

Altered Recovery Process after Fatiguing Exercise and Potential Benefits of Qigong in Patients
with Fibromyalgia

By

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Abstract

Introduction: Fibromyalgia (FM) is a challenging disorder to explore and warrants further study.

This study aimed to determine if the recovery process after isometric fatiguing contractions is altered and if Qigong may be beneficial in this process.

Methods: Twelve healthy controls and eleven FM patients, ages 30 – 63 years completed the isometric fatiguing exercise. Six FM patients randomly assigned into two groups of 3 completed the intervention of Sham Qigong/Qigong.

Results: The data showed a trend towards altered recovery in torque, perceived exertion, and EMG max amplitude in patients with FM in comparison to healthy controls. For the intervention study, the Qigong group showed trends for improvement in fatigue and symptoms.

Conclusion: Favorable trends were observed for altered recovery and symptoms during fatigue testing after the Qigong program. The results support the need for a study with a larger number of participants.

Keywords: Fibromyalgia (FM), Chronic Fatigue Syndrome (CFS)

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Chapter 1. Introduction

1.1 Background and Motivation

Pain management and physical activity are significant problems for those with Fibromyalgia (FM) and can lead to lifelong challenges. Unfortunately, many different clinical evaluations and treatments work for a while, but then a patient tends to fall off the treatment due to increased pain or other reasons. If we were able to develop a way to easily determine if it was due to an altered recovery pattern, then interventions targeting recovery after activity could help reduce the number of patients stopping treatment.

Activity reduction in FM patients is devastating as they can become more depressive and sometimes miss important activities because they want that time to their families. Patients prefer to be more sedentary with dispersed activity, so fewer symptoms and variations occur on the same or next day to complete their goals. However, if they are more active that day or the previous then more symptoms and variability are experienced [1]. Interestingly enough it has been found that more than 60% of women with FM meet physical activity recommendations (30min/day of moderate to vigorous activity on 5 or more days), spend about 71% of waking time on activities expending little energy, and spend 22min or less on sedentary behaviors on the weekend [2]. So if some FM patients can do activities how recovered are they day to day and why do other patients report having difficulty recovering.

Questionnaires of symptoms, fatigue level, and pain are currently the ways of determining how patients are recovering. Studies have shown varying differences depending on the type of exercise whether aerobic, weightlifting, yoga, or some combination with some recovering and others not recovering at all. Torque and EMG data have shown that patients can recover just like healthy controls, but other studies show that they don't recover. Biomarkers

and cytokines have shown similar findings for recovery and non-recovery. However, studies of how the biomarkers or torque change over the course of an intervention looking at solely the recovery pattern have not been studied extensively.

Interventions and exercise prescriptions exist to help improve patient's symptoms and daily life of activities, along with sleep, mood, and pain [3]. Therefore, understanding what is happening in the recovery process could help to improve treatment and provide long term benefits for FM patients.

1.2 Specific Aims

The goal of this study was to investigate the recovery patterns of healthy controls compared to FM patients after an isometric fatiguing exercise in an attempt to understand if an altered recovery pattern exists. Torque, EMG, and ratings of perceived exertion data were collected and analyzed to determine if recovery may be altered in these two groups, plus an FM intervention: FM and healthy controls were age matched and those FM patients that wanted to participate in an intervention split into two groups of Qigong and Sham Qigong. Results were analyzed by; peak torque reduction after muscle fatigue, peak torque recovery at day 1, peak torque recovery at day 2, fatigue index after fatigue, first day recovery fatigue index, second day recovery fatigue index, and perceived exertion at various contractions and recovery.

The short term goal was to determine if an altered recovery pattern may have exist after exercise preventing patients from wanting to continue treatment and also if a mind body intervention of Qigong may change the results for exercise recovery afterwards. This will allow for the design of more improved studies viewing the recovery pattern in order to find better treatment regiments. The long term goal of the study is to provide a reason as to why patients

lack compliance to exercise and how an altered recovery pattern may be assisted in order for a patient to become more compliant.

