Trajectory of Change in Pain, Depression, and Physical Functioning after Physical Activity Adoption in Fibromyalgia

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Clinical trial registration: NCT00573612

Funding/Support: National Institute of Arthritis and Musculoskeletal and Skin Diseases

Grant number: 1RO1AR054324-01A1

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See the final published article at Steiner JL, Bigatti SM, Ang DC. Trajectory of change in pain, depression, and physical functioning after physical activity adoption in fibromyalgia. *Journal of Health Psychology*. 2015;20(7):931-941. doi:10.1177/1359105313504234

Abstract

Fibromyalgia (FM) is associated with widespread pain, depression, and declines in physical functioning. The study purpose was to examine the trajectory of these symptoms over time related to physical activity adoption and maintenance via Motivational Interviewing versus Education, to increase physical activity. There were no treatment group differences, we divided the sample (n = 184) based on changes in physical activity. Repeated measures analyses demonstrated differential patterns in depression, pain, and physical functioning at 24 and 36 weeks. Findings suggest increased physical activity may serve as a multiple-target intervention that provides moderate to large, long-lasting benefits for individuals with FM.

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Introduction

Fibromyalgia (FM) is a condition characterized by persistent musculoskeletal pain, fatigue, and nonrestorative sleep. The condition affects approximately 2-7% of the general population in the United States (Wolfe et al, 1995) and prevalence rates in the United Kingdom are rising (Hughes et al, 2006). Cross-nationally FM is more prevalent among women (Wolfe et al, 1995; Hughes et al, 2006). Due to lack of a biological marker, diagnosis was traditionally based on the presence at least 11 of 18 tender points across all four quadrants of the body (Wolfe et al, 1990). In 2010, the American College of Rheumatology changed the diagnostic criteria to a purely self-report method (Wolfe et al, 2010). Three of the main concerns of FM patients: pain, depression, and physical functioning, are the focus of the present study.

Pain

Diffuse idiopathic pain is a hallmark of FM (Wolfe et al, 1990). Pain seems to be localized to deep tissues and growing evidence suggests that this is related to hypersensitivity of the central nervous system and peripheral fibers (Staud and Rodriguez, 2006). This process, known as *central sensitization,* has come to be thought of as one of the possible mechanisms behind pain in FM. Research has focused on addressing hypersensitivity through electrical stimulation and demonstrated FM patients have lower pain thresholds and higher pain ratings compared to healthy controls (Desmeules et al., 2003; Diers et al, 2008; Granges and Littlejohn, 1993; Petzke et al, 2003).

Depression in FM

Rates of depression among FM patients, estimated at between 24-40% in any given sample (Bennett et al, 2007; Munce and Stewart, 2007), is significantly higher than among other chronic pain patients. Munce and Stewart (2007) sampled 131,535 members of the general

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population and found that depression was present in 22.3% of FM patients, which was significantly greater than that found in those with rheumatoid arthritis (10%) and back pain (12.6%).

Physical functioning

Decline of physical functioning is frequently seen in FM patients (Bennett et al, 2007). Some studies estimate that people with FM self-report functional limitations as much as 2 standard deviations above healthy individuals (Hawley and Wolfe, 1991). Bennett and colleagues (2007) surveyed 2,596 people with FM and found only 7% reported being able to complete "heavy household duties" such as vacuuming or scrubbing (Bennett et al, 2007). FM patients also report high rates of disability awards (Kurtze et al, 2001), lower rates of employment following diagnosis (Burckhardt, et al, 2005), and more missed work days compared to osteoarthritis patients (White et al, 2008). Thus, FM has a fundamental impact on the ability to function in a way that is consistent with the overall population. Furthermore, lower activity levels are associated with higher levels of FM symptomology, especially pain (Kop et al, 2005).

The Relationship between pain, depression, and physical functioning

There is strong evidence that pain and depression co-occur. Munce and Stewart (2007) found depression was more common (11.3%) in the chronic pain subset of their sample compared to the subset without chronic pain (5.3%). FM pain may be related to dysfunction in the *neuromatrix,* or network of nerves that connect the "sensory, cognitive, and affective experiences" associated with pain (Melzack, 1999). Depression is an "affective experience" associated with pain, and the neuro markers for both depression and pain cannot be removed

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from the neuromatrix in isolation but rather by interventions that target *both conditions* and impact the network as a whole (Campbell et al, 2003). Pain intensity is a significant predictor of physical functioning (Arnstein et al, 1999; Bigatti et al, 2008) and impairment is associated with pain reports (Bennett et al, 2009; Jensen et al, 2000). Pain and depression may also co-occur as a consequence of patients recognizing that pain is causing limitations in physical functioning or vice versa (Bigatti et al, 2008; Jones et al, 2010).

