics Review Committee (Ref: 88078318.8.0000.5411). We used the following inclusion criteria, based on participant's answers of these questions in the survey: Brazilian nationals aged 18 years and older reporting a diagnosis of fibromyalgia made by a physician. We excluded participants that did not meet inclusion criteria, those that did not complete the full survey, participants with missing data, and

cases of duplicate records, as determined through the identification information provided by participants. When duplicate records were identified, only the most recent records were kept in the analyses. After excluding duplicates, the study dataset was anonymized.

We used the CD-RISC to measure resilience [17]. The CD-RISC is an assessment of psychological resilience based on self-report that has been used in several research areas, including fibromyalgia [18]. It is composed of 25 items that are scored on a 4-point Likert scale ranging from "Not true at all" to "True nearly all of the time". The final score ranges from 0 to 100 and higher values indicate higher resilience. In this study, we categorized resilience into two groups according to the final score of the CD-RISC: low ($\leq$70), and moderate-to-high resilience (>70) [18, 19].

We used the short form of the BPI to assess the severity of participants' pain and the degree of interference of pain in the lives of participants. The BPI is one of the research instruments recommended by the IMMPACT guidelines for use in clinical trials in pain [8] It has been widely used for the assessment of a variety of chronic pain syndromes, including fibromyalgia [20]. The BPI assesses pain intensity and the degree of interference of pain in the lives of participants on an 11-point Numeric Rating Scale (NRS) [11]. In the present study, average pain was extracted directly from the 5th item of the BPI. The degree of interference of pain in the lives of participants was scored as the mean of the seven pain interference items of the BPI (i.e., working, general activity, walking, sleep, mood, enjoyment of life, and relations with others), as recommended by the developers of that instrument [11].

We also collected a range of sociodemographic, lifestyle and clinical data for adjustment for potential confounding in our statistical models, as described in the next section. Participants were able to review and change their responses through a back button at any time.

Statistical Analyses

We reported categorical data as absolute numbers and proportions. Continuous data were reported as means and standard deviations (SD) when their distribution was approximately normal, or as medians and interquartile ranges (IQR) when otherwise.

Because the residuals from the preliminary multivariable regression models evaluating the association between resilience and participants' average pain, and between resilience and the degree of interference of pain in the lives of participants of participants were substantially skewed, we used robust linear regression with M-estimation for those analyses [21]. We also assessed the presence of an interaction between resilience and average pain on the degree of interference of pain in the lives of participants outcome through a robust linear multivariable model and estimated marginal means of that outcome for all combinations of resilience and average pain as a way to represent that interaction [22]. We performed pairwise comparisons of the marginal means of the degree of interference of pain in the lives of participants' outcome for

the different combinations of resilience and average pain using Tukey's adjustment for multiple comparisons. Finally, we assessed the presence of multicollinearity by examining variance inflation factors for each regression model. In our regression analyses, we did not weight participants according to the age distribution of people with fibromyalgia in the Brazilian population because the rare population-based studies in this area did not produce such data [23].

We adjusted all regression analyses for the following potential confounders according to the disjunctive cause criterion (24) based on their potential role as confounders: gender (male, female, or other), age (coded in years), race (white, black, brown, yellow, indigenous and other[1]), marital status (married/stable union, single, divorced, or widowed), education (did not complete elementary and middle school, completed elementary and middle school, did not complete high school, completed high school, did not complete college, completed college, and graduate education), family income (coded as <1 minimum wage[2], ≥1 and <3 minimum wages, ≥3 and <6 minimum wages, ≥6 and <9 minimum wages, ≥9 and <12 minimum wages, ≥12 minimum wages), working status (inactive, active informal work, active formal work), frequency of alcohol consumption (none, once weekly, twice weekly, thrice weekly, 4 or more times weekly), current smoking (yes or no), frequency of physical activity (none, once weekly, twice weekly, thrice weekly, and four or more times weekly), number of painful areas in the body (coded as a continuous variable), time since the diagnosis of fibromyalgia (coded as <1 year, ≥1 and <3 years, ≥3 and <5 years, ≥5 and <10 years, and ≥10 years), and the following self-reported diagnoses: depression, generalized anxiety disorder, panic disorder, bipolar disorder, rheumatoid arthritis, systemic lupus, ankylosing spondylitis, migraine, and irritable bowel syndrome.

