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Impact of isometric and concentric resistance exercise on pain and fatigue in fibromyalgia

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Abstract

Purpose: The aim of this study was to determine the local and systemic effects of isometric and concentric muscle contractions on experimental pain and performance fatigability in people with and without fibromyalgia.

Methods: Forty-seven fibromyalgia (FM: 51.3 ± 12.3 yr) and forty-seven control (CON: 52.5 ± 14.7 yr) participants performed submaximal isometric and concentric exercise for ten minutes with the right elbow flexors. Assessments before and after exercise included pressure pain thresholds (PPT) of the biceps and quadriceps, central pain summation, self-reported exercising

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All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Giovanni Berardi, and Marie Hoeger Bement. The first draft of the manuscript was written by Giovanni Berardi and Marie Hoeger Bement and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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The authors declare that they have no conflict of interest.

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This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of Marquette University (September 17, 2015 / HR-3035).

Consent to participate (include appropriate statements):

All participants were provided informed consent and voluntarily confirmed his or her willingness to participate in this study, after having been informed of all aspects of the study that were relevant to the participant's decision to participate.

Consent for publication (include appropriate statements):

All participants signed informed consent regarding publishing their data.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Not applicable.

arm and whole-body pain, and maximal voluntary isometric contraction (MVIC) of the right elbow flexors and left handgrip.

Results: People with FM experienced greater reductions in local fatigue (right elbow flexor MVIC: CON: $-4.0 \pm 6.7\%$, FM: $-9.8 \pm 13.8\%$; $p=0.013$) and similar reductions in systemic fatigue (left handgrip MVIC: $-6.5 \pm 10.2\%$; $p<0.001$) as CON participants, which were not different by contraction type nor related to baseline clinical pain, perceived fatigue, or reported pain with exercise. Following exercise both groups reported an increase in PPTs at the biceps (pre: 205.5 ± 100.3 kPa, post: 219.0 ± 109.3 kPa, $p=0.004$) only and a decrease in central pain summation (pre: 6.8 ± 2.9 , post: 6.5 ± 2.9 ; $p=0.013$). FM reported greater exercising arm pain following exercise (CON: 0.7 ± 1.3 , FM: 2.9 ± 2.3 ; $p<0.001$), and both groups reported greater arm pain following concentric (isometric: 1.4 ± 2.0 , concentric: 2.2 ± 2.9 ; $p=0.001$) than isometric exercise. Neither group reported an increase in whole-body pain following exercise.

Conclusion: People with FM experienced greater performance fatigability in the exercising muscle compared to CON that was not related to central mechanisms of fatigue or pain. These results suggest changes in performance fatigability in FM may be due to differences occurring at the muscular level.

Keywords

Fibromyalgia; exercise; fatigue; pain

Introduction

Fibromyalgia (FM) is characterized by reports of chronic widespread pain accompanied by fatigue and other symptoms that impair quality of life (Queiroz 2013; Wolfe et al. 2010a; Wolfe et al. 1995). Clinical guidelines recommend exercise as a front-line intervention to improve self-reported pain and fatigue for patients with FM (Bidonde et al. 2017; Bidonde et al. 2019; Busch et al. 2013; Dowell et al. 2016; Sosa-Reina et al. 2017). While exercise training can alleviate symptoms of pain and fatigue in people with FM, many report pain and fatigue exacerbation during and following a single exercise session (Bachasson et al. 2013; Bidonde et al. 2019; Busch et al. 2011; Ericsson et al. 2016; Häkkinen et al. 2000; Jacobsen et al. 1991; Jones and Liptan 2009). Despite self-reports of increased pain and fatigue with exercise among people with FM, there has been limited investigation to identify objective changes in experimental pain sensitivity (pressure pain sensitivity and pain summation) and performance fatigability (exercise-induced decrease in muscle force) following resistance exercise. Furthermore with resistance exercise (muscle contractions against an external resistance) it is not clear if the pain and fatigue response following resistance exercise is localized to the exercising limb as expected with unaccustomed exercise or associated with changes in clinical symptoms of widespread pain and fatigue (Alvarez-Gallardo et al. 2019; Bidonde et al. 2014; Busch et al. 2007; Geneen et al. 2017; Gowans and deHueck 2004; Jones et al. 2006). Equivocal evidence and anecdotal reports have led to poor symptom management when initiating resistance exercise in FM which contributes to decreased exercise compliance. Understanding the local and systemic changes in experimental pain sensitivity and performance fatigability following an acute bout of resistance exercise will

assist clinicians in tailoring exercise to be a more effective rehabilitation tool in managing pain associated with FM.

Recent advances in experimental pain assessment allow investigation beyond self-reported pain intensity including the peripheral and central mechanisms of pain via mechanical/pressure pain thresholds and pain facilitation (temporal summation of pain). Prior research investigating the acute experimental pain response to a single bout of exercise has primarily focused on healthy young (Koltyn 2002; Koltyn et al. 2014a) and older adults (Lemley et al. 2015; Naugle et al. 2016) showing reduced experimental pain sensitivity (i.e., exercise-induced hypoalgesia) following aerobic, isometric, and dynamic resistance exercise (Koltyn et al. 2014b; Naugle et al. 2012; Vaegter et al. 2015a; Vaegter et al. 2015b; Vaegter et al. 2016). Acute pain relief following exercise occurs locally in the exercising muscle but also systemically in remote, non-exercising regions (Lemley et al. 2015; Vaegter et al. 2014); suggesting pain relief from exercise may be modulated by the central nervous system and/or circulating hormones (Koltyn et al. 2014b; Lima et al. 2017). Evidence of the influence of exercise on experimental pain sensitivity in healthy adults is not generalizable to patients with FM due to changes in central nervous system processing which may lead to exacerbation of pain (Lannersten and Kosek 2010; Sluka and Clauw 2016; Staud et al. 2005). Prior research investigating the acute exercise-induced change in pain sensitivity in people with FM focused on aerobic and isometric resistance exercise of varying intensity and duration; both with variable responses in pain sensitivity (Ge et al. 2012; Hoeger Bement et al. 2011; Kosek et al. 1996; Lannersten and Kosek 2010; Meeus et al. 2015; Rice et al. 2019; Staud et al. 2005; Vierck et al. 2001). Many of these studies incorporated bouts of high-intensity exercise which is not consistent with clinical guidelines that endorse a graduated exercise program of increasing intensity and frequency to limit pain exacerbation, promote adherence, and lead to reductions in pain (Ambrose and Golightly 2015; Bidonde et al. 2014; Geneen et al. 2017; Palstam et al. 2016). Research from our laboratory identified variability in the acute experimental pain response to sustained isometric contractions of varying intensity and duration among patients with FM as some demonstrated increases, decreases, or no change in pain perception to a noxious stimulus that paralleled changes in clinical pain (Hoeger Bement et al. 2011). In addition, low intensity resistance exercise performed for longer duration was effective in reducing acute experimental pain sensitivity in a cohort of patients with FM (Hoeger Bement et al. 2011). Despite traditional resistance training protocols commonly incorporating intermittent contractions, it is unknown whether similar variability of the acute experimental pain response occurs with intermittent isometric and concentric muscle contractions.

Perception of fatigue at rest and during activity is highly prevalent in FM and is termed perceived fatigability, which is commonly measured as the change in self-reported fatigue scales (Enoka and Duchateau 2016). In contrast, performance fatigability is defined as a decline in an objective measure of performance such as a maximal voluntary contraction following a physical task (Enoka and Duchateau 2016). Performance fatigability has not been extensively investigated in people with FM following exercise tasks. In healthy adults and other clinical populations, performance fatigability is expected in the exercising limb following exercise and may vary by contraction type (Babbault et al. 2006; Hunter 2018; Madeleine et al. 2002; Pasquet et al. 2000; Senefeld et al. 2013; Yoon et al. 2013), as the

mode of contraction (i.e. isometric and concentric) performed during a bout of exercise may lead to varying magnitudes of performance fatigability (Ament and Verkerke 2009; Enoka and Duchateau 2008; Hunter 2018). Of the limited evidence, people with FM experience greater perceived fatigue and performance fatigability compared to controls following exercise however, participants in these studies were not matched for baseline strength and activity levels which may have contributed to group differences (Bachasson et al. 2013; Jacobsen et al. 1991; Srikuea et al. 2013). Additionally, it is unknown whether performance fatigability seen in FM is due to limitations of contractile function (muscular fatigue) isolated to the exercising muscle or the central nervous system (central fatigue) that impacts muscle force production in the exercising muscle and remote, non-exercising body regions (Enoka and Duchateau 2016). Finally, the influence of contraction type on performance fatigability is unknown in people with FM.

The primary purpose of this study was to determine the local and systemic effects of intermittent isometric and concentric muscle contractions matched for intensity, duration, and duty cycle on experimental pain and performance fatigability in primarily middle-aged people with and without FM. We aimed to identify whether after exercise, 1) changes in pain sensitivity and performance fatigability were dependent on the muscle contraction type, 2) people with FM have greater pain sensitivity and performance fatigability compared with control participants, and 3) changes in experimental pain and performance fatigability were localized to the exercising limb or evident systemically in remote non-exercising body regions. To mitigate potential confounding effects, baseline characteristics of age, sex, body composition, physical activity, and strength were collected to determine potential baseline differences between people with and without FM. The control participants predominately included middle-aged women, who represent an understudied population in the areas of exercise and pain research.

Methods

Participants

Forty-seven participants with a physician diagnosis of FM (44 female, mean \pm SD: 51.3 \pm 12.3y; range: 24-75y; BMI: 30.2 \pm 6.9) and 47 control (CON) participants (44 female, mean \pm SD: 52.5 \pm 14.7y; range: 20-74y; BMI: 27.7 \pm 5.6) completed this study. Exclusion criteria included known orthopedic, cardiopulmonary, neurological, or unstable medical conditions that would preclude performance of fatiguing exercise or experimental techniques. All participants were screened with the Physical Activity Readiness Questionnaire (ACSM 2018) to verify safety prior to engaging in physical activity. Informed consent was acquired before study initiation and the protocol was approved by the Marquette University Institutional Review Board (HR-3035) according to principles of the Declaration of Helsinki.

Experimental Protocol

Participants completed three sessions, one familiarization that included baseline assessments and two randomized experimental sessions separated by approximately one-week (Figure 1). During the familiarization session, participants were familiarized to pressure algometry and

the custom-made pressure pain device twice, first to a remote site and subsequently to the site used during experimental sessions to mimic the study protocol. The FM participants completed the modified 2010 American College of Rheumatology Modified Diagnostic Criteria for Fibromyalgia (ACR) (Wolfe et al. 2011; Wolfe et al. 2010b) and Revised Fibromyalgia Impact Questionnaire (FIQR) (Burckhardt et al. 1991). All participants performed maximal voluntary isometric contractions (MVICs) of the right elbow flexors and voluntary activation of the biceps brachii with the twitch interpolation technique (Gandevia 2001). All participants were familiarized to performing isometric and concentric contractions with the right elbow flexors. Participants were issued an ActiGraph activity monitor (ActiGraph wGT3X-BT, Pensacola, FL) to quantify physical activity for a seven-day period. During the first experimental session, dual-energy x-ray absorptiometry (DXA) (GE Lunar iDXA, Madison, WI) was completed and each participant completed the Physical Activity Assessment Tool (PAAT) (Meriwether et al. 2006). During both randomized experimental sessions perceived fatigue was measured using the PROMIS Short Form v1.0 – Fatigue 7a (PROMIS Fatigue) (Ameringer et al. 2016; Lai et al. 2011). Experimental pain perception, right elbow flexor MVIC, and left handgrip MVIC were measured before and after submaximal intermittent isometric and concentric contractions performed with the right elbow flexors. Self-reported pain and rating of perceived exertion were measured every minute during performance of isometric and concentric contractions.