1.3 Thesis Content

This document contains five chapters. Chapter 1 consists of an introduction to the area of study. Chapter 2 consists of an extensive background survey of relevant literature published. Chapter 3 consists of a manuscript reporting the background, methods, results, conclusion, and discussion of the healthy controls and patients recovery after fatiguing exercise. Chapter 4 consists of a manuscript reporting the background, methods, results, and conclusion of the two patient groups after Qigong and Sham Qigong intervention and fatiguing exercise. Chapter 5 consists of a summary of this study.

Chapter 2. Background

2.1 Epidemiology of Fibromyalgia and Chronic Fatigue Syndrome

Fibromyalgia (FM) or Chronic Fatigue Syndrome (CFS) are diseases with widespread chronic body pain and persistent fatigue occurring across a number of people. They cover a wide spectrum of ages, ethnic, racial, and socioeconomic groups. The prevalence of CFS varies widely between 0.007% and 2.8% of the general adult population or 0.006% to 3% of the primary care adult population. Approximately 6 million (2-5%) people in the US have FM. Women are more likely to have FM as 80-90% of those diagnosed are women. FM or CFS is diagnosed once widespread chronic musculoskeletal pain lasts for at least three months or fatigue persists beyond 6 months in which it then becomes defined as chronic fatigue. [4-12]

The definitions of FM or CFS have continued to evolve over time, with attempts to find better diagnostic tests. Definitions of CFS were first determined and defined in the mid-1980 by

the US Centers for Disease Control and Prevention (CDC). Symptoms were required to be present for 6 months or longer with a new or definite onset of fatigue that is not life-long. [6] Holmes and colleagues in 1988, created the name, chronic fatigue syndrome, as it was different than current etiological implications of the time [13]. The American College of Rheumatology [14] criteria for defining FM, was based on tender points, in which if a patient was tender in more than 11 out of 18 tender points over the body she/he would be diagnosed with FM [15]. However, there were concerns that the tests may not always be done correctly and that patients could have a smaller number of tender points but still experience severe pain and fatigue daily [16]. Attempts at using diagnostic tests such as laboratory studies to confirm the diagnosis have been reported with no success [6]. There have been suggestions that first-degree relatives of those with FM might have an 8-fold greater risk of developing FM compared with the general population. Genetics have been studied in this regard and have had no clear conclusion. [17] Pain in fibromyalgia is believed by some clinical investigators to result from neurochemical imbalances in the central nervous system that lead to a “central amplification” of pain perceptions [18].

2.2 Major Symptoms of FM or CFS

Patients with FM or CFS usually present with multiple symptoms that may vary person to person, but almost always include excessive fatigue and severe chronic pain. Fatigue is often persistent, un-explained, of definite onset, and is not alleviated by rest. There is a noticeable decline in activities, tender cervical or axillary lymph nodes, muscle pain, chronic widespread pain (right/left side body, above/below waist, and in axial skeleton), and multi-joint. Pain is measured to determine how severe a patient is in the following areas left and right: shoulder

girdle, upper and lower arm, hip, upper and lower leg, jaw, chest, abdomen, upper and lower back, and neck. On diagnostic measures patients must meet criteria including: widespread pain index (WPI) ≥ 7 and symptom severity (SS) ≥ 5 , symptoms must be of a similar level for 3 months, and the patient must not have a disorder that would otherwise explain pain. Symptoms can also include other ailments such as: sleep disturbance, post-exertional malaise, short-term memory issues, myalgia, mood issues, new headaches, morning stiffness, paresthesia, anxiety, irritable bowel syndrome, temporomandibular joint issues, and neurological symptoms. Symptoms can also be accompanied by decreased thresholds to heat, cold, and electrical stimuli. [5, 6, 11, 13, 15-17, 19, 20] A dysfunction in the central nervous system could possibly explain symptoms of widespread pain and tenderness, and why patients feel more fatigued [18].

