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The Complex Relationship between Pain Intensity and Physical Functioning in Fibromyalgia: The Mediating Role of Depression

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Abstract

PURPOSE: Fibromyalgia (FM) is typically associated with the experience of diffuse pain and physical impairment. Depression also commonly co-exists in patients with FM, and has been correlated with pain intensity and physical functioning. Previous research suggests an association between pain intensity and physical functioning; however, the direct causal relationship between improvements in pain intensity and in functioning is not observed in many FM patients. This may suggest that another factor such as depression is mediating this relationship. The present work examined mediating role of depression. METHODS: 216 patients with FM completed measures of pain intensity, depression, and physical function as part of a larger longitudinal study. Assessments were completed at baseline, 12, 24, and 36 weeks. RESULTS: Longitudinal mediational analyses indicated that depression is a partial mediator of the relationship between pain intensity and physical functioning at all four assessment points. Beta coefficients for the path from pain to physical functioning ranged from 0.18 - 0.36, with attenuated path coefficients ranging from 0.03 - 0.08, still showing significant but decreased associations when depression was added as a mediator. CONCLUSIONS: Clinical implication includes the importance of treating co-morbid depression in patients with fibromyalgia early in the course of treatment to prevent engagement in the cycle of disability.

Introduction

Fibromyalgia (FM) is a chronic pain condition characterized by persistent diffuse musculoskeletal pain, fatigue, and non-restorative sleep (Wolfe, Ross, Anderson, Russell, & Hebet, 1995), diagnosed on the basis of self-reported symptoms, as there are no biological markers specific to the condition (Wolfe et al, 2011). Recent prevalence rates suggest the condition affects approximately 2.1% of the general population and is more common among women (Wolfe, Brähler, Hinz, & Häuser, 2013). Partly because of the subjective nature of diagnosing FM, patients often do not receive validation of their pain from those around them. As a result, FM patients may feel isolated, misunderstood, or rejected by loved ones and society (Turk, 2002), which may contribute to the experience of depression.

Physical Functioning and Pain

Decreases in physical functioning are among the most problematic symptoms for FM patients (Bennett, Jones, Turk, Russel, & Matallana, 2007; Turk et al, 2008). A survey of 1735 women with FM found that 25% reported experiencing difficulty completing activity of daily living such as bathing, and 90% reported trouble with heavy household tasks and strenuous activities (Jones, Rutledge, Jones, Matallana, & Rooks, 2008). Bennett and colleagues (2007) found that a mere 7% of their sample reported being able to complete tasks such as vacuuming or scrubbing.

Declines in physical functioning seem to be correlated with severity of FM pain (Kop et al, 2005). Studies have documented pain intensity as a significant predictor of physical functioning among fibromyalgia patients (Bigatti, Hernandez, Cronan, & Rand, 2008).

Despite the documented relationship between pain and functioning, both pharmacological and non-pharmacological interventions aimed at improving physical functioning do not yield consistent positive changes in pain intensity (Häuser, Petzke, & Sommer, 2010). The inconsistencies in the relationships between changes in physical functioning and pain intensity suggest that there may be mediating variables, such as psychological factors, underlying the relationship between pain and physical functioning. This relationship is further complicated by the fact that research demonstrates improvements in physical functioning may in turn create reductions in pain intensity due to reversing or prevention of deconditioning and disuse; however, patients may have difficulty breaking this cycle of perpetuating pain and lack of activity due to pain as well as depression and other psychological factors (Scott, Kroenke, Wu & Yu, 2016). This is further supported by meta-analytic work indicating that psychological interventions produce the largest improvements in daily functioning (Bernardy, Klose, Busch, Choy, & Häuser, 2013), as well as improvements in pain-related behaviors, and psychological factors (Bennett & Nelson, 2006).

The Role of Depression

Co-morbid depression is common among individuals with FM (Gormsen, Rosenberg, Bach, & Jensen, 2010; Thieme, Turk, & Flor, 2007) with estimated prevalence rates between 24-40% (Bennett et al, 2007; Munce and Stewart, 2007). Further, Munce and Stewart (2007) have reported higher rates of comorbid depression in FM (22.3%) compared to other chronic pain conditions such as rheumatoid arthritis (10%) and chronic back pain (12.6%).

The reasons behind the large rates of depression in FM populations are varied. It is not surprising that the experience of chronic pain would lead some individuals to experience depression when contemplating the chronic nature of their condition and the limitations it entails (Harris, Morley, & Barton, 2003). Although depression may lead to more pain among chronic pain patients, longitudinal research demonstrates that chronic illness leads to depression, and not the other way around. Chronic pain specifically has been identified as a risk factor for depression and prolonged depressive episodes in the general population (Ohayon & Schatzberg, 2003). Using ecological momentary assessments, Okifuji, and colleagues (2011) sequenced daily symptoms in FM and found that pain preceded and increased emotional distress.