Intermittent Submaximal Isometric & Concentric Muscle Contractions

Submaximal intermittent isometric and concentric muscle contractions were matched for intensity (20% of maximal voluntary isometric contraction), duration (10-minutes), and duty-cycle (2-s contraction: 1-s relaxation) Each participant matched a target force line indicating 20% of MVIC on a computer monitor placed 1 m from the participant. Verbal encouragement was provided throughout both exercise tasks.

Computerized Pressure Algometer: Biceps and Quadriceps

Pressure pain thresholds (PPTs) were measured before and after exercise with a pressure algometer (Somedic Algometer Type II, Hörby, Sweden) locally at the exercising limb (right biceps) and systemically in the right quadriceps. Two trials separated by a 10-second intertrial interval were performed at each site with a 1-cm² rubber tip using a ramp protocol increasing applied pressure at a rate of 50 kPa/sec. The average of the two assessments at each site were used for data analysis. PPTs were recorded with participants seated upright in a Biodex System 3 Pro (Biodex Medical Systems, Inc., Shirley, New York) with the upper extremity supported in 40° shoulder flexion and 15° elbow flexion, bilateral feet were rested on a footrest with hips and knees at 90° flexion. The right biceps site was marked at 2/3 distance between the anterior border of the acromion to the superior border of the cubital fossa and the right quadriceps site was marked midway between the anterior superior iliac spine and the mid-patella.

Customized Pressure Pain Device: Finger

A custom-made pressure pain device (Romus, Inc, Milwaukee WI) was used to measure pain perception with isometric and concentric muscle contractions (Hoeger Bement et al. 2011; Hoeger Bement et al. 2009). A weighted Lucite edge was placed on the left index

finger for 2-minutes, the equivalent of 1-kg mass was applied to controls while a 0.75-kg mass was applied to participants with FM. A lesser mass was used with FM participants to facilitate completion of the two-minute trial despite their increased pain sensitivity (Hoeger Bement et al. 2011). Participants reported “pain” when they first perceived pain (i.e., pain threshold) and the time in seconds was recorded. Pain ratings were reported every 20-seconds using a 0 to 10 numerical pain rating scale. Summation of pain during the constant noxious stimulus was calculated as the difference from the last pain rating (120 sec) to the first (0 sec).

Self-Reported Arm Pain and Perceived Exertion During Exercise

During both exercise tasks, participants were asked to rate exercising arm pain and perceived exertion upon initiation, every minute during, and at completion of the 10-minute exercise task. Perceived pain was measured with a 0 to 10 numerical rating scale (NRS) with anchors of 0 = no pain; 5 = moderate pain; and 10 = worst pain (Farrar et al. 2001; Turk et al. 1993). Perceived exertion was measured with the modified Borg Rating of Perceived Exertion (RPE) scale with anchors 0 = “nothing at all” and 10 = “very very strong” (Borg 1998).

Self-Reported Exercising Arm and Whole-Body Pain Intensity Before and After Exercise

Self-reported arm and whole-body pain was rated before and after the 10-minute exercise bout with a 0-10 cm visual analogue scale (VAS) with anchors of no pain and worst pain (Turk et al. 1993). Arm and whole-body pain were assessed in reference to performing gross limb and whole-body movement such as mimicking reaching forward a picking up a cup and walking and squatting to pick something up from the floor respectively.

Elbow Flexor Maximal Voluntary Isometric Contractions & Voluntary Activation

Maximal voluntary isometric contractions (MVIC) were performed by each participant with the right elbow flexors while seated in a Biodex System 3 PRO. The participant’s forearm was placed in a modified forearm orthosis attached to the dynamometer. Each participant was seated with their hips and knees flexed to 90° flexion, right shoulder in 40° flexion, right elbow in 90° flexion, and a neutral forearm position. The setup and positioning for maximal voluntary isometric testing was maintained throughout sessions. Participants were verbally encouraged to contract as strong as they could and build as much force for 3-5 seconds with visual feedback of torque production on a computer monitor placed 1m from the participant. Torque recordings from the dynamometer were recorded online and digitized using a Power 1401 analog-to-digital converter and Spike 2 software [Cambridge Electronics Design (CED), Cambridge, UK] at 500 samples per second. Participants were familiarized to MVICs during the familiarization session and two MVICs were performed prior to isometric and concentric muscle contractions to identify a load equivalent of 20% of MVIC. MVICs were performed after isometric and concentric muscle contractions to measure the local exercise-induced decrease in muscle force production (i.e., fatigue of the exercising muscle). Post-exercise MVICs were conducted approximately five minutes following exercise to facilitate completion of experimental and clinical pain assessments.

Voluntary activation was assessed using the interpolated stimulus technique (Gandevia 2001) to evaluate the participants’ ability to maximally activate their biceps muscle and generate

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torque during performance of MVICs. This technique involved superimposing an evoked contraction with electrical stimulation over the biceps brachii during performance of the MVICs. The biceps brachii was stimulated with a paired stimulus (i.e. twitch stimulation) by a constant-current stimulator (Digitimer, DS7AH, Welwyn Garden City, UK) with surface electrodes [30 x 22 mm] (Ambu Neuroline 715, Columbia, MD). Intensity of twitch stimulations were increased by 50mA until there was a plateau in force and no further increase in evoked force with two consecutive stimulations. The stimulation intensity was increased a further 20% to provide supramaximal stimulations during the torque plateau of each MVIC (superimposed twitch) and then while the muscle was relaxed ~3-seconds after cessation of the MVIC (potentiated twitch). To determine voluntary activation using the twitch interpolation technique (Gandevia 2001), the increase in elbow flexion torque evoked by a stimulation during MVIC (superimposed twitch) was expressed as a fraction of the torque amplitude during stimulation while the biceps muscle was relaxed (potentiated twitch) and quantified as a percentage using the following formula: [(1 – superimposed twitch/potentiated twitch) × 100]. The potentiated twitch was further analyzed for peak amplitude and half-relaxation time/rate (Gandevia 2001).

Handgrip Maximal Voluntary Isometric Contraction

Left handgrip MVIC was assessed before and after isometric and concentric muscle contractions with a handgrip dynamometer (JAMAR Hydraulic Hand Dynamometer, Sammons Preston, Bolingbrook, IL). Participants had their left upper extremity unsupported and positioned with their left shoulder in neutral, elbow flexed to 90°, forearm and wrist in neutral, and elbow tucked against the body. Participants were verbally encouraged to squeeze as strong as possible for 3-5 seconds. Maximal contractions were performed prior to and upon completion of each exercise task to measure systemic fatigue following the exercise task.

Physical Activity and Body Composition

Participants wore activity monitors (ActiGraph wGT3X-BT, Pensacola, FL) on the non-dominant wrist for seven days to quantify the percent of time spent in sedentary, light activity, and moderate-to-vigorous activity. Placement on the wrist has shown to increase wear compliance (Freedson & John, 2013; Martin & Hakim, 2011; Troiano et al., 2014; van Hees et al., 2011) and correlate with physical activity measured at the hip (Kamada et al., 2016; Scott et al., 2017). Daily logs tracking sleep time, physical activity, and any removal time were completed by participants. Data were downloaded and analyzed using ActiLife software (ActiLife 6.13.1, Pensacola, FL). Non-wear and sleep time were identified and removed using the Troiano algorithm (Choi et al. 2012) and daily logs to calculate amount of physical activity time. Data from four validated days (wear time of at least 10 hours) were used for analysis as four days has been shown to be representative of a week's average of physical activity (Migueles et al. 2017). Percent of time spent in sedentary, light, and moderate-to-vigorous activity were estimated using cut points based on Freedson's algorithm and the worn-on wrist option was selected to mathematically depress counts (Freedson 1998; Rosenberger 2013). Self-reported physical activity was measured with the Physical Activity Assessment Tool (PAAT) (Meriwether et al. 2006) and time spent in moderate to vigorous intensity activity was reported.

Body composition was quantified using a GE Lunar iDXA (GE, Madison, WI). Participants were instructed to refrain from eating and drinking 1-2 hours prior to scanning. Scans were analyzed using Encore software (GE, Madison, WI) and measures of total lean mass (kg), total fat mass (kg), right arm lean mass (kg), and right arm fat mass (kg) were obtained. Because exercise was performed with the right elbow flexors, right arm fat mass and lean mass were used as an indicator of regional body composition.

Statistical Analysis

All data were analyzed using IBM SPSS (Version 26, IBM, Armonk, NY, USA). Normality and linearity were evaluated with the Shapiro-Wilk test and visual inspection via Q-Q plots. Data are reported as mean \pm SD in text and tables and displayed as mean \pm SEM in figures. Differences between means were tested with paired-samples and independent samples t-test. Repeated measures analysis of variance was used to compare the following variables across session and time with between subject factor of group: elbow MVIC, handgrip MVIC, experimental pain threshold, pain and RPE during exercise, and the change in arm and whole-body pain after exercise. Pressure pain thresholds were analyzed with a repeated measures analysis of variance with variables of session, time, site, and between subject factor of group. Pain summation was analyzed with a repeated measures analysis of variance with variables of session, time, summation, and between subject factor of group. Post hoc tests were applied where appropriate. Pearson product moment correlations were calculated to determine associations between variables. A P-value < 0.02 was used for statistical significance.

Results

Participant Descriptors / Characteristics

Descriptive statistics for the study sample are listed in Table 1. Control (CON) and fibromyalgia (FM) groups were matched for age (CON: 52.5 ± 14.7 ; FM: 51.3 ± 12.3), sex (CON: 44 Female (F), 3 Male (M); FM: 44 F, 3 M), and BMI (CON: 27.7 ± 5.6 ; FM: 30.2 ± 6.9) with both groups falling in the overweight to obese category. Both groups had similar total lean mass, total fat mass, right arm lean mass, and right arm fat mass. Both groups self-reported similar amount of moderate-to-vigorous activity minutes per week via the PAAT. Each group spent similar amount of time in sedentary, light, and moderate-to-vigorous activity as measured by the ActiGraph. The FM group had a mean symptom severity score on the 2010 ACR Diagnostic Criteria for Fibromyalgia at time of enrollment was 16.6 ± 5.8 . The FM group had a mean total FIQR score of 48.5 ± 19.7 . Neither group reported differences in perceived fatigue with the PROMIS Short Form Fatigue 7a across isometric and concentric experimental sessions ($p > 0.05$) therefore, values from the isometric session were used to evaluate differences between groups and correlations to performance fatigue. The FM group reported greater perceived fatigue on the PROMIS Short Form Fatigue 7a ($p < 0.001$) compared to controls.

Voluntary Activation, Muscle Twitch Properties, Elbow Flexor MVIC, & Handgrip MVIC

Baseline Voluntary Activation, Muscle Twitch Properties, & Elbow Flexor Strength: Participants with FM had similar activation properties as the control participants that

included voluntary activation of the right biceps, baseline twitch amplitude, and half-relaxation time (Table 1). MVIC torque of the right elbow flexors was also similar at the beginning of all sessions and between CON and FM participants (Table 2, Figure 2a).