2.3 Exercise Prescription

Research evidence has supported the prescription of exercise for patients with FM and that exercise should be gradually increased up to moderate intensities. Aerobic exercise, resistance exercise, strength training, flexibility training, and movement therapies such as qigong, tai chi, and yoga have all shown positive results in the health of patients. [3, 21] Significant improvements have been noted between exercise groups and control groups in FM patients within measurements of fitness, anaerobic function, tender points, muscle strength, pain, fatigue, and symptom severity, supporting the benefits of exercise. [3, 20] Evidence has shown that moderate intensity aerobic exercise and recreational activity can also improve blood pressure, glucose and lipid profiles, without improving cardiovascular fitness [22]. FM patients can improve aerobic and muscular strength while decreasing symptoms and maintaining function in daily activities by monitoring the intensity of the exercise program. Beginning low and

gradually increasing to a moderate intensity and increasing duration have proven to be beneficial and so has strength training when performed in proper progressions for FM. [3, 11, 20, 23] In addition, methods that could limit exercise induced pain in strengthening programs include: (1) minimize eccentric exercise, (2) include pauses between exercise repetitions, and (3) perform exercise for upper extremity muscle groups and lower extremity muscle groups in separate sessions, with at least 1 day of rest between sessions. Specific methods may include: (1) breath, posture, and relaxation training; (2) flexibility; (3) strength and balance; and (4) aerobics allowing patients to develop over time. [3, 24-28]

Prescribing a successful exercise program is not trivial [11]. Success happens as a clinician evaluates many aspects before deciding on the proper exercise treatment, such as; benefits of exercise, type of exercise training or recreational physical activity, psychological considerations, and any adverse effects precautions, supervision, or monitoring that may need to take place for a specific individual [22]. Clinicians prefer to recommend aerobic exercise over eccentric or isometric muscle work, as the last two are likely to increase hyper-excitability of the central nervous system. They follow some suggested principles in prescribing exercise such as: minimizing aggravation of peripheral pain, posture and body alignment work, stretching, minimizing eccentric muscle use, spending ample time in warm-up, cool down, and breathing practices. These principles, supervising, and individualizing the exercise program to each person may be beneficial in the long run as compliance appears to be an issue in this population and one of the main reasons why treatment is difficult. [3, 11, 20, 25]

2.4 Patients Compliance to Physical Exercise

Although physical exercise is commonly pre-scribed or recommended by health professionals, FM patients are usually reluctant to participate in supervised exercise programs and have low adherence to exercise regimens after a structured supervised program [29-33]. For instance after 12 weeks of a combined exercise program only one-third of the participants with FM continued their exercise program during the follow-up period [34]. In a study of aerobic exercise over a 23-week period, the compliance to 90 minutes/week or longer of aerobic exercise was from 38% to 59% [27]. In a 16-week resistance training program 22% of the participants did not complete the program, even though they could receive gifts at 8 and 16 weeks [35]. In a study using aerobic exercise of walking and cycling only 72% of the patients attended over 1/3 of the classes and only 38% of them continued exercising by the 12-month follow up [36]. In a recent Cochrane review on strengthening exercise in patients with fibromyalgia, only one study reported long-term follow up results that the many benefits of the supervised exercise program diminished [37]. The low compliance to self-maintained exercise was suggested to be an important factor for the dissatisfactory long-term outcomes.

Past researchers have reported positive relationships between exercise compliance and maintenance of exercise induced changes [26]. A positive relationship was reported between the maintained gains in a 6-min walking test measured at a 6-month follow up and minutes of continuing aerobic exercise after a 3-month exercise program [38]. Similar correlations were reported at a 1-year follow-up [26]. At four years after an exercise program, those who continued to exercise had maintained exercise-improvements compared to those who stopped exercising [33]. The long-term benefit for physical function and self-efficacy may depend on the compliance with aerobic exercise [26].