For depressed FM patients, reductions in physical functioning are compounded. Okifuji et al (2000) found that depressed patients reported greater impairment in household tasks and physical activities outside of the home and higher levels of perceived disability than those FM patients without depression.

These findings suggest that depression may mediate the relationship between pain and physical functioning in chronic pain populations. Wegener and colleagues (2011), found in limb trauma patients that psychological distress mediated pain and function, and similar relationships with psychological mediators have been noted in other pain populations as well (Craig, Tran, Siddall, Wijesuriya, Lovas, Bartrop, & Middleton, 2013; Kop et al, 2005; Peters, Vlaeyen, & Weber, 2004). Specific to FM, many studies have examined potential mediators of pain and functioning. For example, Miró and colleagues (2011) found that sleep quality mediated the relationship between pain and emotional distress, as well as pain and physical functioning, suggesting a possible relationship between distress and physical functioning via sleep, and other studies have suggested that variables related to depression such as catastrophic thinking about pain (Crombez et al, 2004) may play a role. Additionally, exercise interventions for Fibromyalgia have suggested positive correlations between improvements in depression and increased activity (Gowans, deHueck, Voss, Silaj, Abbey, & Reynolds, 2001; Tomas-carus et al, 2008). However, we could not find any study that explicitly examined depression as a statistical mediator of the pain and physical functioning relationship. Given that depression is so prevalent in FM, and so disruptive to quality of life, it is important to consider its role in the relationship between pain and functioning.

In a sample of FM patients we hypothesized that pain, depression and physical functioning would be correlated. We expected that depression would mediate the relationship between pain intensity and physical functioning across multiple time points.

Materials and Methods

Design

This is a secondary data analysis of a completed randomized controlled trial entitled, Research to Encourage Exercise in Fibromyalgia (REEF) (Ang et al, 2013). The study approved by the university Institutional Review Board, examined motivational interviewing as an intervention to enhance physical activity in patients with Fibromyalgia; no effects of the intervention were found (Ang et al, 2011). As part of a battery of questionnaires self-report measures of pain intensity, physical functioning, and depression collected and completed at 4 time points: baseline, immediately following an intervention period (12 weeks), 3- month followup (24 weeks), and 6- month follow-up (36 weeks). All four assessment points were examined to test our hypotheses.

Participants

Participants were recruited from various primary care clinics or specialty medicine practices (rheumatology, pain management, and neurology). To be eligible to participate in the study, individuals were required to meet the following inclusion criteria: 1) must be between 18-65 years of age, 2) must be diagnosed with FM by a board-certified rheumatologist, 3) must be on stable doses of all medications, and 4) must have an average pain level of 4 or above on a scale from 0-10. Exclusion criteria included diagnosis of another rheumatic condition such as rheumatoid arthritis; full exclusion criteria are described elsewhere (Ang et al, 2013). The study enrolled 216 FM patients. Informed consent was obtained from all participants prior to the onset of the study. Given that the intervention had no effects on any of the relevant variables participants in both the intervention and attention control arms were included in the present analyses as one single group.

Measures

Physical functioning. The Fibromyalgia Impact Questionnaire Physical Impairment Subscale (FIQ-PI; Burckhardt, Clark, & Bennett, 1991) consists of 10 items that focus primarily on the patient's ability to perform large muscle tasks (i.e. doing yard work, vacuuming a rug) in the week leading up to the assessment, presented in a Likert-type scale format ranging from 0 (always able to do) to 3 (never able to do). The sum of these 10 items is divided by the number of valid scores and then multiplied by 3.33 to provide one physical impairment score that ranges from 0-9.99. The items are specific to ability over the past week. The scale has demonstrated test-retest reliability (0.56 to 0.95). Both content and construct validity have previously been established [29]. It should be noted that this is the original version of the scale.

Depression. The Personal Health Questionnaire Depression Scale (PHQ-8) is an eight item self-report measure designed to assess depressive symptoms over the two week period

leading up to the assessment (Kroenke, Strine, Spitzer, Williams, Berry, & Mokdad, 2009). The eight items are designed to map onto the diagnostic criteria for a depressed episode in the DSM-IV-TR, with the exception of suicidal ideation. The measure is short and easy to score, making it an ideal measure for both patients and clinicians to use. Scores range from 0-24 with lower scores representing milder levels of depression. Additionally, the measure has specified cut-off scores for various levels of symptom severity: $(0-4 = \text{minimal}; 5-9 = \text{mild}; 10-14 = \text{moderate}; 15-19 = \text{moderately severe}; \geq 20 = \text{severe}$).