Right Elbow Flexor Performance Fatigability: Right elbow flexor MVIC torque decreased following exercise (i.e. performance fatigability) (Time (pre- to post-exercise): $F(1,92) = 42.47$, $p < 0.001$, $\eta_p^2 = 0.316$) with a mean decline of 7.2% (Figure 2a, Table 2). The performance fatigability differed by group (Time (pre- to post-exercise) x Group: $F(1,92) = 5.88$, $p = 0.017$, $\eta_p^2 = 0.060$), with post hoc analysis showing people with FM showing greater declines in MVIC torque (performance fatigability) than CON (CON: $-4.0 \pm 6.7\%$, FM: $-9.8 \pm 13.8\%$; $t(66.44) = 2.56$, $p = 0.013$). The reduction in MVIC torque was similar after the isometric and concentric exercise (Contraction (Iso v Conc) x Time: $F(1,92) = 1.53$, $p = 0.219$).

Left Handgrip Strength and Performance Fatigability: Baseline handgrip MVIC was similar across sessions and between CON and FM participants ($p > 0.05$) (Table 2, Figure 2b). Left handgrip MVIC decreased following exercise (Time (pre- to post-exercise) $F(1,92) = 53.04$, $p < 0.001$, $\eta_p^2 = 0.368$) with a mean decline of $6.5 \pm 10.2\%$. The change in left handgrip MVIC was not different between exercise types (Contraction (Iso v Conc) x Time (pre- to post-exercise): $F(1,92) = 2.17$, $p = 0.144$) or groups (Group x Time (pre- to post-exercise): $F(1,92) = 1.61$, $p = 0.208$).

Perceived Arm Pain and Exertion During Exercise

Perceived arm pain increased during isometric and concentric exercise (Time (during exercise): $F(1.71, 157.7) = 154.67$, $p < 0.001$, $\eta_p^2 = 0.627$) and arm pain ratings differed by exercise type (Contraction (Iso v Conc) x Time (during exercise): $F(2.75, 253.05) = 21.3$, $p < 0.001$, $\eta_p^2 = 0.188$) with post hoc demonstrating greater change in arm pain with concentric (mean change = 5.0 ± 3.6) compared to isometric (mean change = 3.3 ± 3.3) ($t(93) = -6.34$, $p < 0.001$) (Table 2, Figure 3a). Arm pain differed by group (Group (CON v FM) X Time (during exercise): $F(1.71, 157.7) = 17.85$, $p < 0.001$, $\eta_p^2 = 0.162$); post hoc showed a greater increase in arm pain for FM (mean change = 5.8 ± 2.8) compared to CON (mean change = 2.6 ± 2.7) ($t(92) = -5.63$, $p < 0.001$). A significant interaction of Contraction (Isometric v Concentric) x Time (during Ex) x Group (CON v FM) ($F(2.75, 253.05) = 7.10$, $p < 0.001$, $\eta_p^2 = 0.072$) was demonstrated for arm pain during exercise. Post hoc demonstrates the change in arm pain in FM during concentric exercise (6.3 ± 3.3) was greater than the change in arm pain in FM during isometric (5.2 ± 2.9 , $t(46) = -3.07$, $p = 0.004$), CON during concentric (3.7 ± 3.4 , $t(92) = 3.84$, $p < 0.001$), and CON during isometric (1.4 ± 2.5 , $t(85.6) = 8.19$, $p < 0.001$). The change in arm pain in FM during isometric exercise (5.2 ± 2.9) was greater than the change in arm pain in CON during concentric (3.7 ± 3.4 , $t(92) = 2.35$, $p = 0.02$) and CON during isometric (1.4 ± 2.5 , $t(92) = 6.77$, $p < 0.001$). The CON reported greater arm pain during concentric (3.7 ± 3.4) compared to isometric (1.4 ± 2.5) ($t(46) = -6.03$, $p < 0.001$).

Rating of perceived exertion increased during exercise (Time (during exercise): $F(2.63, 241.82) = 327.66$, $p < 0.001$, $\eta_p^2 = 0.781$) and differed by exercise type (Contraction (Iso v Conc) x Time (during exercise): $F(3.25, 22.56) = 7.88$, $p < 0.001$, $\eta_p^2 = 0.079$) with

post hoc demonstrating greater change in RPE with concentric (mean change = 6.5 ± 5.5) compared to isometric (mean change = 5.5 ± 2.8) ($t(93) = -3.63$, $p < 0.001$) (Table 2, Figure 3b). RPE was greater for FM than CON (Group X Time (during Ex); $F(2.63, 241.82) = 5.89$, $p = 0.001$, $\eta_p^2 = 0.060$ with post hoc showing a greater increase in RPE for FM (mean change = 6.7 ± 2.5) compared to CON (mean change = 5.2 ± 2.0) ($t(92) = -3.15$, $p = 0.002$).

Change in Self-Reported Arm and Whole-Body Pain Following Exercise

Self-reported arm pain relative to movement was assessed immediately before and after the exercise protocol increased (Time: $F(1, 92) = 88.49$, $p < 0.001$, $\eta_p^2 = 0.490$), which was greater for participants with FM (Group (CON v FM) x Time (pre- to post-exercise): $F(1, 92) = 33.38$, $p < 0.001$, $\eta_p^2 = 0.266$) (Table 2). Post-hoc analysis reveals that participants with FM reported a greater increase in arm pain following exercise (CON: 0.7 ± 1.3 , FM: 2.9 ± 2.3 ; $t(71.74) = -5.78$, $p < 0.001$). Exercise type also led to differences in arm pain following exercise (Contraction (Iso v Conc) x Time (pre- to post-exercise): $F(1, 92) = 11.31$, $p = 0.001$, $\eta_p^2 = 0.110$) with greater increases following concentric contractions than the isometric exercise (Iso: 1.4 ± 2.0 , Conc: 2.2 ± 2.9 ; $t(93) = -3.35$, $p = 0.001$).

Self-reported whole-body pain relative to movement increased following exercise (Time (pre- to post-exercise): $F(1, 92) = 10.53$, $p = 0.001$, $\eta_p^2 = 0.103$) however, post-hoc analysis showed no increase ($p > 0.05$) (Table 2). The change in whole body pain was similar across exercise types (Time (pre- to post-exercise) x Contraction (Iso v Conc): $F(1, 92) = .467$, $p = 0.496$) and groups (Time (pre- to post-exercise) x Group: $F(1, 92) = 5.03$, $p = 0.027$).

Computerized Pressure Algometer: Biceps and Quadriceps

Control participants reported higher baseline PPTs compared with FM participants at the biceps and quadriceps across all three sessions ($p < 0.01$) (Figure 4a & 4b). Baseline PPTs were similar across sessions for both groups ($p > 0.05$). Higher PPTs were assessed at the quadriceps than the biceps (Site (bicep v quad): $F(1, 92) = 164.82$, $p < 0.001$, $\eta_p^2 = 0.642$). Following exercise, the change in PPTs differed by site (Site (bicep v quad) x Time (pre- to post-exercise: $F(1, 92) = 6.41$, $p = 0.013$, $\eta_p^2 = 0.065$) with post hoc analysis showing PPT at the biceps increased following exercise (Pre: 205.5 ± 100.3 , Post: 219.0 ± 109.3 , $p = 0.004$) and remained unchanged at the quadriceps (Pre: 310.4 ± 139.5 , Post: 306.5 ± 146.1 , $p = 0.370$). The change in PPTs were not different between groups (Group x Time (pre- to post-exercise): $F(1, 92) = 1.92$, $p = 0.169$) or exercise type (Contraction (Iso v Conc) x Time: $F(1, 92) = 0.007$, $p = 0.933$). The change in PPTs (absolute and relative) at the biceps and quadriceps were not correlated with any of the self-report pain assessments (change in arm and whole-body pain, or pain during exercise).

Customized Pressure Pain Device: Finger

Baseline (pre-exercise) pain threshold with the two-minute pressure pain device was similar between groups and consistent across all three sessions (Table 2). There were no changes in pain threshold following performance of isometric and concentric exercise (Time: $F(1, 87) = 1.37$, $p = 0.246$) and change in pain threshold was not related to exercise type (Time (pre- to post-exercise) x Contraction (Iso v Conc): $F(1, 87) = 2.37$, $p = 0.127$) or groups (Time (pre- to post-exercise) x Group: $F(1, 87) = 1.15$, $p = 0.286$) (Figure 5a). Summation of pain from

the constant noxious stimulus occurred during all assessments in CON and FM (Summation: (0 to 2-min): $F(1.88, 173.10) = 309.53, p < 0.001, \eta_p^2 = 0.771$) (Table 2 & Figure 5b). Control and FM participants demonstrated similar baseline (pre-exercise) pain summation across sessions (CON: $6.9 \pm 3.0, 6.3 \pm 3.1, 6.4 \pm 3.0$; FM: $7.3 \pm 2.9, 7.3 \pm 2.8, 7.2 \pm 3.1$). (Figure 5b). Summation of pain decreased following exercise (Summation X Time (pre- to post-exercise): $F(3.30, 303.65) = 5.88, p < 0.001, \eta_p^2 = 0.060$) with post hoc demonstrating a reduction in pain summation from pre-exercise (6.8 ± 2.9) to post-exercise (6.5 ± 2.9) ($t(93) = 2.52, p = 0.013$). The change in summation did not differ by exercise type (Contraction x Time x Summation: $F(3.86, 352.0) = 1.43, p = 0.227$) or between groups (Group x Time x Summation: $F(3.30, 303.65) = 1.10, p = 0.351$). The change in pain summation (absolute and relative) was not correlated with any self-report pain assessments (change in whole-body pain or pain during exercise).

Relation between Baseline Clinical Pain, Perceived Fatigue, & Pain during Exercise to Performance Fatigability

Correlations to performance fatigability for isometric and concentric contractions were combined due to lack of task specificity for elbow flexor and handgrip fatigability. Correlations between baseline clinical pain (ACR, FIQR, whole-body pain VAS) did not correlate with performance fatigability of the right elbow flexors (ACR: $r = -0.141, p = 0.345$; FIQR: $r = 0.009, p = 0.951$; whole-body pain VAS: $r = 0.041, p = 0.783$) or left handgrip (ACR: $r = -0.289, p = 0.049$; FIQR: $r = -0.227, p = 0.124$; whole-body pain VAS: $r = -0.161, p = 0.280$). Baseline perceived fatigue (PROMIS-Fatigue) did not correlate with performance fatigability at the right elbow flexors ($r = -0.011, p = 0.942$) or left handgrip ($r = -0.108, p = 0.468$). Self-reported pain during exercise (NPRS) did not correlate with performance fatigability at the elbow flexors ($r = -0.088, p = 0.558$) or handgrip ($r = -0.065, p = 0.664$).