Reasons for low compliance with physical exercise given by patients with FM or CFS are primarily increases in sensations of pain, fatigue, and stiffness immediately after exercise, and a fear that exercise may worsen the condition [36]. Women living with FM often claim that symptoms get worse after exercise that previously led to no worsening in symptoms [22]. Such a phenomenon may be partially explained by the fact that patients with FM or CFS have shown in most exercise tests a significantly reduced exercise capacity (VO_2 max, maximal exertion, anaerobic threshold etc.), when compared to sedentary controls [39-42]. Patients prefer to exercise at much lower levels than prescribed, but such low levels can potentially diminish the benefits of physical exercise [28, 43, 44]. Despite the levels of exercise, many patients suffer from post-exertional malaise after exercise and recover at a slower pace [45, 46]. All severe CFS patients and 60% of the less severe patients have reported an aggravation of symptoms after minor exertion [47]. Setting exercise limits has been unable to prevent short-term symptom worsening [44]. Within 24 hours of an exercise test 85% of the controls indicated full recovery, in contrast to none of the CFS patients [48]. The slower rate of “recovery” may be one of the main reasons why FM or CFS patients are reluctant to increase their physical activities over time [49]. Another major reason for the low compliance to physical exercise, especially observed in long-term follow-up, could be due to the fact that a set of key symptoms including pain, fatigue, sleep disorder, etc. would not be sufficiently released through long-term physical exercise as shown in recent literature reviews of aerobic and resistance exercise trials [50, 51]. For instance, there was no improvement in pain levels after 12-week supervised or unsupervised aerobic exercise regimens in 74 patients with FM [32]. Physical exercise may also negatively affect the cognitive functions of patients with FM or CFS [52-54]. Although physical exercise leads to improvement in multiple aspects of one’s health condition, many patients with FM or CFS may

suffer from delayed recovery and symptom worsening when participating in moderate physical exercise in order to maintain their fitness. If key symptoms, such as pain, fatigue, and/or sleep disturbance showed no sign of relief over time, they may then choose to stop the exercise.

2.5 Factors for Low Compliance to Exercise: Psychological

Some FM or CFS patients are willing to do exercise and others are not and in turn their psychological feelings vary and many therapies have been tried in an attempt to improve feelings to exercise. Cognitive behavior therapy (CBT) represents a wide variety of interventions commonly used in the management of chronic pain, with empirical literature supporting it, aimed at decreasing pain and distress as well as increasing social and physical functioning [55, 56]. CBT has been significantly better than other psychological treatments in short-term pain reduction, coping with pain and some Fibromyalgia Impact Questionnaire elements [57, 58]. Short-term improvements have been found and fewer in long-term but they are present as 25% of patients have achieved clinically meaningful long term improvements [59, 60]. Sleep disturbance has also been improved and with all of these facts CBT favorably influences physical function improvement in patients [60, 61]. Additionally within CBT there is acceptance and commitment therapy (ACT), emphasizing the usefulness of acceptance and mindfulness strategies. [55].

Some investigators believe that the fear of symptom worsening and other psychological issues may lead to low compliance to exercise [27, 29, 32, 33, 38]. It has been seen in healthy controls that those using behavioral processes to help regulate their physical activity were more likely to adhere at a level that was clinically meaningful for their health [62]. ACT may help patients with FM in pain-related functioning, FM impact, mental health-related quality of life,

self-efficacy, depression, anxiety, and psychological inflexibility [55]. In a cycling exercise, which included increasing intensity until the individual's target heart rate was achieved, found that mental/physical fatigue and ratings of perceived exertion were higher along with psychological symptoms of anxiety and depression in patients than healthy controls [63]. Patients are usually overwhelmed with perceptions of pain that may blur over time leading to higher levels of pain and reduced tolerances for exercise or activity that may exacerbate the pain. This creates a problem in which patients become less compliant to exercise due to psychological feelings, but physiological aspects could be influencing the psychological.

2.6 Factors for Low Compliance to Exercise: Physiological

2.6.1 Healthy Controls

Studies of exercise-induced changes in physiological processes have shown consistent patterns in healthy adults. These patterns range from increased soreness, delayed onset muscle soreness, increase in force reduction, increase in EMG amplitude, increase in feelings of fatigue, and varying results for biomarkers making usefulness of the values questionable.