Pain. The Brief Pain Inventory (BPI; Cleeland, 1989) is a self-report measure designed to assess pain on two dimensions: pain intensity and pain interference. The BPI pain intensity is an average of 4 items (i.e., worse pain, least amount of pain, average pain and pain right now) that ask participants to rate their pain on a scale of 0-10 (0= no pain and 10 = pain as bad as you can imagine) during the past 7 days. For the present study, only the BPI pain intensity domain was examined. Higher scores are associated with greater levels of pain.

Statistical Analyses

Longitudinal mediation analyses were performed to determine if the association between pain and physical function is mediated by depression. First, Structural Equation Modeling (SEM) techniques were used to set up the longitudinal design; at each time period, direct effect paths were tested from pain to depression and depression to function. An indirect path between pain and function was tested at each time point as well, so that both the direct and indirect effects were evaluated to determine the presence of mediation. The longitudinal aspect was analyzed by adding paths between the variables from each time point to the next follow-up (i.e. from pain at baseline to week 12, pain from week 12 to week 24, and pain from week 24 to week 36, with similar paths for the associations between depression outcomes and physical function outcomes). The model was also adjusted for treatment group: Motivational Interviewing intervention to enhance physical activity engagement (MI) vs. an educational attention control intervention (AC), with treatment group having paths leading to the functional outcome at each time point (MacKinnon, 2008). Although the sample size necessary for such a model is relatively large, due to the number of paths and parameters, bootstrapping methods were used to resample the data in order to more accurately estimate the parameters, including path coefficients. To further clarify the longitudinal relationships, a second model, where paths were added from both pain and depression to the next assessment's function outcome, was also performed. The longitudinal mediation analysis was performed using Mplus software and is consistent with modeling outlined by Muthen (1997).

Results

Descriptive Statistics

Participants were 216 individuals with FM, of which 95.8% were female. The average age of participants was 45.81 (SD = 11.18), and the average number of years since diagnosis with FM was 9.01 year (SD = 7.02). A complete description of the participant characteristics is presented in Table 1.

Physical Functioning

As a group, the level of impairment in physical functioning at baseline was moderate with a group FIQ-PI mean score of 5.37 (SD = 1.57) at baseline. However scores ranged from 2.12-9.99 indicating that for some individuals the level of functional impairment was very severe. Of the specific tasks listed on the FIQ-PI, washing dishes, vacuuming, walking several blocks, and yard work had the highest group means for difficulty. Across all visits, FIQ-PI ranged from 0 to 9.99, with follow-up visits having mean scores just under four (3.86, 3.93, and 3.80). Means, standard deviations, and ranges of scores for all assessment time points can be seen in Table 2.

Pain Intensity

The mean baseline score for pain intensity on the BPI was 5.95 (SD = 1.27), with scores ranging from 0.25 to 10 throughout the study, with mean BPI values close to five across the study time (4.90, 5.05, and 4.71 at the three follow-up visits, respectively). Pain intensity scores ranged from 4-10, with 78.2% rating their pain as 5 or greater, and 7.9% rating their pain as an 8 or above indicated very severe level of pain. The most commonly reported amount of pain was a rating of 5.5, accounting for 9.3% of the sample. Means, standard deviations, and ranges of scores for all assessment time points can be seen in Table 2.

Depression

The mean score on the PHQ-8 at baseline was 12.54 (SD = 4.92), ranging from 0 – 24 across the study, and with mean values at follow-up visits staying between 9 and 10 (9.33, 9.77, and 9.81, respectively), which represents a moderate level of depression for the group as a whole. Scores ranged from 1-24 indicating that our sample varied greatly with respect to depressive symptoms. The most frequently endorsed items were related to energy level and/or sleeping. A very small portion of the sample (3.2%) reported a minimal level of depression; the majority of the sample fell somewhere in the middle of the continuum. Means, standard deviations, and ranges of scores for all assessment time points can be seen in Table 2.

Mediational Analyses

Using the structural equation modeling approach described above, we tested the mediating role of depression in the relationship between pain intensity and physical functioning using longitudinal data. Model 1 analyzed each mediation cross-sectionally, while adjusting for each variable's measure at the previous time point (i.e., depression at 12 week visit was adjusted for by depression at baseline); additionally, these relationships were tested adding longitudinal steps to functioning, at each visit, from the previous visit's pain and depression outcomes (Model 2). Figure 1 provides an illustration of the model and the beta weights for each path and Table 3 includes beta weights for all paths. In both models, the effect of treatment group was added, with paths to each visit's functioning outcome. Overall, beta coefficients for the path from pain to function ranged from 0.18 - 0.36, with attenuated path coefficients ranging from 0.03 - 0.08, still showing significant associations. Beta coefficients for paths from depression to function ranged from 0.15 - 0.28 and from pain to depression ranged from 0.23 - 0.31. Longitudinal paths, from each variable to itself at the next visit, ranged from 0.26 - 0.67, with a median coefficient of 0.49.