Discussion

The novel findings of this study are that people with and without FM did not experience detrimental changes in experimental pain sensitivity following isometric or concentric exercise of clinically appropriate intensity; pressure pain thresholds were similar at the exercising muscle (locally) and remotely. The FM group did report greater pain locally in the exercising muscle however, neither controls nor people with FM experienced changes in widespread body pain which was supported by a small reduction in pain summation. In addition to pain, we show that people with and without FM experience similar central fatigue in response to isometric and concentric fatiguing contractions while people with FM show greater performance fatigability in the exercising muscle that was not related to baseline clinical symptoms or pain experienced during exercise. These results suggest the greater performance fatigability in the exercising muscle of people with FM was not related to central mechanisms of fatigue or pain but specific to changes occurring locally in the exercising muscle.

Despite our participants with FM reporting clinical symptoms of pain and perceived fatigue, we showed performance of submaximal resistance exercise did not adversely influence

clinical widespread pain, regardless of contraction type. Furthermore, the pain response to resistance exercise was predominately localized in the exercising muscle in people with and without FM. Similar to prior work, changes in pressure pain sensitivity following exercise may be dependent on assessment site (Melia et al. 2019), thus assessment of local and remote sites may provide a better scope of local and systemic changes from exercise. The novel finding of a reduction in pain summation is in contrast to prior work demonstrating increased pressure pain sensitivity and pain summation with sustained submaximal isometric contractions and exercise to exhaustion (Lannersten and Kosek 2010; Staud et al. 2005; Vierck et al. 2001). Results of reduced pain summation in this study were supported by a lack of increase in widespread body pain assessed via self-report and with PPTs at the quadriceps. This indicates the pain response following submaximal resistance exercise may be due to a local post-exercise muscle soreness that is commonly experienced in those who are naïve with exercise and may be attributed to mechanical, chemical, and noxious stimuli in the exercising muscle (MacIntyre et al. 1995). Additionally, the local pain response was not sufficient to lead to augmented pain facilitation from repeated afferent nociceptive input from the exercising muscle. Changes in pain summation following resistance exercise may be dose dependent as prior studies show exercise of higher intensity may lead to heightened pain summation (Staud et al. 2005; Vierck et al. 2001). Exercise performed to maximal intensity or to exhaustion leads to metabolic by-product accumulation such as fatigue metabolites (Pi, H⁺, Mg²⁺, Ca²⁺, K⁺, lactate, creatine kinase) (Ament & Verkerke, 2009; Feher, 2017; Pollak et al., 2014; Radák, 2018) which may lead to greater nociceptor sensitivity, increased group III and IV afferent feedback, and greater pain summation with exercise (Mense, 2008; Pollak et al., 2014; Ross et al., 2018; Staud et al., 2009). Exercise in this study was performed at a submaximal intensity which may have reduced the impact of these metabolic effects.

In contrast to experimental pain sensitivity, contraction type did influence self-reported arm pain during and following exercise and perceived exertion during exercise for CON and FM participants. Concentric contractions lead to greater perceived pain compared to isometric despite same intensity of exercise relative to the MVIC possibly because concentric contractions require greater metabolic demand compared with isometric contractions (Feher 2017; MacIntosh et al. 2012; Radák 2018). Despite both groups having elevated arm pain during exercise, greater perceived pain and exertion was reported by FM participants as they achieved clinically relevant increases in arm pain following both contraction types (>2-point change) (Farrar et al. 2001), while control participants did not. The increase in local arm pain may be due to augmented sensory feedback associated with accumulation of fatigue metabolites (Ge et al. 2012; Staud 2010; Staud et al. 2009). Neither group reported a significant increase in whole-body pain following isometric or concentric exercise, reinforcing the local effects of resistance exercise within exercising muscle tissue on perceived pain in FM versus changes in systemic clinical symptoms associated with central pain facilitation. Despite increased perceived pain locally in the exercising arm, submaximal isometric or concentric exercise did not lead to increased pressure pain sensitivity. Reinforcing the need of evaluating both clinical and experimental pain as each construct may provide unique attributes of the pain experience (Backonja et al. 2013).

People with and without FM experienced performance fatigability in the exercising elbow flexors and remotely in the non-exercising, contralateral hand which was similar between concentric and isometric tasks. These reductions in MVICs were still evident in both groups despite being assessed approximately 5 minutes after exercise (following all pain assessments). Performance fatigability of the elbow flexors was greater in the FM group while similar changes were seen systemically measured via handgrip. The greater performance fatigability in FM was not explained by clinical symptoms of pain, perceived fatigue, or pain experienced during the exercising task. These results are in contrast to previous studies reporting relationships between elevated clinical symptoms and inhibition of force production following exercise (Cardinal et al. 2019; Chimenti et al. 2018; Mastaglia 2012). Further evaluation of neuromotor function showed both groups were comparable in their ability to activate the right biceps brachii as similar neural drive (voluntary activation) and muscle contractile properties (twitch amplitude and half relaxation time) were assessed at baseline. These findings corroborate similar baseline elbow flexor and handgrip MVIC, indicating FM participants were not at a reduced neuromuscular capacity compared to controls. Therefore, both groups performed similar intensity of exercise when matched at 20% of MVIC during each exercise bout. The lack of differences in resting measures of central neural drive and peripheral contractile properties in combination with greater local performance fatigability in the exercising elbow flexors without greater systemic change in performance fatigability suggests there may be local metabolic changes within the exercising muscle during exercise that contributes to performance fatigability. Although evidence for muscle pathology in FM is inconclusive, evidence suggests potential structural and metabolic changes, and abnormal inflammatory responses in muscle fibers of people with FM (Bengtsson, 2002; Conti et al., 2020; Le Goff, 2006; Mastrangelo et al., 2018; Ruggiero et al., 2018). These physiological changes may heighten nociceptive feedback during exercise, thus explaining increased reductions in strength in an exercising muscle in people with fibromyalgia. In addition to local changes occurring in the muscle, central nervous system input to the exercising muscle may be reduced with heightened nociceptive feedback during exercise (Aboodarda et al., 2020; Amann, 2012; Blain et al., 2016; Hureau et al., 2018; Taylor et al., 2016), thus also contributing to strength reductions in the exercising muscle.

Lack of differences in performance fatigability between the two contraction types provides evidence that isometric and/or concentric based resistance exercise may be implemented in FM with similar effects on motor function. The exercise protocols used in this study are similar to rehabilitation practices where single limb exercise is initially prescribed at submaximal levels prior to progression to whole-body/multi-joint exercise. These results indicate resistance exercise leads predominately to local effects on motor performance following exercise. Clinicians should be cognizant when initiating submaximal resistance exercise in people with FM as greater reductions in local motor function may inhibit subsequent exercise that is directed to similar muscle groups. Although similar systemic reductions in force generation occurred in CON and FM, clinicians should be aware that muscle groups in remote body regions may demonstrate physiological fatigue that may influence systemic muscle performance during subsequent daily activity and exercise bouts directed to previously non-exercised muscle groups.

A strength of this study was the ability to examine changes in experimental pain, clinical pain, and performance fatigability in primarily middle-aged people with and without FM matched for age, sex, body composition, physical activity, and strength thereby reducing the influence of each factor on the response to exercise. Both groups had comparable elbow flexor and handgrip force generating capacity, indicating similar physical fitness levels despite increased symptomology in the FM group. The similarities between the groups allows for better comparison of the influence of clinical pain and fatigue commonly experienced in FM on the response to exercise as well as the opportunity to advance knowledge of the pain and fatigue response to exercise in an understudied population of primarily middle-aged women. Furthermore, our FM participants were of similar age and symptom severity as prior clinical studies (Bennett et al. 2009; Hauser et al. 2011; Walitt et al. 2015). These results are generalizable to middle-aged people with and without FM, which contrasts with prior reports investigating the influence of exercise on pain and fatigue in fit, young healthy adults (Babault et al., 2006; Dannecker & Koltyn, 2014; Hunter, 2018; Kirk et al., 2019; Koltyn et al., 2014a; Kosek & Lundberg, 2003; Naugle et al., 2012; Senefeld et al., 2013; Vaegter et al., 2014, 2015; Vaegter et al., 2017). Both groups reported increased self-reported arm pain and experienced performance fatigability localized to the exercising limb which may be expected when performing novel exercise in a sample who are overweight-obese and of primarily middle age.

The results of this study hold significant clinical implications because intermittent muscle contractions are routinely performed with resistance exercise training. The results of this study show people with FM may partake in light intensity resistance exercise without increases in widespread pain and fatigue which contrasts with anecdotal reports suggesting exacerbation of whole-body pain with resistance exercise. Clinicians may consider initiating resistance exercise in FM with isometric based contractions to reduce the impact perceived pain and exertion during bouts of exercise. This study highlights the importance of prescribing light intensity resistance exercise to a limited body region prior to progressing towards whole-body resistance exercise in order to prevent systemic changes in whole-body pain. Clinicians should assess and manage localized exercise-evoked pain and fatigue during and after a bout of submaximal resistance exercise. Adjunct pain management techniques devoted to the exercising limb may be beneficial in reducing pain during bouts of resistance exercise (Dailey et al. 2013; Dailey et al. 2020), which may lead to improved tolerance during single sessions of resistance exercise and improve compliance with repeated sessions of exercise as required for training. Additionally, patient education directed towards localized muscle pain following resistance exercise can set appropriate expectations of the exercise response for people with FM.

Limitations

Fibromyalgia symptom severity may have fluctuated throughout the three weeks of study participation as prior research demonstrates people with FM experience fluctuating intensity of symptomology (Harris et al. 2005; Wolfe et al. 2011) which may have influenced experimental and clinical assessments. However, our study design included assessment of pain and fatigue before each exercise session and differences were not seen between sessions. Experimental pain was evaluated immediately after each exercise bout, though

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further research needs to investigate whether longer time durations are needed to capture systemic changes in pressure pain sensitivity following resistance exercise. Post-exercise assessment of elbow flexor and handgrip MVIC were performed after completion of all post-exercise clinical and experimental pain assessments. Post-exercise assessment of elbow flexor and handgrip MVIC were performed after completion of all post-exercise clinical and experimental pain assessments. Therefore, 5 minutes separated the completion of the exercise task and reassessment of MVICs which likely resulted in some recovery of elbow flexor and handgrip strength. The magnitude of exercise-induced reductions in force production may be underestimated in this study. Despite this limitation, both groups experienced exercise-induced decreases in force production. Further research should investigate whether exercise-induced reductions in muscle force persist for longer duration in people with FM.

Conclusion

We assessed clinically recommended light-intensity exercise, with isometric and concentric contractions, and showed similar changes in experimental pain sensitivity in people with and without FM that was not dependent on the type of muscle contraction performed. People with FM however, reported greater pain locally in the exercising limb during and following exercise with no changes in systemic widespread body pain which was supported by small decreases in pain summation. If people with FM have a primary limitation of pain during exercise then isometric contractions may be beneficial to start with for an individually tailored approach.

People with and without FM experience performance fatigability following resistance exercise irrespective of contraction type. Greater performance fatigability in the exercising muscle of people with FM was not attributed to central fatigue or related to baseline clinical symptoms and exercise-induced pain. Our study suggests the local performance fatigability is attributed to changes occurring in the muscle that are specific to FM; these changes are independent of previously known factors that contribute to fatigue including sex, body composition, physical activity, and baseline strength.