Despite relationships among these variables, interventions aimed at one have not always produced effects in the others. An intervention study examining the effect of CBT on physical functioning led to improvements in functional status but not pain intensity (Williams et al, 2002). Another recent randomized controlled trail of guided imagery with FM patients demonstrated no significant effects on pain, functional status, or self-efficacy (Verkaik et al, 2013). Conversely, many FM treatments produce improvements in pain but not functional status (Rossy et al, 1999). These findings suggest the need to find interventions that improve multiple symptoms.

Physical activity as a multiple-target intervention

Exercise is a promising intervention for FM. Moderate levels of physical activity are associated with improvement of physical symptoms, physical functioning, decreases in pain intensity (Busch et al, 2008), and improvements in depression (Busch et al., 2008; Hauser et al, 2010; Tomas-Carus et al, 2008) and overall well-being for FM patients (Kelley et al, 2010), although these outcomes have mostly been studied separately. Benefits are likely to be enduring when activity is continued regularly (Gowans et al, 2004; King et al, 2002). Of note, exercise and physical activity are two distinct constructs. Exercise refers to "a type or subcategory of leisure-time physical activity in which planned, structured, and repetitive bodily

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movements are performed to improve or maintain… physical fitness" (Caspersen et al, 1985). A common definition of physical activity is "any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level (Caspersen et al, 1985)". Most research examines benefits of exercise specifically; how much benefit can be obtained through increases in general physical activity is not yet understood, and is the focus here.

We examined pain, depression and physical functioning over a 36 week period among a sample of FM patients who were relatively inactive prior to participation in a study to increase exercise behavior. The purpose of this study was to examine the trajectory of pain, depression and physical functioning over time related to physical activity adoption and maintenance, in an originally inactive group.

Method

Design

This was a secondary analysis of data from a completed randomized control trial of Motivational Interviewing to increase moderate to vigorous physical activity (MVPA) in patients with FM (Ang et al, 2010). The RTC was conducted from 2008 to 2010. In the primary study, participants were randomized to either a MI intervention or an educational Attention Control (AC) condition. Both groups received two supervised exercise sessions and an individualized exercise prescription from a qualified fitness instructor who was blinded to treatment assignment. . The exercise sessions consisted of 10 minutes of stretching and approximately 10 minutes of aerobic exercise. Exercise prescriptions were based on the individual's symptoms severity and prior experience. A detailed description of the intervention and the formula for the exercise prescription can be found elsewhere (Ang et al, 2010). It should be noted that the individualization of the exercise prescription was made based on a formula with set goals, rather

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than the personal goals of the participants. Thus, none of the participants received any messages that would be consistent with MI until after the exercise sessions. This was followed by six telephone-delivered intervention sessions. Outcome assessments were conducted at baseline, post-treatment, 3-month follow-up and 6-month follow-up.

Participants

All potential participants were referred from specialty (Rheumatology, Neurology, Pain Management) or primary care clinics. The majority of referrals came from the greater Indianapolis metropolitan area. Inclusion/exclusion criteria has been described elsewhere (Ang et al, 2010). A total of 996 patients were screened for potential participation in the study. Of these, 216 (22%) met the inclusion criteria, enrolled and were randomized to MI (n=107) and AC (n=109). The majority of screening failures were: (a) exercising for ≥3 days a week (30%); (b) use of heart rate lowering medications (19%); (c) aged ≥ 65 years (12%); and (d) presence of medical condition that contraindicated exercise participation. There were no significant differences between groups following randomization.

Measures

Community health activities model program for seniors (CHAMPS). CHAMPS (Stewart et al, 1997) is a survey that assesses frequency and duration of physical activity in a typical week over the past month. The CHAMPS provides a list of activities ranging from light to vigorous intensity. Research supports the validity, reliability and sensitivity to change of CHAMPS as a measure of physical activity among older adults (Harada et al, 2001). The CHAMPS provides an estimate of the *typical* number of hours per week spent performing sedentary-light activity, MVPA, and total physical activity. In the current study, total CHAMPS hours/week was used

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due to its ability to assess a wide range of physical activities, including daily tasks and structured exercise.

*Patient health questionnaire (PHQ-8).*The PHQ-8 is a self-report measure designed to assess depression. The measure consists of 8 items corresponding to the DMS-IV criteria for a major depressive episode. Items are rated on frequency of each issue over the past two weeks. This scale is an abbreviated version of the PHQ-9 which is a widely used brief measure of depression (Kronke and Spitzer, 2002); however the PHQ-8 omits the suicidal ideation item, making it ethically appropriate for research. The scale has demonstrated good reliability (Kronke and Spitzer, 2002).