Fatigue occurs during activity and is verbalized by a feeling of soreness that has varying recovery rates. In an experiment untrained university students completed 6 sets of 10 maximal voluntary eccentric contractions. Torque decreased immediately after exercise and soreness was confirmed at 24 hours [64]. Healthy sedentary men performed as many reps as possible at 40% of their maximal voluntary contraction of the biceps until voluntary exhaustion for 3 sets which in turn resulted in reduced repetitions per set. Soreness was found to be present for 24 hours and beyond [65]. Becoming accustomed to exercise can reduce soreness as seen in healthy physically active men [66]. Soreness also reduces during recovery in 8 untrained subjects [67].

EMG parameters were found to increase in amplitude, which correlated with soreness found in the torque measurements of fatigue testing. In healthy physically active men electromyography (EMG) was measured 72 hours after the first bout and 1 day and 3 days after the last bout of the 7 days of 6 sets of 15 repetitions of isokinetic eccentric contractions at 60°/s between 20° and 80 ° of knee flexion. A significant increase in amplitude occurred after the 3rd training session when muscle soreness was also present, along with increasing force reduction [66]. Previous investigations reported that fatigue induced exercise increases EMG amplitude, yet that is contradictory to studies finding a decrease or no change in EMG amplitude across repetitions. Changes in EMG during fatigue testing could be due to varying activation strategies, non-maximal effort, or changes in subject motivation with higher exertion levels, making it difficult to relate fatigue to a specific parameter of the EMG measure. [68]

Other measurements of physiological factors for muscle soreness and feelings of fatigue may include some biomarkers, even though their roles are still being debated. Biomarkers are used to objectively measure physiological or pathogenic processes in the body that occur during health, disease or in response to pharmacological treatment. [69] Exercise type and duration are determining factors for the concentrations and types of biomarkers that appear and dictate the rates of recovery of muscle performance and thus how soon a biomarker returns to normal. [69]

Interleukin-6 (IL-6), an inflammatory cytokine, and Creatine Kinase (CK), a muscle enzyme, are two biomarkers that have been studied with their relation to exercise, fatigue, and recovery. IL-6 has been thought to be released during intense or prolonged exercise. A 20min repetitive, low-force exercise performed with dominant arm and hand moving sticks on a peg board has shown IL-6 to increase and have its highest level during the last 10 min of recovery, suggesting that IL-6 may be a systemic response rather than local response [70]. Several studies

have shown increases and decreases due to exercise and recovery phase [71, 72]. The same pattern exists over the course of training, whether resistance training, endurance training, or a combination of the two with IL-6 being increased higher before training than after training.

Intensity and duration of exercise may play a key role in the changes of IL-6 concentration. Fifteen recreationally active males completed 6 weeks of high-intensity interval running 4 times per week with; groups 1 and 2 whom trained twice per day, 2 days per week and group 3 trained once per day for 4 days. For all groups it was found that IL-6 following the protocol was significantly greater before training than after training, showing that IL-6 levels after acute exercise are reduced with training [72]. In a study involving 47 inactive males undergoing resistance training (RT) (3 sets, 10 reps upper/lower body), endurance training (ET) (60min walk/run), or concurrent training (CT) (both) found IL-6 to increase exponentially during and after exercise depending on the type of exercise [73]. Altering intensities of exercise produced different increases in IL-6 concentration after acute exercise from 2 fold up to 20-fold [72, 73].

Creatine kinase is released due to muscle damage from an exercise designed to create fatigue in which an increased elevation at 24 hours is expected and may continue for several days. Untrained university students completing 6 sets of 10 maximal voluntary eccentric contractions, showed delayed onset muscle soreness and after 7 days CK levels were still 25% above baseline [64]. Other studies have reported that CK will be elevated 24 hours post-exercise, but recovery depends on the intensity of the exercise ranging from 72-96 hours [65].

2.6.2 FM or CFS

Studies of FM patients have shown similar patterns to that of controls in soreness, force reduction, and feelings of fatigue. However, patients complete fewer reps, have higher pain ratings that last longer, show fatigue increases on a different scale, while results about some biomarkers are mixed.