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Abbreviations

ACR	2010 American College of Rheumatology Modified Diagnostic Criteria for Fibromyalgia
BMI	Body mass index
CON	Control
Conc	Concentric

DXA	Dual-energy x-ray absorptiometry
FIQR	Revised Fibromyalgia Impact Questionnaire
FM	Fibromyalgia
Iso	Isometric
MVIC	Maximal voluntary isometric contraction
NRS	Numerical rating scale
PAAT	Physical Activity Assessment Tool
PPT	Pressure pain threshold
PROMIS Fatigue	PROMIS Short Form v1.0 – Fatigue 7a
RPE	Rating of perceived exertion
VAS	Visual analogue scale

References

Aboodarda SJ, lannetta D, Emami N, Varesco G, Murias JM, & Millet GY (2020). Effects of pre-induced fatigue vs. concurrent pain on exercise tolerance, neuromuscular performance and corticospinal responses of locomotor muscles. *J Physiol*, 598(2), 285–302. 10.1113/JP278943 [PubMed: 31826296]

ACSM (2018) ACSM's Health/Fitness Facility Standards and Guidelines. 5th edn. Human Kinetics, Champaign, IL.

Alvarez-Gallardo IC et al. (2019) Therapeutic validity of exercise interventions in the management of fibromyalgia *J Sports Med Phys Fitness* 59:828–838 doi:10.23736/s0022-4707.18.08897-7 [PubMed: 30293405]

Amann M (2012). Significance of Group III and IV muscle afferents for the endurance exercising human. *Clin Exp Pharmacol Physiol*, 39(9), 831–835. 10.1111/j.1440-1681.2012.05681.x [PubMed: 22300329]

Ambrose KR, Golightly YM (2015) Physical exercise as non-pharmacological treatment of chronic pain: Why and when *Best Pract Res Clin Rheumatol* 29:120–130 doi:10.1016/j.berh.2015.04.022 [PubMed: 26267006]

Ament W, Verkerke GJ (2009) Exercise and fatigue *Sports Med* 39:389–422 doi:10.2165/00007256-200939050-00005 [PubMed: 19402743]

Ameringer S et al. (2016) Psychometric Evaluation of the Patient-Reported Outcomes Measurement Information System Fatigue-Short Form Across Diverse Populations *Nursing research* 65:279–289 doi:10.1097/nnr.0000000000000162 [PubMed: 27362514]

Babault N, Desbrosses K, Fabre MS, Michaut A, Pousson M (2006) Neuromuscular fatigue development during maximal concentric and isometric knee extensions *Journal of applied physiology* (Bethesda, Md: 1985) 100:780–785 doi:10.1152/japplphysiol.00737.2005

Bachasson D, Guinot M, Wuyam B, Favre-Juvin A, Millet GY, Levy P, Verges S (2013) Neuromuscular fatigue and exercise capacity in fibromyalgia syndrome *Arthritis Care & Research* 65:432–440 doi:10.1002/acr.21845 [PubMed: 22965792]

Backonja MM et al. (2013) Value of quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus *Pain* 154:1807–1819 doi:10.1016/j.pain.2013.05.047 [PubMed: 23742795]

Bengtsson A (2002). The muscle in fibromyalgia. *Rheumatology (Oxford)*, 41(7), 721–724. 10.1093/rheumatology/41.7.721 [PubMed: 12096218]

Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL (2009) The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. In: *Arthritis Res Ther*, vol 11, vol 4, p R120. doi:10.1186/ar2783 [PubMed: 19664287]

Bidonde J, Busch AJ, Bath B, Milosavljevic S (2014) Exercise for adults with fibromyalgia: an umbrella systematic review with synthesis of best evidence *Current Rheumatology Reviews* 10:45–79 [PubMed: 25229499]

Bidonde J et al. (2017) Aerobic exercise training for adults with fibromyalgia *Cochrane Database Syst Rev* 6: Cd012700 doi:10.1002/14651858.cd012700 [PubMed: 28636204]

Bidonde J et al. (2019) Mixed exercise training for adults with fibromyalgia *Cochrane Database Syst Rev* 5: Cd013340 doi:10.1002/14651858.cd013340 [PubMed: 31124142]

Blain GM, Mangum TS, Sidhu SK, Weavil JC, Hureau TJ, Jessop JE, Bledsoe AD, Richardson RS, & Amann M (2016) Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. *J Physiol*, 594(18), 5303–5315. 10.1113/JP272283 [PubMed: 27241818]

Borg G (1998) Borg's perceived exertion and pain scales. *Human Kinetics*,

Burckhardt CS, Clark SR, Bennett RM (1991) The fibromyalgia impact questionnaire: development and validation *J Rheumatol* 18:728–733 [PubMed: 1865419]

Busch AJ, Barber KA, Overend TJ, Peloso PMJ, Schachter CL (2007) Exercise for treating fibromyalgia syndrome *The Cochrane Database of Systematic Reviews*: CD003786 doi:10.1002/14651858.CD003786.pub2 [PubMed: 17943797]

Busch AJ et al. (2011) Exercise therapy for fibromyalgia *Current Pain and Headache Reports* 15:358–367 doi:10.1007/s11916-011-0214-2 [PubMed: 21725900]

Busch AJ et al. (2013) Resistance exercise training for fibromyalgia *The Cochrane Database of Systematic Reviews*: CD010884 doi:10.1002/14651858.CD010884 [PubMed: 24362925]

Cardinal TM et al. (2019) Differential Neuroplastic Changes in Fibromyalgia and Depression Indexed by Up-Regulation of Motor Cortex Inhibition and Disinhibition of the Descending Pain System: An Exploratory Study *Front Hum Neurosci* 13:138 doi:10.3389/fnhum.2019.00138 [PubMed: 31105542]

Chimenti RL, Frey-Law LA, Sluka KA (2018) A Mechanism-Based Approach to Physical Therapist Management of Pain *Phys Ther* 98:302–314 doi:10.1093/ptj/pzy030 [PubMed: 29669091]

Choi L, Ward SC, Schnelle JF, Buchowski MS (2012) Assessment of wear/nonwear time classification algorithms for triaxial accelerometer *Med Sci Sports Exerc* 44:2009–2016 doi:10.1249/MSS.0b013e318258cb36 [PubMed: 22525772]

Conti P, Gallenga CE, Caraffa A, Ronconi G, & Kritas SK (2020). Impact of mast cells in fibromyalgia and low-grade chronic inflammation: Can IL-37 play a role? *Dermatol Ther*, 33(1), e13191. 10.1111/dth.13191 [PubMed: 31837249]

Dailey DL et al. (2013) Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia *Pain* 154:2554–2562 doi:10.1016/j.pain.2013.07.043 [PubMed: 23900134]

Dailey DL et al. (2020) Transcutaneous Electrical Nerve Stimulation Reduces Movement-Evoked Pain and Fatigue: A Randomized, Controlled Trial *Arthritis Rheumatol* 72:824–836 doi:10.1002/art.41170 [PubMed: 31738014]

Dannecker EA, & Koltyn KF (2014). Pain during and within hours after exercise in healthy adults. *Sports Med*, 44(7), 921–942. 10.1007/s40279-014-0172-z [PubMed: 24668291]

Dowell D, Haegerich TM, Chou R (2016) CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016 *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control* 65:1–49

Enoka RM, Duchateau J (2008) Muscle fatigue: what, why and how it influences muscle function *J Physiol* 586:11–23 doi:10.1113/jphysiol.2007.139477 [PubMed: 17702815]

Enoka RM, Duchateau J (2016) Translating Fatigue to Human Performance *Med Sci Sports Exerc* 48:2228–2238 doi:10.1249/mss.0000000000000929 [PubMed: 27015386]

Ericsson A et al. (2016) Resistance exercise improves physical fatigue in women with fibromyalgia: a randomized controlled trial *Arthritis Res Ther* 18:176 doi:10.1186/s13075-016-1073-3 [PubMed: 27473164]

Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM (2001) Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale *Pain* 94:149–158 [PubMed: 11690728]

Feher J (2017) *Skeletal Muscle Mechanics*. In: *Quantitative Human Physiology: An Introduction*. 2nd edn. Academic Press,

Freedson PM E. Sirard J (1998) Calibration of the Computer Science and Applications, Inc. Accelerometer Medicine and science in sports and exercise 30 doi:10.1097/00005768-199805000-00021

Freedson PS, & John D (2013). Comment on “Estimating activity and sedentary behavior from an accelerometer on the hip and wrist”. *Med Sci Sports Exerc*, 45(5), 962–963 10.1249/MSS.0b013e31827f024d [PubMed: 23594509]

Gandevia SC (2001) Spinal and supraspinal factors in human muscle fatigue *Physiological Reviews* 81:1725–1789 [PubMed: 11581501]

Ge HY, Nie H, Graven-Nielsen T, Danneskiold-Samsøe B, Arendt-Nielsen L (2012) Descending pain modulation and its interaction with peripheral sensitization following sustained isometric muscle contraction in fibromyalgia *Eur J Pain* 16:196–203 doi:10.1016/j.ejpain.2011.06.008 [PubMed: 22323372]

Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH (2017) Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews *The Cochrane Database of Systematic Reviews* 1:CD011279 doi:10.1002/14651858.CD011279.pub2 [PubMed: 28087891]

Gowans SE, deHueck A (2004) Effectiveness of exercise in management of fibromyalgia *Curr Opin Rheumatol* 16:138–142 [PubMed: 14770100]

Häkkinen A, Häkkinen K, Hannonen P, Alen M (2000) Force production capacity and acute neuromuscular responses to fatiguing loading in women with fibromyalgia are not different from those of healthy women *The Journal of Rheumatology* 27:1277–1282 [PubMed: 10813301]

Harris RE et al. (2005) Characterization and consequences of pain variability in individuals with fibromyalgia *Arthritis Rheum* 52:3670–3674 doi:10.1002/art.21407 [PubMed: 16258905]

Hauser W, Kuhn-Becker H, von Wilmosky H, Settan M, Braehler E, Petzke F (2011) Demographic and clinical features of patients with fibromyalgia syndrome of different settings: a gender comparison *Gend Med* 8:116–125 doi:10.1016/j.genm.2011.03.002 [PubMed: 21536230]

Hoeger Bement MK, Weyer A, Hartley S, Drewek B, Harkins AL, Hunter SK (2011) Pain perception after isometric exercise in women with fibromyalgia *Archives of Physical Medicine and Rehabilitation* 92:89–95 doi:10.1016/j.apmr.2010.10.006 [PubMed: 21187210]

Hoeger Bement MK, Weyer A, Hartley S, Yoon T, Hunter SK (2009) Fatiguing exercise attenuates pain-induced corticomotor excitability *Neuroscience letters* 452:209–213 doi:10.1016/j.neulet.2009.01.038 [PubMed: 19383441]

Hunter SK (2018) Performance Fatigability: Mechanisms and Task Specificity *Cold Spring Harb Perspect Med* 8 doi:10.1101/cshperspect.a029728

Hureau TJ, Romer LM, & Amann M (2018). The 'sensory tolerance limit': A hypothetical construct determining exercise performance? *Eur J Sport Sci*, 18(1), 13–24. 10.1080/17461391.2016.1252428 [PubMed: 27821022]

Jacobsen S, Wildschiodtz G, Danneskiold-Samsøe B (1991) Isokinetic and isometric muscle strength combined with transcutaneous electrical muscle stimulation in primary fibromyalgia syndrome *J Rheumatol* 18:1390–1393 [PubMed: 1757942]