*Brief pain inventory (BPI).*The BPI (Tan et al, 2004) is a self-report measure to assess pain on two dimensions: pain intensity and pain interference. The measure consists of 9 items, of which 4 ask participants to rate their worst, least, and average pain on a scale of 0-10 (0= no pain and 10 = pain as bad as you can imagine) during the past 7 days. The last item is current pain. Other items address the type of treatments used to deal with pain and amount of relief from said treatments. Item 9 consists sub-items of the impact of pain in seven life domains, such as sleep, which are ranked on a 0-10 scale. Higher scores are associated with greater interference. For the present study, only pain intensity was examined.

Fibromyalgia impact questionnaire (FIQ)-physical impairment subscale. The Fibromyalgia Impact Questionnaire (FIQ) is a brief, self-administered measure of disease impact (Burckhardt et al, 1991). The first section consists of 10 items that focus on ability to perform large muscle tasks (i.e. doing yard work, vacuuming a rug), presented as a Likert-type scale ranging from 0 (always able to do) to 3 (never able to do). The sum of these 10 sub-items is divided by the

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number of valid scores to provide a total physical impairment score. Both content and construct validity were demonstrated in the development of the scale (Burckhardt et al., 1991).

Results

A total of 184 participants completed all assessments with complete data and were included in these analyses. Demographic and study variable means and standard deviations are detailed in Table 1. When examining all participants, the CHAMPS (total score, hours/week), showed increases from baseline (mean = 6.96, SD = 6.86) to week 12 (mean = 11.19, SD = 8.58), and then declined at week 24 (mean = 10.88, SD = 8.42) and again at week 36 (mean = 9.85, SD = 7.88). A repeated measures analysis of variance multivariate test showed significant differences over time for the entire sample, $F(3,181) = 19.01$, $p \leq 0.01$. At every time point the distribution of scores was skewed, with most participants showing low scores. To show the range of physical activities reported by participants over time, Table 1 reports the *number* of participants who reported engaging in each type of activity at each assessment point.

Table 1. Number of participants who reported engaging in each type of activity at each time point.

Type of Physical Activity	1	2	3	4
LIGHT				
Light household work	178	163	157	160
Light gardening	83	78	74	66
Walk for errands	126	125	125	134
Walk leisurely for exercise or pleasure*	79	118	99	108
Stretching or flexibility*	64	132	107	113

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Yoga or tai chi	16	16	19	16
General conditioning exercises*	12	43	32	33
MODERATE				
Dance	9	13	16	8
Heavy household work	31	38	41	42
Heavy gardening	11	24	25	21
Work on machinery	10	8	15	11
Walk fast or briskly for exercise*	23	112	87	84
Ride bicycle or stationary cycle	14	26	25	21
Aerobic machines such as rowing or step	8	16	19	15
Water exercises	10	10	8	10
Swimming gently	16	12	9	14
Aerobics or aerobic dancing	8	20	16	13
Moderate to heavy strength training	10	13	14	15
Light strength training	17	23	30	25
VIGOROUS				
Run or jog*	4	14	9	6
Walk or hike uphill*	16	25	32	31

Note: 1: baseline; 2: post-treatmetn; 3: 3 month follow up; 4: 6 month follow up; only activities with a count of 10 participants or higher at any time point are included; * $p < .05$.

When comparing the MI and Education groups, a repeated measures analysis of variance multivariate test showed no differences in trajectory of physical activity over time ($p > 0.05$).

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Differences in means between groups were 0.35 at baseline, 1.72 at 12 months, 0.43 at 24 weeks, and 1.18 at 36 weeks.

Because there were no differences in physical activity levels between treatment groups, we divided the sample into participants whose physical activity had increased from baseline to 36 weeks versus those whose physical activity had not, by computing a change score (36 week total CHAMPS - baseline total CHAMPS), then creating groups based on whether the change score was above zero (*increased activity*, n = 121) or at or below zero (*no increased activity*, n = 63), regardless of intervention group. When examining demographic and clinical variables by new groups, we found differences only in time since diagnosis; those who did not increase activity had a diagnosis of FM an average 3 years longer than those who increased activity (Table 1).

Examination of the trajectory of physical activity per group supported appropriateness of this categorization. The trajectories were significantly different as identified by a time by group interaction in a repeated measures analysis of variance, $F(3,180) = 55.71$, $p \leq 0.01$ (Figure 1a). Adding intervention group as a covariate did not change these findings. Differences in means between groups were 4.55 at baseline, 2.32 at 12 weeks, 3.76 at 24 weeks, and 7.18 at 36 weeks.