It is known that muscle fatigue occurs due to any exercise-induced reduction in the maximal capacity to generate force or power output [74]. In a study that compared responses of cycling exercise between FM patients and healthy controls it was found that fewer patients completed higher watt levels of cycling and their median performance was 92.5W compared to 130W in controls. [75] During an isometric handgrip task at 25% maximal strength for 3min, patients reported a greater intensity of muscle pain which was inversely correlated with the level of physical activity [76].

A plethora of objective markers have been found to not be abnormal in patients vs. controls, however they are abnormal in FM and change in response to symptoms, and could be possible biomarkers [17]. Changes in some biomarkers after aerobic exercise have been inconsistent in literature. An incremental cycling test showed that levels of CK were similar in patient and healthy control groups after exercise. [75, 77] An exercise of 15 minutes stepping on and off a platform induced a slight but significant increase in IL-6 secretion, but the responses of the CFS patients were not different from the controls [78]. However, in a recent study after exhaustive treadmill exercise, FM participants failed to show an expected anti-inflammatory response to exercise and experienced a worsening of symptoms, along with a delayed returning of IL-6 to baseline levels compared to healthy controls [79]. In a long duration exercise study of FM women in an aquatic fitness program, IL-6 levels were increased during the first 4-months,

but after 8-months had decreased with respect to basal measures and 4-month measures [80]. Thus, the responses of the body to dysfunctional stress in patients implies that recovery following exercise is delayed and needs to be further explored [25].

2.7 Significance of Present Work

We planned to evaluate muscle torque, EMG, and rating of perceived exertion among healthy sedentary controls and patients with FM, in an attempt to see if an altered muscle fatigue recovery pattern may exist. In past studies patients with FM or CFS had more fatigue and delayed recovery, even though results of the measured muscle force, EMG, and some biomarkers after exercise were mixed, depending on the type and intensity of exercise. More studies are required on the issue, especially for a specific research question: whether an altered recovery pattern exists in patients with FM or CFS after physical activity or exercise.

Therefore it is clinically important to test a theory of altered recovery after exercise in patients with FM or CFS in order to determine if the type and progression of exercise could be beneficial in keeping patients motivated and compliant to exercise therapy. Patients have frequently reported negative feelings in response to interactions with health care professionals, partially due to the difficulty of seeing positive results or having increased symptoms [22]. A better understanding of the recovery process after exercise may help clinicians in improving therapeutic relationships. Also, there is an importance on individualizing duration and intensity of physical activity to match with an individual's pain and movement capabilities. Simply beginning by addressing poor sleep, mood, and pain with medical therapy, the patient may be more compliant with an exercise program and gain the full benefits [3]. Our study could provide a good insight to clinicians by informing them of an altered recovery pattern.

Chapter 3. Altered Fatigue Recovery in Patients with Fibromyalgia

3.1 Abstract

Introduction: Fibromyalgia (FM) is a challenging disorder to explore and warrants further study.

This study aimed to determine if the recovery process after isometric fatiguing contractions was altered.

Methods: Twelve healthy controls and eleven FM patients, ages 30 – 63 years completed the isometric fatiguing exercise. Day 1 consisted of 18, ten-second contractions with 2 ten-second recovery contractions, followed 24 hours later by 3 ten-second contractions. Measurements of torque, EMG, and perceived exertion were gathered.

Results: The data had a trend towards altered recovery in torque, perceived exertion, and EMG max amplitude existing in study patients while healthy controls recovered better. Healthy controls were less fatigued on day 2, while study patients had data resembling more fatigue on day 2.

Conclusion: Favorable trends were noted for altered recovery supporting the need for further studies with a larger number of participants as we were only able to recruit 12 healthy controls and 11 fibromyalgia patients. A different evaluation of the EMG measures may prove to be more beneficial with torque and fatigue changes. Studies should continue to be done on the recovery issue with various types of exercise and evaluation of the participant's feelings and perceptions of pain.