Results of Model 1 indicated that depression is a significant partial mediator of the relationship between pain intensity and physical functioning at all four time points. The mediation is viewed as partial, given that this relationship maintained significance even in the presence of depression, but the strength of the relationship decreased at each point in time. There were significant positive associations between each outcome and its respective value at the next follow-up (i.e. physical functioning at baseline was associated with physical functioning at subsequent time points). As stated previously, there were no significant effects of the intervention on the originally randomized group, thus all participants were treated as one group in the present analyses. However, exploratory analyses were conducted both with and without

treatment group and treatment group was not significantly associated with functioning. Analyses were performed without treatment group yielded similar results.

For Model 2, although depression was significantly associated with functioning at the following visit, for all visits, pain was not. In addition, the main mediation analyses were not attenuated and remained similar to Model 1's results. With the added path from pain and depression to physical functioning at the next time point Model fit statistics (using both Akaike and Bayesian information criteria) showed similar results between the models, with Model 2 having a slight, but non-significant, worse fit, due to the number of added paths. Both models are presented in Figure 1.

Additionally, both mediation models (cross-sectional and longitudinal) were run in reverse, looking at the association of function on pain, being mediated by depression. Results were similar in both models, indicating that pain and physical functioning are significantly associated, with depression being a significant partial mediator, regardless of direction.

Discussion

The aim of the present study was to examine the relationships between pain intensity, physical functioning, and depression in a group of FM patients and to determine the potential mediating effect of depression on the pain intensity- physical functioning relationship over time.

Our findings that depression partially mediates the relationship between pain intensity and physical functioning support the extant literature that shows improvements in physical and mental health with reduced pain (Moore et al, 2010). The fact that depression emerged as only a

partial mediator highlights the importance of pain intensity to deficits in physical functioning. Given that pain and physical functioning are the two most common physical symptoms and complaints of patients, they are, and should be, the focus on treatment planning.

However, clinically significant pain reduction is difficult to achieve in FM. Meta-analyses suggest current pharmacological treatments for FM pain have small effect sizes and serious side effects (Häuser et al, 2014; Sebastian, Derry, Moore, & McQuay, 2010). Cognitive Behavioral Therapy (CBT), the most common behavioral approach to pain reduction in FM has had mixed results in terms of efficacy with some meta-analyses suggesting that CBT is effective for only *short-term* pain reduction (Glombieski et al 2010), or that the intervention yields only small effects on pain, functioning, and mood (Bernardyet al, 2013).

Regular exercise and moderate levels of physical activity are considered to be important components in the management of FM (Clauw, 2014; Häuser, Thieme, & Turk, 2010). Both aerobic and strength enhancing exercise yield moderate to large effects on physical functioning (Busch et al, 2011), and lower pain has been related to better muscle strength and flexibility (Soriano-Maldonado et al., 2015). However, FM patients are often reluctant to adopt a physical activity program because of fear of pain and activity-avoidance beliefs (de Bruijin et al, 2011). This is further evidenced by the finding that the average dropout rate in clinical trials of exercise for FM is greater for those assigned to aerobic exercise (22%) compared to those assigned to a control condition (10%; Busch et al, 2011). Thus although treatments aimed at pain and functioning have some effect, these findings provide compelling evidence for the need to find other target for treatment. One of these may be a greater focus on depressive symptoms in FM patients. Our data provide compelling evidence for emphasizing treatment of depression in the treatment of FM. Present results showed a significant partial mediation of the pain intensity-physical functioning relationship via depression across multiple assessment points. It is important to note that the means for each of these variables changed across assessment points, and strength of the relationships also changed, but the mediation of depression remained similarly strong at each time point. Even with the addition of longitudinal paths assessing associations between the same variable across time points, depression at any time point remained a significant partial mediator of pain intensity-physical functioning relationship at that same time point. The temporal directions of these relationships were tested as well, by testing in reverse order, yielding no significant associations and providing greater evidence for the direction of the relationships between variables.

Treating depression in an effort to improve functioning may also help decrease pain, or perception of pain. The pain-depressive symptoms relationship has been extensively established, and recent research suggest a bidirectional relationship between these two experiences (Chang et al, 2015). However, understanding that this relationship may lead to physical functioning problems had not been explicitly established in FM to date.

Depressed mood may also make patients more aware of their symptoms and more likely to react to these symptoms in a maladaptive manner (Wegener et al, 2011). According to Wegener et al. (2011), depressed mood may lead patients to more negatively appraise their abilities, or to avoid activities altogether, leading to lower functioning. These researchers examined individuals who had experienced lower limb trauma and found that depressed mood played a larger role in decreased functioning as time passed from the time of injury.

Other factors associated with depression such as pain catastrophizing and low self-efficacy (Börsbo, Gerdle, & Peolsson, 2010) and fatigue (Lukkahatai et al., 2016) are also related to disability among FM and chronic pain patients, suggesting avenues through which depression may contribute to poorer physical functioning.