We used the R software (version 4.1.2) for all statistical analyses [25], and a two-tailed alpha of 0.05 as the criterion for statistical significance. We used R's *MASS* and *emmeans* packages for the performance of robust linear regressions and the estimation of marginal effects, respectively [26, 27].

RESULTS

We obtained 2605 responses of which 2176 (83.5%) were included in this study. We excluded 128 participants due to lack of medical diagnosis, 32 participants due to age below 18 years, 40 duplicates, and 229 individuals due to missing data.

The studied population is predominantly female of working age, white, living in a stable union, with at least complete high school education and family income that was inferior to three minimum wages. Most participants were diagnosed with fibromyalgia for more than three years

[1] Race categories were taken from the reference standards of the Brazilian Institute of Geography and Statistics, the country's most important governmental agency for the study of demography.
[2] Specific income ranges based on the value of the minimum wage were provided to participants in the survey questionnaire.

(n=1351, 62.1%). Table 1 presents the main sociodemographic characteristics of the research participants.

Table 1. Characteristics of participants.

The median (IQR) average pain score reported in the survey, on an 11-point NRS, was 7 (6 to 8). The median (IQR) values of the weakest and worst pain in the 24h before the survey were 5 (4 to 7) and 9 (8 to 10), respectively. Fifty-eight (2.7%), 770 (35.4%), and 1348 (61.9%) reported their average pain level as mild (NRS: 1 to 3), moderate (NRS: 4 to 6), and intense (NRS: 7 to 10), respectively. Participants reported a median (IQR) of 6 (5 to 8) painful areas out of a list of 8 body areas. The degree of interference of pain in the lives of participants is described in Table 2. The median (IQR) global resilience score in the CD-RISC scale among participants was 58 (45 to 70) and 534 (24.5%) were classified as having moderate-to-high resilience.

Table 2. Description of the degree of interference of pain in the lives of participants on an 11-point scale, according to the different domains of the Brief Pain Inventory and overall.

In comparison with participants with low resilience, those with moderate-to-high resilience did not report different average pain scores in the simple (β: -0.14, 95% CI: -0.29 to 0.02, p=0.09) and multivariable robust linear regression models (β: -0.01, 95% CI: -0.18 to 0.16, p=0.92). On the other hand, moderate-to-high resilience was associated with a decreased degree of interference of pain in the lives of participants (Table 3) in both simple and multivariable regression models.

Table 3. Results of multivariable robust linear regression of resilience and average pain on the degree of interference of pain in the lives of participants.

The adjusted analysis showed that participants with moderate-to-high resilience had, on average, less 0.38 points (95% CI: -0.54 to -0.22, p<0.001) in the 11-point total interference scale than individuals with low resilience. That main effect was almost equivalent, and in the opposite direction, to the detrimental effect of an increase of one unit of average pain in the NRS for that outcome (β: 0.39, 95% CI: 0.35 to 0.43, p<0.001).

Figure 1. Effect modification plot of resilience on the association between average pain levels and the degree of interference of pain in the life of patients with fibromyalgia.

The multivariable robust linear regression analysis including an interaction term for resilience and average pain revealed that resilience was a significant effect modifier of the

association between average pain and its degree of interference of pain in the lives of participants (Figure 1). For each level of average pain, individuals with moderate-to-high resilience reported significantly less interference of pain in their lives than individuals with low resilience (Table 4). However, the difference between the mean degree of interference of pain in the lives of participants reporting different levels of average pain is higher among those with moderate-to-high levels of resilience than those with low resilience (Table 5).

Table 4. Estimated marginal mean* levels of the interference of pain in the lives of participants according to their average pain levels and resilience, with contrasts.