The 36 week trajectory of depression, pain and physical functioning were compared between those who increased activity and those who did not with repeated measures analysis of variance. Physical activity group (increased vs. not increased) was the between-subjects factor and time was the within-subject factor, with four assessment periods. Intervention group (MI vs. AC) and years since diagnoses were included as covariates. Multivariate tests revealed a main effect of time, $F(9,172) = 2.59$, $p \leq 0.01$, partial $eta^2 = .12$, but not of physical activity group (increased vs. not increased; $p > 0.05$) or of the covariates ($p > 0.05$). The time by covariate

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interactions were not significant ($p > 0.05$) but the time by physical activity group interaction was, $F(9,172) = 2.41$, $p \leq 0.01$, partial $eta^2 = .11$, suggesting that those who increased their activity differed from non-increasers in trajectory of depression, pain, and physical functioning.

Depression

Univariate follow-up tests showed the interaction between time and physical activity group was significant for depression, $F(3,181) = 2.85$, $p \leq 0.05$, partial $eta^2 = .02$. Figure 1b shows that from baseline to 24 weeks, groups moved in the same direction, but by week 36 the activity increasers' depression scores leveled off whereas the non-increasers' depression scores continued upwards. By week 36, the difference in PHQ-8 scores from baseline in the increased activity group was 3.08, for those who did not increase it was 0.93. Within subjects contrasts showed this difference between the groups' changes in depression from baseline to week 36 was statistically significant, $F(1,183) = 6.45$, $p \leq 0.01$, partial $eta^2 =0 .04$.

Pain

Univariate tests showed the interaction between time and physical activity group was significant for pain, $F(3,181) = 3.25$, $p \leq .05$, partial $eta^2 = .02$. Figure 1c shows that from baseline to 24 weeks, groups moved in the same direction, possibly due to non-specific intervention effects and/or regression toward the mean, but by week 36 the activity increasers' pain scores decreased further whereas for those who did not increase their pain scores had leveled off. By week 36, the difference in pain from baseline in the activity increasers was 3.45, for the non-increasers it was 1.84. Within subjects contrasts showed this difference between the group changes in pain from baseline to week 36 was statistically significant, $F(1,183) = 6.47$, $p \leq 0.01$, partial $eta^2 = 0.04$.

Physical functioning

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Univariate tests showed the interaction between time and physical activity group was significant for physical functioning, $F(3,181) = 7.92$, $p \leq 0.01$, partial $eta^2 = 0.04$. Figure 1d shows that from baseline to 12 weeks, groups moved in the same direction, possibly due to non-specific intervention effects and/or regression toward the mean, but then the activity increasers continued to improve, whereas those who did not increase activity began to move back to baseline scores $F(1, 183) = 10.79$, $p \leq 0.04$. By week 36, the difference in FIQ-PI scores from baseline in the activity increasers was 2.09, for the other group it was 0.53. Within subjects contrasts showed this difference between groups in physical functioning from baseline to week 36 was statistically significant, $F(1,183) = 19.02$, $p \leq 0.01$, partial $eta^2 = .10$.

Discussion

This study examined the correspondence between the trajectory of pain, depression and physical functioning with increased physical activity and maintenance, in an originally relatively inactive group. Participants received exercise sessions and were randomly assigned to receive Motivational Interviewing or education; however, group assignment had no significant impact on the adoption and maintenance of increased physical activity. There were individuals in both groups who increased and maintained physical activity over the 36 week period. These individuals were compared to those who did not increase physical activity. Note, the "non-increasers" reported approximately twice the hours/week of physical activity at baseline compared to the "increasers" group. This may reflect regression to the mean for these individuals, rather than lack of physical activity (Figure 2a). Despite this possibility, the "non-increasers" group activity fell far below their baseline level over the course of the study, while the "increaser" group maintained a higher level of physical activity.

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Depression, pain, and physical functioning followed a similar pattern from baseline to the 12-week assessment, demonstrating significant improvements for all participants, regardless of group. Because the 12-week assessment marked the end of the active intervention, it is possible that improvement over that period is related to participating weekly individual contact with an interventionist.