A multidisciplinary treatment plan that also addresses depression and its impact on functioning may be the best approach for FM. Although guidelines for the management of FM have long included the use of CBT and psychological interventions, greater emphasis may need to be placed on psychological intervention that focus on depressive symptoms and thought processes in addition to maladaptive beliefs about pain, as is often the focus in most CBT for chronic pain interventions. Interventions aimed at emotional expression may also be effective in reducing depression, pain, and pain interference (Burger et al., 2016; Lumley, 2011). Importantly, all the treatment modalities mentioned above, pharmacological, behavioral and physical activity, may work better if they are combined with a focus on reducing depressive symptoms along with improvements in pain and functioning. Given our mediation findings it may well be that a slight change in approach, the addition of components focused on mood, may increase the treatment effectiveness.

Limitations

An important limitation to the present study is the fact that all of the variables were assessed by self-report. Self-report measures are often criticized for being subject to response bias and inaccurate reporting (Greenwald et al, 2002). Physical functioning and pain can be measured in a more objective manner, such as activity monitors which have been used in other studies (Ang et al, 2010) to assess the experience of pain in a more objective manner. It should also be noted that within our sample, participants reported a mean depression score indicative of only moderate levels of depression; thus, it is plausible that this relationship may be more pronounced in a more depressed sample, though further work is needed to confirm this assumption. It bears mention that several other factors may play a role in explaining the relationship between pain intensity and physical functioning; previous research in other chronic pain populations has indicated that catastrophizing, fear of reinjury, and pain-related anxiety may impact this relationship as well (Denison, Asenlof, & Lindberg, 2004; Peters et al, 2004; Scott, Kroenke, Wu & Yu, 2016); and there is evidence that these factors contribute to the experience of depression as well (Sturgeon & Zautra, 2013). Another plausible relationship worth exploring is the role of fatigue/decreased energy; fatigue is a hallmark symptom of fibromyalgia, with some estimates suggesting prevalence rates as high as 76% in FM patients (Vincent, Benzo, Whipple, McAllister, Erwin, & Saligan, 2013). It stands to reason that fatigue may also play a role in the relationship between depression/negative affect and physical functioning/disability as it is correlated with both (Vincent et al, 2013). Although we were unable to examine these factors in the present study, future research should attempt to further illustrate the complex relationships between psychological constructs, pain, fatigue, and functioning with FM patients; this work may involve looking for subgroups within the populations that exhibit various patterns of these other factors; this work would be especially important given the only partial mediation of our depression mediator. Furthermore, we cannot generalize these findings to individuals with different demographic characteristics than our sample, or to non-patient populations.

Conclusions

The present research is congruent with the existing literature on the strong relationships between pain intensity, physical functioning and depression. Furthermore, the data support our hypothesis that depression mediates the relationship between pain intensity and physical functioning in FM patients, and that this pattern held across multiple times points as well as when individual variables were assessed overtime. To our knowledge, this is the first study to explicitly examine this relationship in a sample of FM patients, as well as the first to do so using a longitudinal design. The study results significantly add to our understanding of the complexities behind efforts to improve physical functioning in this population. Given that our findings regarding the mediational role of depression in the pain intensity-physical functioning relationship are largely aligned with research in nonspecific chronic pain populations, coupled with the consistency of our findings over time, we can assume confidence in the mediational role of depression. Clinical implications for these findings include focusing on depression and more specifically psychological correlates of depression as first line therapeutic targets in improving physical functioning of patients with FM. Depression and other psychological factors should be assessed and intervened upon early in the treatment of FM, before the individual has an opportunity to engage in the disability cycle.

References

- Ang, D.C., Chakr, R., Mazzuca, S., France, C.R., Steiner, J.L., & Stump, T. (2010). Cognitive behavioral therapy attenuates nociceptive responding in patients with fibromyalgia: a pilot study. *Arthritis & Rheumatism*, 62(5), 618-623.
- Ang, D. C., Kaleth, A. S., Bigatti, S., Mazzuca, S. A., Jensen, M. P., Hilligoss, J., ... & Saha, C. (2013). Research to Encourage Exercise for Fibromyalgia (REEF): Use of Motivational Interviewing, Outcomes from a Randomized Controlled Trial. *The Clinical journal of pain*, 29(4), 296.
- Ang, D. C., Kaleth, A. S., Bigatti, S., Mazzuca, S., Saha, C., Hilligoss, J., ... & Bandy, R. (2011).
 Research to Encourage Exercise for Fibromyalgia (REEF): use of motivational interviewing design and method. *Contemporary clinical trials*, 32(1), 59-68.
- Bennett, R., & Nelson, D. (2006) Cognitive behavioral therapy for fibromyalgia. Nature Clinical Practice Rheumatology, 2(8), 416-424.
- Bennett, R.M., Jones, J., Turk, D.C., Russell, I.J., & Matallana, L. (2007). An internet survey of 2596 people with fibromyalgia. *BMC Musculoskeletal Disorders*, 8(1), 1.
- Börsbo, B., Gerdle, B., & Peolsson, M. (2010). Impact of the interaction between self-efficacy, symptoms and catastrophising on disability, quality of life and health in with chronic pain patients. *Disability and rehabilitation*,*32*(17), 1387-1396.
- Burger, A. J., Lumley, M. A., Carty, J. N., Latsch, D. V., Thakur, E. R., Hyde-Nolan, M. E., ... & Schubiner, H. (2016). The effects of a novel psychological attribution and emotional awareness and expression therapy for chronic musculoskeletal pain: A preliminary, uncontrolled trial. *Journal of psychosomatic research*, *81*, 1-8.