Because statistical interactions are symmetric [28], our findings can be interpreted both in the sense that resilience modifies the effect of average pain on the degree of interference of pain in the lives of participants, and also as that average pain modifies the effect of resilience on that very outcome. As shown in Table 4, resilience demonstrated a much stronger protective association among participants with average null-to-mild pain than among those with more intense levels of pain.

Table 5. Comparisons among the estimated marginal mean* levels of interference of pain in the lives of participants reporting different levels of average pain according to their level of resilience.

DISCUSSION

This study assessed the association between resilience, pain, and the degree of interference of pain in the lives of participants living with fibromyalgia. Although we did not find any association between resilience and average pain, the main effect (i.e., from the regression model without the interaction term) of moderate-to-high resilience on the degree of interference of pain in the lives of participants was almost equivalent and in the opposite direction as the effect of a 1-unit increase in the intensity of average pain on the same outcome. Most interestingly, we also found a significant interaction between average pain and resilience for that outcome, so that when comparing the degree of interference of pain in the lives of participants with null-to-mild pain and those with moderate pain, that difference among people with moderate-to-high resilience was almost five times more intense than among those with low resilience. This means that the intensity with which resilience was associated with decreased degree of interference of pain in the lives of participants was strongest when the average level of pain experienced by participants was low, and less marked for moderate and severe levels of pain. Those findings are important for shedding light on the complexity of the interrelationships between resilience, pain and functionality, and may signal both the relevance and the limits of resilience in the management of chronic pain in fibromyalgia.

A few empirical studies explored the role of resilience in fibromyalgia [10, 15, 16, 18, 29]. However, to our best knowledge, only Torma et al evaluated the association between resilience with pain and functional impairment in fibromyalgia while probing for an interaction between pain and resilience [16]. Those authors investigated the association between resilience and physical functioning in 224 older adults with fibromyalgia. In line with our results, they did not find any association between resilience and pain and identified a protective association between resilience and physical functioning. However, they did not find any significant interaction between resilience and pain regarding physical functioning. Several factors may explain the differences between our results. For example, Torma et al studied older adults and their main outcome was physical functioning as measured by the Late Life Function and Disability Index. On the other hand, most participants from our study were younger than 65 years old and our main outcome was the degree of interference of pain in the lives of participants with fibromyalgia [16]. Finally, our sample size was almost 10 times larger than theirs, and it is well known that the study of interactions requires large sample sizes to attain sufficient power [28].

Bauer and colleagues studied a sample of 724 older adults in Germany and evaluated the interaction between resilience with two forms of pain presentation (chronic widespread pain and chronic localized pain) regarding their association with depressive symptoms [30]. They found significant interactions between resilience and chronic widespread pain, but not with chronic localized pain, concerning the median number of depressive symptoms. However, that study did not use a diagnosis of fibromyalgia among its inclusion criteria and did not evaluate pain intensity or its degree of interference of pain in the lives of participants.

Our study has some relevant implications for research and clinical practice. Our findings suggest that people living with fibromyalgia who report milder pain may be most likely to experience substantial benefits from resilience-strengthening interventions to decrease the impact of pain in their lives. Additionally, our findings suggest a more limited effect of resilience among people with fibromyalgia reporting moderate and intense pain than among those with milder pain. This is important for two main reasons. First, fibromyalgia patients with moderate to intense pain may benefit more from interventions aimed at decreasing the pain rather than aimed at increasing resilience. Second, given the lack of association between pain intensity and resilience, these findings dispute beliefs that the pain reported by people with fibromyalgia is psychosomatic [6, 31]. Regrettably, such beliefs are still common and represent additional sources of suffering for people with fibromyalgia [2, 32]. Finally, our results suggest that future studies of psychological interventions for decreasing the impact of pain in people with fibromyalgia should consider evaluating how those interventions interact with patients' baseline levels of pain and resilience. More specifically, future clinical trials trying to untangle

the relationship between resilience and pain levels on the degree of interference of pain in the lives of people with fibromyalgia would be particularly welcome.