Jones KD, Adams D, Winters-Stone K, Burckhardt CS (2006) A comprehensive review of 46 exercise treatment studies in fibromyalgia (1988–2005) *Health and quality of life outcomes* 4:67 doi:10.1186/1477-7525-4-67 [PubMed: 16999856]

Jones KD, Liptan GL (2009) Exercise interventions in fibromyalgia: clinical applications from the evidence *Rheum Dis Clin North Am* 35:373–391 doi:10.1016/j.rdc.2009.05.004 [PubMed: 19647149]

Kamada M, Shiroma EJ, Harris TB, & Lee IM (2016). Comparison of physical activity assessed using hip- and wrist-worn accelerometers. *Gait Posture*, 44, 23–28. 10.1016/j.gaitpost.2015.11.005 [PubMed: 27004628]

Kirk BJC, Trajano GS, Pulverenti TS, Rowe G, & Blazevich AJ (2019). Neuromuscular Factors Contributing to Reductions in Muscle Force After Repeated, High-Intensity Muscular Efforts. *Front Physiol*, 10, 783. 10.3389/fphys.2019.00783 [PubMed: 31293449]

Koltyn KF (2002) Exercise-induced hypoalgesia and intensity of exercise *Sports Medicine* (Auckland, NZ) 32:477–487

Koltyn KF, Brellenthin AG, Cook DB, Sehgal N, Hillard C (2014a) Mechanisms of exercise-induced hypoalgesia *J Pain* 15:1294–1304 doi:10.1016/j.jpain.2014.09.006 [PubMed: 25261342]

Koltyn KF, Brellenthin AG, Cook DB, Sehgal N, Hillard C (2014b) Mechanisms of exercise-induced hypoalgesia *The Journal of Pain: Official Journal of the American Pain Society* 15:1294–1304 doi:10.1016/j.jpain.2014.09.006

Kosek E, Ekholm J, Hansson P (1996) Modulation of pressure pain thresholds during and following isometric contraction in patients with fibromyalgia and in healthy controls *Pain* 64:415–423 [PubMed: 8783304]

Kosek E, & Lundberg L (2003). Segmental and plurisegmental modulation of pressure pain thresholds during static muscle contractions in healthy individuals. *Eur J Pain*, 7(3), 251–258. 10.1016/S1090-3801(02)00124-6 [PubMed: 12725848]

Lai JS, Celli D, Choi S, Junghaenel DU, Christodoulou C, Gershon R, Stone A (2011) How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example *Arch Phys Med Rehabil* 92:S20–27 doi:10.1016/j.apmr.2010.08.033 [PubMed: 21958919]

Lannersten L, Kosek E (2010) Dysfunction of endogenous pain inhibition during exercise with painful muscles in patients with shoulder myalgia and fibromyalgia *Pain* 151:77–86 doi:10.1016/j.pain.2010.06.021 [PubMed: 20621420]

Le Goff P (2006). Is fibromyalgia a muscle disorder? *Joint Bone Spine*, 73(3), 239–242. 10.1016/j.jbspin.2005.03.022 [PubMed: 16488643]

Lemley KJ, Hunter SK, Bement MKH (2015) Conditioned pain modulation predicts exercise-induced hypoalgesia in healthy adults *Medicine and Science in Sports and Exercise* 47:176–184 doi:10.1249/MSS.0000000000000381 [PubMed: 24870571]

Lima LV, Abner TSS, Sluka KA (2017) Does exercise increase or decrease pain? Central mechanisms underlying these two phenomena *The Journal of Physiology* doi:10.1113/JP273355

MacIntosh BR, Holash RJ, Renaud JM (2012) Skeletal muscle fatigue--regulation of excitation-contraction coupling to avoid metabolic catastrophe *J Cell Sci* 125:2105–2114 doi:10.1242/jcs.093674 [PubMed: 22627029]

MacIntyre DL, Reid WD, McKenzie DC (1995) Delayed muscle soreness. The inflammatory response to muscle injury and its clinical implications *Sports Med* 20:24–40 doi:10.2165/00007256-199520010-00003 [PubMed: 7481277]

Madeleine P, Jorgensen LV, Sogaard K, Arendt-Nielsen L, Sjogaard G (2002) Development of muscle fatigue as assessed by electromyography and mechanomyography during continuous and intermittent low-force contractions: effects of the feedback mode *Eur J Appl Physiol* 87:28–37 doi:10.1007/s00421-002-0578-4 [PubMed: 12012073]

Martin JL, & Hakim AD (2011). Wrist actigraphy. *Chest*, 139(6), 1514–1527. 10.1378/chest.10-1872 [PubMed: 21652563]

Mastaglia FL (2012) The relationship between muscle pain and fatigue *Neuromuscul Disord* 22 Suppl 3:S178–180 doi:10.1016/j.nmd.2012.10.003 [PubMed: 23182635]

Mastrangelo F, Frydas I, Ronconi G, Kritas SK, Tettamanti L, Caraffa A, C DO, Younes A, Gallenga CE, & Conti P (2018). Low-grade chronic inflammation mediated by mast cells in fibromyalgia: role of IL-37. *J Biol Regul Homeost Agents*, 32(2), 195–198. www.ncbi.nlm.nih.gov/pubmed/29684996 [PubMed: 29684996]

Meeus M et al. (2015) Endogenous pain modulation in response to exercise in patients with rheumatoid arthritis, patients with chronic fatigue syndrome and comorbid fibromyalgia, and healthy controls: a double-blind randomized controlled trial *Pain Practice: The Official Journal of World Institute of Pain* 15:98–106 doi:10.1111/papr.12181 [PubMed: 24528544]

Melia M, Geissler B, Konig J, Ottersbach HJ, Umbreit M, Letzel S, Muttray A (2019) Pressure pain thresholds: Subject factors and the meaning of peak pressures *Eur J Pain* 23:167–182 doi:10.1002/ejp.1298 [PubMed: 30076659]

Mense S (2008). Muscle pain: mechanisms and clinical significance. *Dtsch Arztebl Int*, 105(12), 214–219. 10.3238/artebl.2008.0214 [PubMed: 19629211]

Meriwether RA, McMahon PM, Islam N, Steinmann WC (2006) Physical activity assessment: validation of a clinical assessment tool *American journal of preventive medicine* 31:484–491 doi:10.1016/j.amepre.2006.08.021 [PubMed: 17169709]

Miguel JH et al. (2017) Accelerometer Data Collection and Processing Criteria to Assess Physical Activity and Other Outcomes: A Systematic Review and Practical Considerations *Sports Med* 47:1821–1845 doi:10.1007/s40279-017-0716-0 [PubMed: 28303543]

Naugle KM, Fillingim RB, Riley JL (2012) A meta-analytic review of the hypoalgesic effects of exercise *The Journal of Pain: Official Journal of the American Pain Society* 13:1139–1150 doi:10.1016/j.jpain.2012.09.006

Naugle KM, Naugle KE, Riley JL (2016) Reduced Modulation of Pain in Older Adults After Isometric and Aerobic Exercise *The Journal of Pain: Official Journal of the American Pain Society* 17:719–728 doi:10.1016/j.jpain.2016.02.013

Palstam A et al. (2016) Decrease of fear avoidance beliefs following person-centered progressive resistance exercise contributes to reduced pain disability in women with fibromyalgia: secondary exploratory analyses from a randomized controlled trial *Arthritis Res Ther* 18 doi:10.1186/s13075-016-1007-0

Pasquet B, Carpentier A, Duchateau J, Hainaut K (2000) Muscle fatigue during concentric and eccentric contractions *Muscle & nerve* 23:1727–1735 doi:10.1002/1097-4598(200011)23:11<1727::aid-mus9>3.0.co;2-y [PubMed: 11054752]

Pollak KA, Swenson JD, Vanhaitsma TA, Hughen RW, Jo D, White AT, Light KC, Schweinhardt P, Amann M, & Light AR (2014). Exogenously applied muscle metabolites synergistically evoke sensations of muscle fatigue and pain in human subjects. *Exp Physiol*, 99(2), 368–380. 10.1113/expphysiol.2013.075812 [PubMed: 24142455]

Queiroz LP (2013) Worldwide epidemiology of fibromyalgia *Current Pain and Headache Reports* 17:356 doi:10.1007/s11916-013-0356-5 [PubMed: 23801009]

Radák Z (2018) Skeletal Muscle, Function, and Muscle Fiber Types. In: *The Physiology of Physical Training*. 1st edn. Academic Press.

Rice D et al. (2019) Exercise induced hypoalgesia in pain-free and chronic pain populations: State of the art and future directions *J Pain* doi:10.1016/j.jpain.2019.03.005

Rosenberger MH WL, Albinali F, Mota S, Nawyn J, Intille S. (2013) Estimating Activity and Sedentary Behavior From an Accelerometer on the Hip or Wrist *Medicine and Science in Sports and Exercise* 45 doi:10.1249/MSS.0b013e31827f0d9c

Ross JL, Queme LF, Lamb JE, Green KJ, & Jankowski MP (2018). Sex differences in primary muscle afferent sensitization following ischemia and reperfusion injury. *Biol Sex Differ*, 9(1), 2. 10.1186/s13293-017-0163-5 [PubMed: 29298725]

Ruggiero L, Manganelli F, & Santoro L (2018). Muscle pain syndromes and fibromyalgia: the role of muscle biopsy. *Curr Opin Support Palliat Care*, 12(3), 382–387. 10.1097/SPC.0000000000000355 [PubMed: 29912728]

Scott JJ, Rowlands AV, Cliff DP, Morgan PJ, Plotnikoff RC, & Lubans DR (2017). Comparability and feasibility of wrist- and hip-worn accelerometers in free-living adolescents. *J Sci Med Sport*, 20(12), 1101–1106. 10.1016/j.jsams.2017.04.017 [PubMed: 28501418]

Senefeld J, Yoon T, Bement MH, Hunter SK (2013) Fatigue and recovery from dynamic contractions in men and women differ for arm and leg muscles *Muscle & nerve* 48:436–439 doi:10.1002/mus.23836 [PubMed: 23494882]

Sluka KA, Clauw DJ (2016) Neurobiology of fibromyalgia and chronic widespread pain *Neuroscience* 338:114–129 doi:10.1016/j.neuroscience.2016.06.006 [PubMed: 27291641]

Sosa-Reina MD, Nunez-Nagy S, Gallego-Izquierdo T, Pecos-Martin D, Monserrat J, Alvarez-Mon M (2017) Effectiveness of Therapeutic Exercise in Fibromyalgia Syndrome: A Systematic Review

and Meta-Analysis of Randomized Clinical Trials *Biomed Res Int* 2017:2356346 doi:10.1155/2017/2356346 [PubMed: 29291206]

Srikuea R et al. (2013) Association of fibromyalgia with altered skeletal muscle characteristics which may contribute to postexertional fatigue in postmenopausal women *Arthritis Rheum* 65:519–528 doi:10.1002/art.37763 [PubMed: 23124535]

Staud R (2010) Is it all central sensitization? Role of peripheral tissue nociception in chronic musculoskeletal pain *Current Rheumatology Reports* 12:448–454 doi:10.1007/s11926-010-0134-x [PubMed: 20882373]

Staud R, Nagel S, Robinson ME, Price DD (2009) Enhanced central pain processing of fibromyalgia patients is maintained by muscle afferent input: a randomized, double-blind, placebo-controlled study *Pain* 145:96–104 doi:10.1016/j.pain.2009.05.020 [PubMed: 19540671]