- Burckhardt, C.S., Clark, S., & Bennett, R.M. (1991). The fibromyalgia impact questionnaire: development and validation. *The Journal of Rheumatology*, *18*(5), 728-733.
- Bernardy, K., Klose, P., Busch, A. J., Choy, E. H., & Häuser, W. (2013). Cognitive behavioural therapies for fibromyalgia. *The Cochrane Library*.
- Bigatti, S.M., Hernandez, A.M., Cronan, T.A., & Rand, K.L. (2008). Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. *Arthritis & Rheumatism*, 59(7), 961-967.
- Busch, A. J., Webber, S. C., Brachaniec, M., Bidonde, J., Dal Bello-Haas, V., Danyliw, A. D., ...
 & Schachter, C. L. (2011). Exercise therapy for fibromyalgia. *Current pain and headache reports*, 15(5), 358-367.
- Chang, M. H., Hsu, J. W., Huang, K. L., Su, T. P., Bai, Y. M., Li, C. T., ... & Chen, M. H. (2015). Bidirectional association between depression and fibromyalgia syndrome: a nationwide longitudinal study. *The Journal of Pain*, *16*(9), 895-902.
- Clauw, D. J. (2014). Fibromyalgia: a clinical review. Jama, 311(15), 1547-1555.
- Cleeland, C.S. (1989). Measurement of pain by subjective report. In: C.R. Chapman & J.D. Loeser (Eds.). Advances in Pain Research and Therapy. Vol. 12. Issues in Pain Measurement (391-403). New York, Raven Press.
- Craig, A., Tran, Y., Siddall, P., Wijesuriya, N., Lovas, J., Bartrop, R., & Middleton, J. (2013).
 Developing a model of associations between chronic pain, depressive mood, chronic fatigue, and self-efficacy in people with spinal cord injury. *The Journal of Pain*, *14*(9), 911-920.

- Crombez, G., Eccleston, C., Van den Broeck, A., Goubert, L., & Van Houdenhove, B. (2004).Hypervigilance to pain in fibromyalgia: the mediating role of pain intensity and catastrophic thinking about pain. *The Clinical journal of pain*, 20(2), 98-102.
- de Bruijin, S.T., van Wijck, A.J.M., Geenan, R., Snijders, T.J., van der Meulen, W.J.T.M., Jacobs, J.W.G., & Veldhuijzen, D.S. (2011). Relevance of physical fitness levels and exercise-related beliefs for self-reported and experimental pain in fibromyalgia: an explorative study. *The Clinical Journal of Rheumatology*, *17*(6), 295-301.
- Denison, E., Asenlof, P., & Lindberg, P (2004). Self-efficacy, fear avoidance, and pain intensity as predictors of disability in subacute and chronic musculoskeletal pain patients in primary health care. *Pain*, *111*(3), 245-252.
- Glombieski, J.A., Sawyer, A.T., Gutermann, J., Koenig, K., Rief, W., & Hofmann S.G. (2010). Psychological treatments for fibromyalgia: a meta-analysis. *Pain*, *151*(2), 280-295.
- Gormsen, L., Rosenberg, R., Bach, F.W., & Jensen, T.S. (2010). Depression, anxiety, healthrelated quality of life and pain in patients with chronic fibromyalgia and neuropathic pain. *The European Journal of Pain*, *14*(2), 127-e1.
- Gowans, S. E., deHueck, A., Voss, S., Silaj, A., Abbey, S. E., & Reynolds, W. J. (2001). Effect of a randomized, controlled trial of exercise on mood and physical function in individuals with fibromyalgia. *Arthritis Care & Research*, *45*(6), 519-529.
- Greenwald, A.G., Rudman, L.A., Nosek, B.A., Banaji, M.R., Farnham, S.D., & Mellott, D.S.
 (2002). A unified theory of implicit attitudes, stereotypes, self-esteem, and self-concept.
 Psychological Review, 109(1),3-25.
- Harris, S., Morley, S., & Barton, S.B. (2003). Role loss and emotional adjustment in chronic pain. *Pain*, 105(1),363-370.