Our study has some limitations. First, this was a cross-sectional study, and it is not possible to infer causality. Second, our recruitment was restricted to fibromyalgia virtual support groups on Facebook. For example, the online nature of our survey probably excluded participants unfamiliar with technology and social media. Besides, it has been estimated that around 20% of the Brazilian population did not have access to the internet in 2019[33]. Hence, our findings may not be generalizable to the population of people living with fibromyalgia in Brazil. However, we argue that the importance of our findings lies not in their generalizability to the overall population of fibromyalgia patients in Brazil but rather in its contribution to the understanding of the interrelationships between resilience, pain, and functioning in patients with fibromyalgia. Our findings are relevant for providing initial evidence showing that those relationships may be more complex than was previously believed. Furthermore, for a disease with an enormous amount of underdiagnosis, such as fibromyalgia, generalizability to the whole population is often not feasible even in studies conducted in primary care or in clinical trials because patients enrolled in those studies are those who sought diagnosis and treatment for their symptoms. Third, because the invitation to the survey was disseminated through social media, we were unable to determine the total population size reached with the study promotional materials. As such, we are unable to calculate the true response rate to our survey. We therefore cannot compare demographic characteristics of responders with non-responders. Fourth, to maximize confidentiality, we did not collect data on the IP addresses of participants or use specific cookies in the survey website to collect further data from participants beyond the information that they provided voluntarily by responding to the survey questions and did not measure the time participants took to complete the survey questionnaire. Fifth, we did not evaluate pain catastrophizing behavior among participants, however we would expect a high collinearity between resilience and pain catastrophizing because they may be understood as opposite manifestations of coping behaviors and including both variables in the regression models could have compromised their accuracy [13]. Sixth, although our analyses were adjusted for a large range of potential confounders, as in other epidemiological studies, it is not possible to rule out the possibility of residual confounding. Finally, we relied on self-reports of fibromyalgia diagnosis made by physicians, which is common practice in surveys on fibromyalgia and other rheumatologic and non-rheumatologic diseases [34-38]. Moreover, the high levels of average pain as well as the high number of painful bodily areas reported by the participants of this study are consistent with the fibromyalgia diagnosis. It is also worth pointing out that the diagnostic criteria for fibromyalgia have changed numerous times during the last two decades, that there is no hard laboratory gold standard to confirm that diagnosis and that conditioning the participation in this study to a diagnosis of fibromyalgia based on a

questionnaire adopting the most current diagnostic criteria would represent not only an unnecessary burden to the survey process but could bias our results by excluding patients with fibromyalgia who happened to have a good level of symptom control during their participation in our study.

On the other hand, our study also has some relevant strengths. First, most studies involving fibromyalgia patients were conducted in high-income countries, we studied those patients in a middle-income country from Latin America and thereby contributed to widening the geographical boundaries of the knowledge base around that disease. This is relevant because several social, economic, and cultural differences between countries may influence the experience of living with fibromyalgia around the world. For example, a survey comparing people living with fibromyalgia in Latin America and Europe found that patients in Latin America reported higher levels of pain, more impairment in their ability to work, took less medications and that it took them on average one year longer to be diagnosed than those living in Europe [39]. Second, we used validated scales to assess resilience, pain, and its impact in the lives of participants, and the BPI was particularly well-suited to the assessment of the impact of pain in the lives of participants. Third, we were able to retrieve a relatively large number of responses, which allowed sufficient power to assess the interaction between resilience and average pain on the degree of interference of pain in the lives of participants. Fourth, we were able to adjust our regression models by a large number of demographic and clinical variables.

In conclusion, in this study resilience was not associated with the average level of pain experienced by people with fibromyalgia but interacted with pain in its association with the degree of interference of pain in the lives of participants in such a way that resilience showed a stronger protective association among participants with average milder pain than among those with more intense levels of pain. Future studies evaluating behavioral interventions for the management of fibromyalgia should consider how those interventions interact with baseline levels of pain and resilience in different populations.

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