Staud R, Robinson ME, Price DD (2005) Isometric exercise has opposite effects on central pain mechanisms in fibromyalgia patients compared to normal controls *Pain* 118:176–184 doi:10.1016/j.pain.2005.08.007 [PubMed: 16154700]

Taylor JL, Amann M, Duchateau J, Meeusen R, & Rice CL (2016). Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again. *Med Sci Sports Exerc*, 48(11), 2294–2306. 10.1249/MSS.0000000000000923 [PubMed: 27003703]

Troiano RP, McClain JJ, Brychta RJ, & Chen KY (2014). Evolution of accelerometer methods for physical activity research. *Br J Sports Med*, 48(13), 1019–1023. 10.1136/bjsports-2014-093546 [PubMed: 24782483]

Turk DC, Rudy TE, Sorkin BA (1993) Neglected topics in chronic pain treatment outcome studies: determination of success *Pain* 53:3–16 [PubMed: 8316386]

Vaegter HB, Handberg G, Graven-Nielsen T (2014) Similarities between exercise-induced hypoalgesia and conditioned pain modulation in humans *Pain* 155:158–167 doi:10.1016/j.pain.2013.09.023 [PubMed: 24076045]

Vaegter HB, Handberg G, Graven-Nielsen T (2015a) Isometric exercises reduce temporal summation of pressure pain in humans *European Journal of Pain (London, England)* 19:973–983 doi:10.1002/ejp.623

Vaegter HB, Handberg G, Jørgensen MN, Kinly A, Graven-Nielsen T (2015b) Aerobic exercise and cold pressor test induce hypoalgesia in active and inactive men and women *Pain Medicine (Malden, Mass)* 16:923–933 doi:10.1111/pme.12641

Vaegter HB, Hoeger Bement M, Madsen AB, Fridriksson J, Dasa M, Graven-Nielsen T (2016) Exercise increases pressure pain tolerance but not pressure and heat pain thresholds in healthy young men *European Journal of Pain (London, England)* doi:10.1002/ejp.901

van Hees VT, Renstrom F, Wright A, Gradmak A, Catt M, Chen KY, Lof M, Bluck L, Pomeroy J, Wareham NJ, Ekelund U, Brage S, & Franks PW (2011). Estimation of daily energy expenditure in pregnant and non-pregnant women using a wrist-worn tri-axial accelerometer. *PloS One*, 6(7), e22922. 10.1371/journal.pone.0022922 [PubMed: 21829556]

Vierck CJ, Staud R, Price DD, Cannon RL, Mauderli AP, Martin AD (2001) The effect of maximal exercise on temporal summation of second pain (windup) in patients with fibromyalgia syndrome *The Journal of Pain: Official Journal of the American Pain Society* 2:334–344 doi:10.1054/jpai.2001.25533

Walitt B, Nahin RL, Katz RS, Bergman MJ, Wolfe F (2015) The Prevalence and Characteristics of Fibromyalgia in the 2012 National Health Interview Survey *PloS One* 10:e0138024 doi:10.1371/journal.pone.0138024 [PubMed: 26379048]

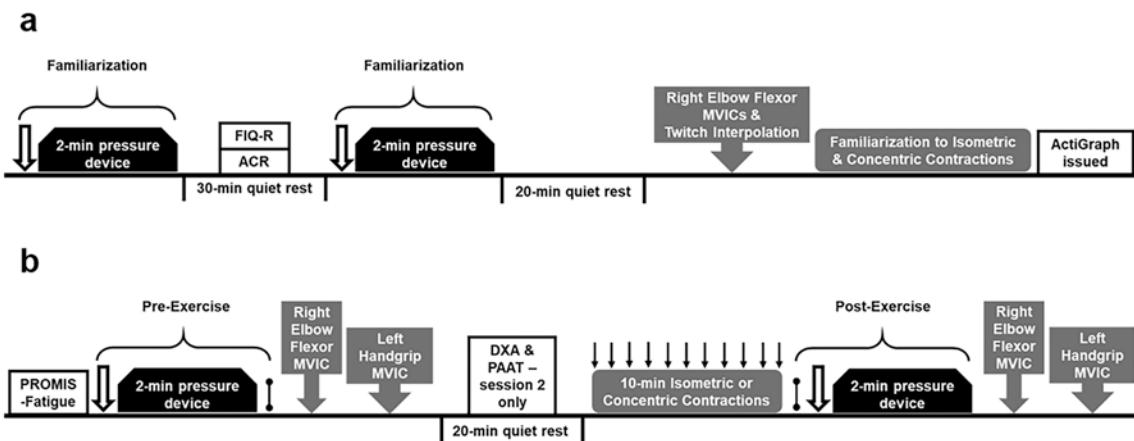
Wolfe F et al. (2011) Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia *The Journal of Rheumatology* 38:1113–1122 doi:10.3899/jrheum.100594 [PubMed: 21285161]

Wolfe F et al. (2010a) The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity *Arthritis Care & Research* 62:600–610 doi:10.1002/acr.20140 [PubMed: 20461783]

Wolfe F et al. (2010b) The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity *Arthritis Care Res (Hoboken)* 62:600–610 doi:10.1002/acr.20140 [PubMed: 20461783]

Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L (1995) The prevalence and characteristics of fibromyalgia in the general population *Arthritis and Rheumatism* 38:19–28 [PubMed: 7818567]

Yoon T, Schlinder-Delap B, Hunter SK (2013) Fatigability and recovery of arm muscles with advanced age for dynamic and isometric contractions *Exp Gerontol* 48:259–268 doi:10.1016/j.exger.2012.10.006 [PubMed: 23103238]

**Figure 1:**

Design of experimental sessions, a) familiarization session (session 1), b) experimental session (session 2 & 3).

↓ = PPTs at the biceps and quadriceps, ↓ = arm pain (NRS) and RPE, ↓ = arm and whole-body pain (VAS), FIQR = Fibromyalgia Impact Questionnaire – Revised, ACR = American College of Rheumatology Modified Diagnostic Criteria for Fibromyalgia, PROMIS – Fatigue = PROMIS Short Form v1.0 – Fatigue 7a, DXA = dual-energy x-ray absorptiometry, PAAT = Physical Activity Assessment Tool, MVIC = maximal voluntary isometric contraction.

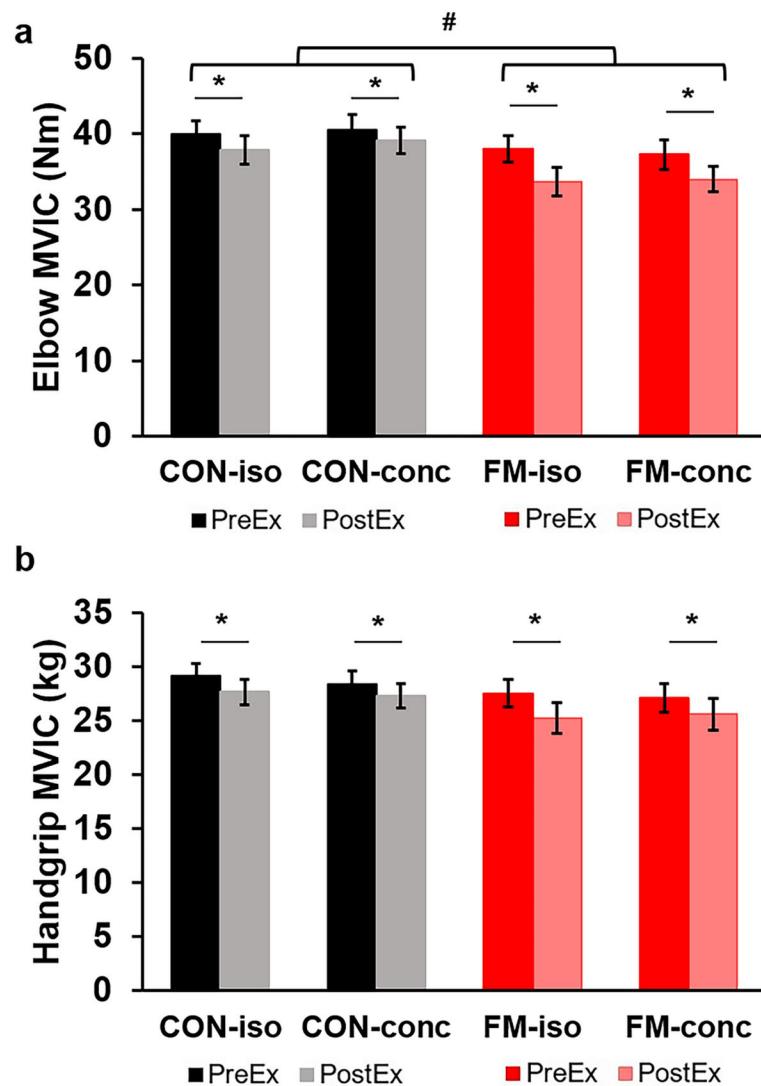


Figure 2:
 Exercise-induced fatigue measured by changes in maximal voluntary isometric contractions (MVIC) before and after isometric (iso) and concentric (conc) exercise for a) right elbow flexors (Nm) and b) left handgrip (kg). Significant effect of time (pre-to-post exercise = *) and differences between groups (Time x Group = #).