Significant group differences in depression were observed after the 12-week assessment. Activity increasers showed a leveling off in depression and less depression compared to baseline, whereas their counterparts showed increases in depression at subsequent assessments. The difference in depression among those who increased activity was a *clinically* significant difference with improvements of a full clinical category (Kronke and Spitzer, 2002). This is an impressive finding as these gains were maintained at 36 weeks. Meta-analysis of other treatments for depression in FM indicates that improvements are generally not significant at follow-up, and effect sizes are generally small (Bernardy et al, 2010; Glombiewski et al, 2010), in comparison to those found in the present study which were moderate in size. Depression is a common experience in FM and it is often hard to create lasting improvements; however our results suggest that increased physical activity may be a potential option with meaningful, lasting effects.

For pain, activity increasers experienced stabilization from week 12 to week 24, followed by continued decreases at week 36. The group that did not increase activity experienced an increase in pain from week 12 to week 24 which stayed constant at week 36. Although both groups showed improvements in pain, only activity increasers showed a meaningful difference from baseline at 36 weeks.

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For physical functioning we saw a marked difference between those who increased activity and those who did not; increasers reported continued improvements in physical functioning at weeks 24 and 36, and non-increasers reported continued increases in physical interference. A noteworthy finding is that the two groups reported opposite effects following the post intervention assessment, with the non-increased activity group returning to baseline levels of physical functioning.

Previous research suggests inconsistent long-term effects of exercise related pain reductions and physical functioning for FM (Busch et al, 2008). However, in the present study, increases in physical activity do not necessarily reflect increased *exercise*. This distinction is meaningful in that while a regimented exercise plan may be challenging to maintain over time (Busch et al, 2008) maintaining an increased general level of physical activity may be easier to sustain. Our effect sizes for pain reductions and physical functioning are considerably larger than those from psychological interventions (Bernardy et al, 2010; Glombiewski et al, 2010) and pharmaceutical interventions (Hauser et al, 2010), which provides new insight into the potential lasting benefits of physical activity for individuals with FM.

Although there are likely physiological reasons why physical activity is related to these improvements, there are likely psychological as well, and attention to these may improve intervention outcomes. Multidisciplinary pain management programs which included physical activity components have been shown to be uniquely beneficial for chronic pain patients with mild to moderate depression (Orenius et al, 2013), and a systematic review of these programs (Miles et al, 2011) suggested that pretreatment depression predicts functional outcomes regardless of intervention. Perhaps, improvement in symptoms serves as a motivator to continue physical activity, thus creating a cyclical effect, or that as participants begin to feel better, the

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behavior is rewarded either through the reduction of symptoms (both depression and pain) or increases in self-efficacy (Arnstein et al, 1999). Perhaps future work should include well controlled qualitative studies that examine patients' thoughts and reactions to experiences that accompany increases in physical activity in order to better understand the immediate rewards and possible mechanisms of change.

Limitations

There are several limitations that require consideration. Due to the primarily female sample, results may not generalize to men with FM; however, the gender distribution of participants was comparable to other psychological-based clinical trials in FM (Glombiewski et al, 2010) and consistent with rates in the general population (Yunus, 2001). Further research comparing potential gender differences in response to increased physical activity overtime is warranted. Additionally, the majority of the sample was Caucasian, thus results may not generalize to individuals of other races. Importantly, because the data for this study were correlational, we cannot draw conclusions about the causal impact of changes in physical activity and symptoms of FM or various pathways that may explain the relationship between variables over time. Further exploration regarding the direction of these relationships would enhance our understanding of the associations found. Finally, the CHAMPS has not been specifically validated for use in patients with FM. However, the measure has been previously validated in samples of older, sedentary adults (Stewart et al, 1997), healthy middle-aged adults (King et al, 2008), and individuals with other chronic illnesses (Foy et al, 2005). Given that the low level of activity in samples used in existing research is comparable to that seen in a relatively inactive FM population, the use of CHAMPS was considered acceptable.

Conclusions

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The present study adds to the growing literature demonstrating physical activity is associated with positive changes in FM-related symptoms. Two main conclusions regarding physical activity can be gleaned from our findings. First, it appears that the increase in physical activity does not need to be substantial to produce positive effects. Those who increased activity reported on average approximately 12 hours per week of physical activity, which may include a variety of activities where body movement is involved. This has important implications for fibromyalgia as vigorous activity may temporarily increase pain, and reduce the probability of adoption of a regular, structured exercise routine. Second, improvements associated with increased physical activity may be maintained over the long-term, albeit the benefits may not be sustained if the activity does not continue. This is important for medical practitioners to note as they may advise patients that physical activity is not a time-limited intervention. Overall, the present study suggests physical activity is an effective behavioral intervention for both the physical and emotional symptoms associated with FM. Physical activity may indeed serve as a multiple-target intervention that provides moderate to large, long-lasting benefits for individuals with FM.

No conflicting interests

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