Keywords: Fibromyalgia (FM), Chronic Fatigue Syndrome (CFS)

3.2 Introduction

Fibromyalgia (FM) is characterized by widespread chronic pain and persistent fatigue occurring across a wide spectrum of people. Approximately 6 million (2-5%) people in the US have FM. Women are more likely to have FM as 80-90% of those diagnosed are women. [4, 6-11] Pain in fibromyalgia is believed by some clinical investigators to result from neurochemical imbalances in the central nervous system that lead to a “central amplification” of pain perceptions [18].

Most symptoms of FM include excessive fatigue and severe chronic pain. Fatigue is often persistent, un-explained, has a definite onset, and is not alleviated by rest. Symptoms often include other ailments such as: sleep disturbance, post-exertional malaise, short-term memory issues, myalgia, mood issues, new headaches, morning stiffness, paresthesia, anxiety, irritable bowel syndrome, temporomandibular joint issues, and neurological symptoms. [5, 6, 11, 13, 15-17, 19, 20] A dysfunction in the central nervous system could possibly explain symptoms of widespread pain and tenderness [18].

Exercise is the most commonly recommended treatment option for FM by healthcare professionals [11]. However, even with attempts to minimize aggravation, and individualizing the exercise program, compliance to exercise prescriptions is low and maintenance of exercise over long periods of time is unlikely. Compliance varies greatly and many women claim that they don't exercise in order to avoid exceeding their physical limits. The common reasons for not attending exercise programs are that pain and stiffness increase after exercise, patients believe exercise simply makes the symptoms worse, and exercise is not beneficial. [22, 36]

Factors contributing to low compliance are believed to be psychological, physiological, or some combination of the two. Past studies have attempted to determine why patients with FM

have negative perceptions of physical activity or exercise, however results vary and are inconclusive [55, 62, 63]. Evidence supports that there may be some type of alteration in the physiological system that can explain why patients do not want to exercise. Studies of cycling have shown that patients did not produce the same level of exercise intensity and were fatigued sooner than sedentary healthy controls [75]. Patients reported greater levels of muscle pain in a simple exercise of maximal isometric handgrip strength [76]. Studies of isometric muscle contractions have reported that patients were not completely recovered in muscle force and EMG 24 hours after exercise within which healthy controls recovered, however a cycling study reported complete recovery in patients and healthy controls [81, 82]. Discrepancies in past findings prompted the need for further research to explore a possible altered recovery pattern in patients with FM.

Our study evaluated muscle torque, EMG, and ratings of perceived exertion immediately and one day after a fatigue test in healthy sedentary controls and patients with FM, in order to determine whether an altered recovery pattern may exist.

3.3 Methods

Participants

A total of eleven patients with FM (10 Females, 1 Male; mean age 51.5 ± 10.2 years) participated in the fatiguing exercise test. Their mean weight was 101.6 ± 20.7 kg and time since diagnosis ranged from 1.5 – 12 years (mean 5.7 ± 4.8 years). The FM patients were all ambulatory and fulfilled the established criteria for fibromyalgia [15, 16]. None of the patients had a history of severe mental illness or any other neurological disability. FM participants were recruited from patients who had previously provided their contact information to our research

team, were seen at the Rheumatology Clinic at the University of Kansas Medical Center (KUMC) outpatient clinic for diagnosis and treatment, or registered in the Heron Database. Patients with a diagnosis of primary FM, based on the 1990 American College of Rheumatology criteria by Wolfe *et al.*, between the ages of 18 and 63 years; willing to remain on current CNS-active therapies (medications) for non-severe depression or others and not add any new ones that are commonly used to treat FM; willing to discontinue treatment with transcutaneous electrical nerve stimulation, biofeedback, tender- and trigger-point injections, acupuncture, and anesthetic or narcotic patches; with a raw score ≥ 4 on physical function component of the Fibromyalgia Impact Questionnaire (FIQ), [83] and a mean visual analog scale (VAS) pain score ≥ 40 on a scale from 0 to 100 were able to be included in the study. Patients who met the criteria for any of the following were excluded from the study: severe psychiatric illness; a current history of severe depression; abuse of alcohol, benzodiazepines, or other drugs; a history of behavior that would prohibit compliance for the duration of the study; active cardiovascular, pulmonary, hepatic, renal, gastrointestinal, or autoimmune disease (except Hashimoto's or Grave's disease that had been stable for 3 months before screening); current systemic infection; active cancer (except basal cell carcinoma); unstable endocrine disease; severe sleep apnea; prostate enlargement or other genitourinary disorder (male patients); or pregnancy or breastfeeding (female patients). (Appendix B – Phone script FM) All participants gave their informed consent as approved by the institutional IRB.