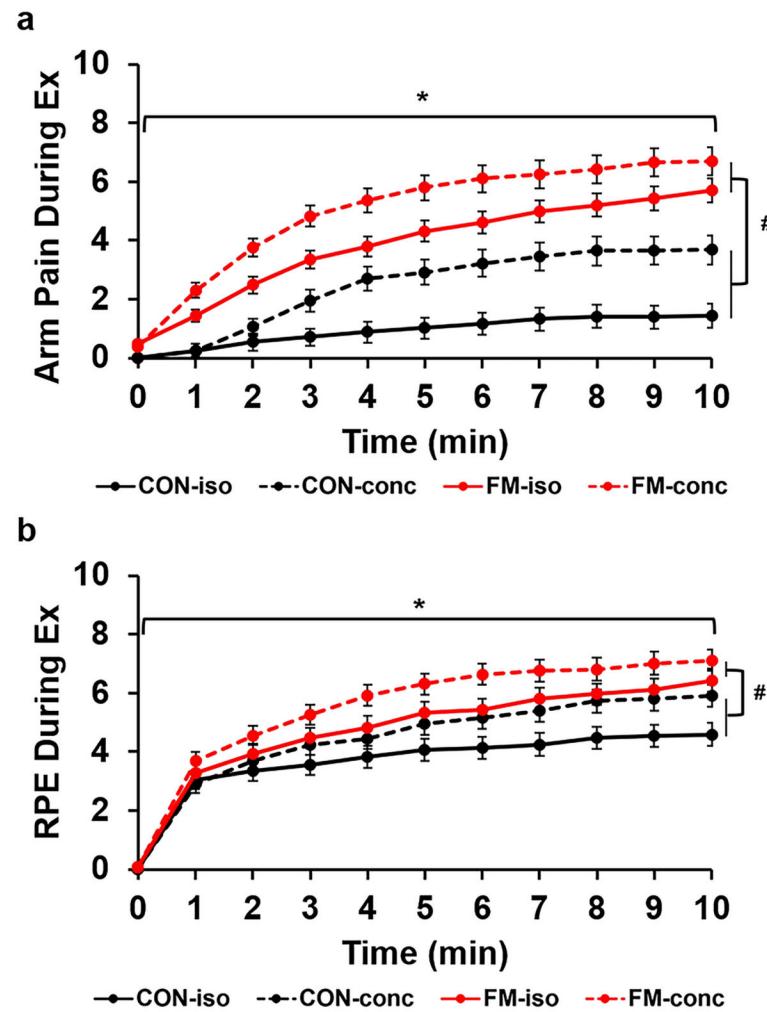
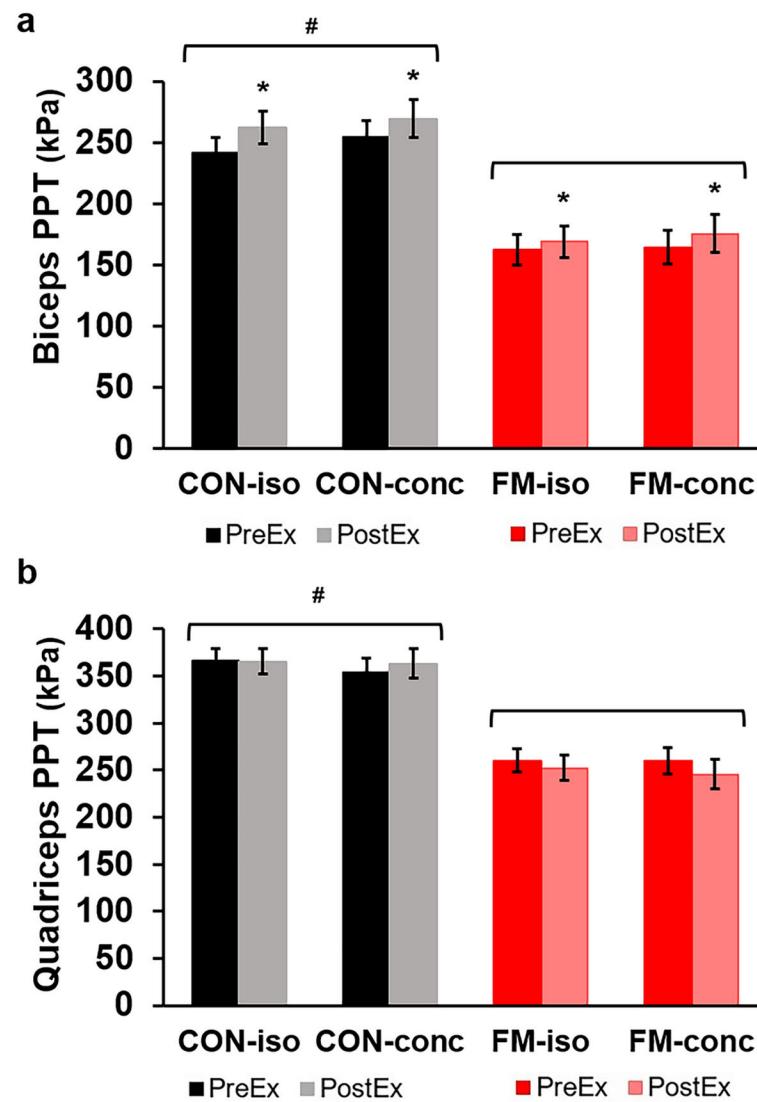
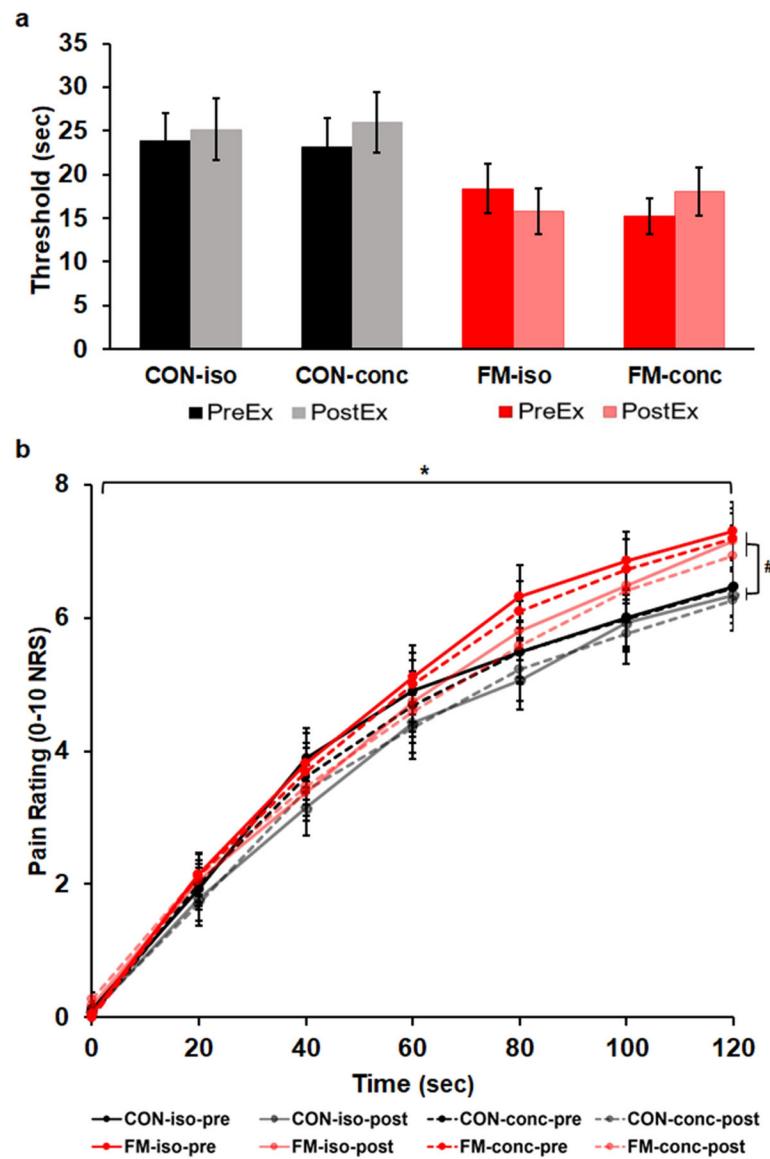


Figure 3:
 Change in a) pain (0-10 numerical pain rating scale) and b) rating of perceived exertion (modified Borg Scale) during isometric (iso) and concentric (conc) exercise. Pain and RPE increased during the 10-minute exercise (time = *). People with FM had greater pain and RPE during exercise compared to CON (Time x Group = #). There was a greater increase in pain and RPE during concentric exercise compared to isometric (Time x Contraction). Ex = exercise, RPE = rating of perceived exertion, min = minutes, iso = isometric, conc = concentric, CON = control, FM = fibromyalgia.

**Figure 4:**

Change in pressure pain thresholds (kPa) before to after exercise a) locally at the exercising biceps and b) systemically at the quadriceps. CON had higher PPTs than FM (Group effect = #). Following exercise there was an increase in PPTs at the bicep (Site x Time = *) and not the quadriceps. (PPT = pressure pain threshold, Ex = exercise, iso = isometric, conc = concentric, CON = control, FM = fibromyalgia).

**Figure 5:**

Change in a) pain threshold (sec) and b) pain summation (0-10 numerical pain rating scale) before and after isometric (iso) and concentric (conc) exercise. Significant pain summation (*) and differences in summation by time (pre- to post-exercise = #). CON = control, FM = fibromyalgia, sec = seconds, iso = isometric, conc = concentric, Ex = exercise.

Table 1:

Participant Characteristics

	Control (mean \pm SD)	Fibromyalgia (mean \pm SD)
Number of Participants	47	47
Age	52.5 \pm 14.7	51.3 \pm 12.3
Sex	44 F, 3 M	44 F, 3 M
Body Mass Index	27.7 \pm 5.6	30.2 \pm 6.9
Total Lean Mass (kg)	43.7 \pm 7.2	44.3 \pm 7.5
Right Arm Lean Mass (kg)	2.4 \pm 0.6	2.4 \pm 0.7
Total Fat Mass (kg)	28.5 \pm 12.2	33.6 \pm 12.8
Right Arm Fat Mass (kg)	1.5 \pm 0.7	1.8 \pm 0.7
PAAT Mod-Vig Activity (min/week)	420.2 \pm 424.0	413.9 \pm 591.2
ActiGraph		
% Time in Sedentary	31.5 \pm 10.3	35.3 \pm 11.7
% Time in Light Activity	48.3 \pm 7.3	45.7 \pm 8.0
% Time in Mod-Vig Activity	20.2 \pm 9.2	19.0 \pm 8.5
ACR Diagnostic Criteria for Fibromyalgia		
Met Criteria	---	32
Did Not Meet Criteria	---	15
Severity Scale	---	16.6 \pm 5.8
Revised Fibromyalgia Impact Questionnaire	---	48.5 \pm 19.7
PROMIS Short Form Fatigue 7a	13.4 \pm 5.1	22.1 \pm 5.6*
Voluntary Activation (%)	93.9 \pm 8.0	93.5 \pm 8.7
Potentiated Twitch Amplitude (Nm)	5.6 \pm 2.5	5.9 \pm 2.5
Half-Relaxation Time (ms)	44.9 \pm 15.0	51.0 \pm 14.3
Half-Relaxation Rate	-1.0 \pm 0.7	-0.9 \pm 0.6

*
=p<0.001

Table 2:

Clinical Pain, Experimental Pain, RPE, and MVIC Before and After Exercise

	Control		Fibromyalgia	
	Isometric (mean \pm SD)	Concentric (mean \pm SD)	Isometric (mean \pm SD)	Concentric (mean \pm SD)
Mean Change Arm Pain During Exercise (0-10 NPRS)	1.4 \pm 2.5	3.7 \pm 3.4	5.2 \pm 2.9	6.3 \pm 3.3
Mean Change RPE During Exercise (0-10 modified Borg)	4.6 \pm 2.6	5.9 \pm 2.2	6.4 \pm 2.4	7.1 \pm 2.4
	Pre	Post	Pre	Post
Elbow Flexor MVIC (Nm)	40.0 \pm 12.2	38.0 \pm 12.2	40.6 \pm 13.0	39.2 \pm 11.2
Handgrip MVIC (kg)	29.2 \pm 8.4	27.7 \pm 7.9	28.5 \pm 8.1	27.4 \pm 8.0
Arm Pain (0-10 cm VAS)	0.0 \pm 0.0	0.7 \pm 1.4	0.0 \pm 0.0	1.4 \pm 2.0
Whole Body Pain (0-10 cm VAS)	0.1 \pm 0.4	0.2 \pm 0.7	0.0 \pm 0.2	0.2 \pm 0.6
PPT – Biceps (kPa)	241.8 \pm 80.3	262.4 \pm 87.5	254.0 \pm 105.9	269.3 \pm 108.3
PPT – Quadriceps (kPa)	366.6 \pm 132.7	365.3 \pm 129.5	354.3 \pm 128.5	362.9 \pm 132.8
Pressure Pain Device-Threshold (sec)	23.8 \pm 21.1	25.2 \pm 23.7	23.1 \pm 22.3	26.0 \pm 23.4
Pressure Pain Device-Summaton (0-10)	6.3 \pm 3.1	6.3 \pm 2.9	6.4 \pm 3.0	6.2 \pm 3.2