- Häuser, W., Petzke, F., & Sommer, C. (2010). Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *The Journal of Pain*, *11*(6),505-521.
- Häuser, W., Walitt, B., Fitzcharles, M. A., & Sommer, C. (2014). Review of pharmacological therapies in fibromyalgia syndrome. *Arthritis research & therapy*, 16(1), 1.
- Häuser, W., Thieme, K., & Turk, D. C. (2010). Guidelines on the management of fibromyalgia syndrome–a systematic review. *European Journal of Pain*, *14*(1), 5-10.
- Jones, J., Rutledge, D.N., Jones, K.D., Matallana, L., & Rooks, D.S. (2008) Self-assessed physical function levels of women with fibromyalgia: a national survey. *Journal of Women's Health Issues and Care, 18*(5),406-412.
- Kop, W.J., Lyden, A., Berlin, A.A., Ambrose, K., Olsen, C., Gracely, R.H., ... & Clauw, D.J. (2005). Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. *Arthritis & Rheumatism*, 52(1), 296-303.
- Kroenke, K., Strine, T. W., Spitzer, R. L., Williams, J. B., Berry, J. T., & Mokdad, A. H. (2009).The PHQ-8 as a measure of current depression in the general population. *Journal of affective disorders*, *114*(1), 163-173.
- Lumley, M. A. (2011). Beyond cognitive-behavioral therapy for fibromyalgia: addressing stress by emotional exposure, processing, and resolution. *Arthritis research & therapy*, *13*(6), 1.
- Lukkahatai, N., Walitt, B., Espina, A., Gelio, A., & Saligan, L. N. (2016). Understanding the association of fatigue with other symptoms of fibromyalgia: Development of a cluster model. *Arthritis Care & Research*, 68(1), 99-107.
- MacKinnon, D.P. (2008) Introduction to Statistical Mediation Analysis. New York: Taylor & Francis.

- Miró, E., Martínez, M. P., Sánchez, A. I., Prados, G., & Medina, A. (2011). When is pain related to emotional distress and daily functioning in fibromyalgia syndrome? The mediating roles of self-efficacy and sleep quality. *British journal of health psychology*, *16*(4), 799-814.
- Moore, R.A., Straube, S., Paine, J., Phillips, C.J., Derry, S., & McQuay, H.J. (2010).
 Fibromyalgia: Moderate and substantial pain intensity reduction predicts improvement in other outcomes and substantial quality of life gain. *Pain*, 149(2), 360-364.
- Munce, S.E.P., & Stewart, D.E. (2007). Gender difference in depression and chronic pain conditions in a national epidemiologic survey. *Psychosomatics*, *48*(5), 394-399.
- Ohayon, M.M., & Schatzberg, A.F. (2003) Using chronic pain to predict depressive morbidity in the general population. *Archives of General Psychiatry*, *60*(1), 39-47.
- Okifuji, A., Bradshaw, D.H., Donaldson, G.W., & Turk, D.C. (2011). Sequential analyses of daily symptoms in women with fibromyalgia syndrome. *The Journal of Pain*, *12*(1), 84-93.
- Okifuji, A., Turk, D.C., & Sherman, J.J. (2000). Evaluation of the relationship between depression and fibromyalgia syndrome: Why aren't all patients depressed?. *The Journal* of Rheumatology, 27(1), 212-219.
- Peters, M.L., Vlaeyen, J.W.S., & Weber, W.E.J. (2004). The joint contribution of physical pathology, pain-related fear and catastrophizing to chronic back pain disability. Pain, 113(1), 45-60.
- Scott, E. L., Kroenke, K., Wu, J., & Yu, Z. (2016). Beneficial Effects of Improvement in Depression, Pain Catastrophizing, and Anxiety on Pain Outcomes: A 12-Month Longitudinal Analysis. *The Journal of Pain*, 17(2), 215-222.

- Sebastian, S., Derry, S., Moore, R.A., & McQuay, H.J. (2010). Pregabalin in fibromyalgia: metaanalysis of efficacy and safety from company clinical trial reports. *Rheumatology*, 49,706-715.
- Soriano-Maldonado, A., Ruiz, J. R., Aparicio, V. A., Estévez-López, F., Segura-Jiménez, V., Álvarez-Gallardo, I. C., ... & Ortega, F. B. (2015). Association of Physical Fitness With Pain in Women With Fibromyalgia: The al-Ándalus Project. Arthritis care & research, 67(11), 1561-1570.
- Sturgeon, J. A., & Zautra, A. J. (2013). Psychological resilience, pain catastrophizing, and positive emotions: perspectives on comprehensive modeling of individual pain adaptation. *Current pain and headache reports*,17(3), 1-9.
- Thieme, K., Turk, D.C., & Flor, H. (2007). Responder criteria for operant and cognitivebehavioral treatment for fibromyalgia syndrome. *Arthritis* & Rheumatism, 57(5), 830-836.
- Tomas-Carus, P., Gusi, N., Häkkinen, A., Häkkinen, K., Leal, A., & Ortega-Alonso, A. (2008).
 Eight months of physical training in warm water improves physical and mental health in women with fibromyalgia: a randomized controlled trial. *Journal of Rehabilitation Medicine*, 40(4), 248-252.
- Turk, D.C. (2002). Suffering and dysfunction in fibromyalgia syndrome. *The Journal Musculoskeletal* Pain, 10(1-2), 85-96.
- Turk, D.C., Dworkin, R.H., Revicki, D., Harding, G., Burke, L.B., Cella, D., ... & Max, M.B.
 (2008). Identifying important outcome domains for chronic pain clinical trials: an
 IMMPACT survey of people with pain. *Pain*, *137* (2), 276-285.

- Vincent, A., Benzo, R. P., Whipple, M. O., McAllister, S. J., Erwin, P. J., & Saligan, L. N. (2013). Beyond pain in fibromyalgia: insights into the symptom of fatigue. *Arthritis research & therapy*, 15(6), 1.
- Wegener, S.T., Castillo, R.C., Haythornthwaite, J., MacKenzie, E.J., Bosse, M.J., & LEAP Study Group. (2011). Psychological distress mediates the effect of pain on function. *Pain*,152(6), 1349-1357.
- Wolfe, F., Brähler, E., Hinz, A., & Häuser, W. (2013). Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. *Arthritis Care & Research*, 65, 777-785.
- Wolfe, F., Clauw, D. J., Fitzcharles, M. A., Goldenberg, D. L., Häuser, W., Katz, R. S., ... & Winfield, J. B. (2011). Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. *The Journal of rheumatology*, *38*(6), 1113-1122.
- Wolfe, F., Ross, K, Anderson, J., Russell, I.J., & Hebert, L. (1995). The prevalence and characteristics of fibromyalgia in the general population. *Arthritis & Rheumatism*, 38, 19-28.

Variable	Mean	SD
Age	45.81	11.18
Years since diagnosis	9.01	7.02
Variable	Percentage	N
Sex		
Female	95.8	207
Male	4.2	9
Race		
Caucasian	88.4	191
African American	9.3	20
American Indian	0.9	2
Pacific Islander	0.5	1
Other	0.9	2
Education		
< High school	2.8	6
High School or GED	19.4	42
>High School	77.9	168
Employment Status		
Employed	45.4	98
Self-employed	8.3	18
Retired	3.7	8
Homemaker	11.6	25
Student	4.2	9
Unable to work	19.0	41
Currently out of work	3.7	8

Table 1. Demographic Characteristics of Participants

Table 2.

Descriptive Statistics

	FIQ-PI		BPI		PHQ-8	
Week	M (SD)	Range	M (SD)	Range	M (SD)	Range
1	5.37 (1.57)	2.12- 9.99	5.95 (1.27)	4.00 - 10.00	12.54 (4.92)	1-24
12	3.86 (2.04)	0.00- 8.78	4.90 (1.75)	1.25 - 10.00	9.33 (5.36)	0-24
24	3.93 (2.24)	0.00- 9.99	5.05 (1.84)	0.25 - 10.00	9.77 (5.92)	0-24
36	3.80 (2.41)	0.00 - 9.99	4.71 (1.91)	0.25 - 9.50	9.81 (5.97)	0-24

FIQ-PI = Fibromyalgia Impact Questionnaire- Physical Interference Subscale; BPI = Brief Pain Inventory (pain intensity measure); PHQ-8 = Patient Health Questionnaire- 8 (depression measure); M = Mean; SD = standard deviation

Table 3.

Mediational Analyses

	Path A	Path B	Path C	Path C'
Week 1	$\beta = 0.279 * *$	$\beta = 0.284 * *$	$\beta = 0.177*$	$\beta = 0.081*$
Week 12	$\beta = 0.308 * *$	$\beta = 0.270^{**}$	$\beta = 0.264 * *$	$\beta = 0.082*$
Week 24	$\beta = 0.236^{**}$	$\beta = 0.177*$	$\beta = 0.224 * *$	$\beta = 0.044*$
Week 36	$\beta = 0.234 * *$	$\beta = 0.147*$	$\beta = 0.360 * *$	$\beta = 0.034*$
	•	•		,

*significant at *p* < 0.01; ** significant at *p* < 0.001

Path A = Direct effect of Pain Intensity on Depression; Path B = Direct effect of Depression on Physical Functioning; Path C = Direct effect of Pain Intensity on Physical Functioning; Path C' = Relationship between Pain Intensity and Physical Functioning with Depression as a mediator. All path coefficients are standardized, based on longitudinal analyses.

Figure 1. The mediating role of depression in the relationship between pain intensity and physical functioning.