Twelve sedentary healthy controls (7 females, 4 males; mean age 48.3 ± 10.1 years) participated in the fatigue exercise test. The controls had a mean weight of 79.3 ± 16.2 kg. Individuals in the healthy control group were selected from a group of sedentary individuals who did not do physical exercise or exercised at a frequency less than twice a week with a caloric

expenditure below 3 metabolic equivalents of task (METs) [24, 84]. Sedentary controls were chosen in order to be similar to FM patients in regards to the lack of exercise and potentially similar lifestyle. Control participants had no history of neurological or neuromuscular disease. The age range of our healthy control participants reflected the age range of the majority of the patient participants. The specific inclusion criteria included: 1) Age 30-63 years (age range that was recruited), 2) not currently ill, 3) with body mass index (BMI) < 30, 4) living sedentary lifestyle, 5) no apparent medical conditions that would interfere with participation in the study, and 6) not on any medication that would interfere with participation in this study. The exclusion criteria included: 1) medical or surgical conditions including medication that preclude participation in the study and 2) presence of motor or neuromuscular deficits that may preclude participating in the fatiguing exercise. (Appendix A – Phone script Healthy) All participants gave their informed consent as approved by the institutional IRB.

Study Procedure

Fatigue testing was conducted on all patients and healthy controls (Figure 3-1). The participants came to our campus during their testing day 1 and 2 between 9-11am. The participants walked up a slight incline outdoors to our research laboratory for about 10-15 minutes as a warm-up. The participants then sat on the chair of the Biodex System 3 Pro (Biodex Medical Systems, Inc., Shirley, New York) which included a dynamometer used in the experiment. The dynamometer's axis of rotation was lined up with the flexion/extension axis of rotation for the right knee, which was set at a flexion angle of 90°. A Telemyo™ 900 EMG System (U.S.A Inc., Scottsdale, AZ) was used in the experiment. Electrodes were placed in the appropriate locations above the knee to record the EMG signal from the Vastus Medialis (VM),

Rectus Femoris (RF), and Vastus Lateralis (VL) muscles, with the ground electrode placed on the styloid process of the ulna. Data of torque and EMG were recorded at a sampling frequency of 1000Hz. The participant was given instructions about how to complete the fatiguing exercise, which was similar to that of Paul et al., 1999. Briefly, participants were instructed to produce a maximal effort on each of 18 consecutive 10-second knee extension contractions with a 10-second rest between each. Followed by two additional contractions of a 10-second duration at 5-minutes and 30-minutes of the recovery phase. Participants were also shown a ratings of perceived exertion chart (modified Borg scale) and asked to give their rating before and after warm-up, at the 6th, 12th, and 18th contractions, 5-minute recovery and 30-minute recovery.

(Figure 3-1)

On day 2 each participant produced the maximal effort contraction for three 10-second contractions with a 1-minute rest between each. Participants were also shown a ratings of perceived exertion chart (modified Borg scale) and asked to give their rating before and after warm-up, and after each of the 3 contractions. Participants were also asked to rate their pain/soreness on a scale of 0-10 (10 highest) at the end of day 1 and on day 2 before and after exercise. Verbal encouragement was given to the participants on both days during each of the contractions in order to ensure that maximum contractions were obtained. (Appendix C – step-by-step details)

Data Processing

The data of torque and EMG were processed using a lab-made program in Matlab. The raw data was first divided into each 10-second contraction plus 1-second before and after the contraction.

Torque data was filtered using a 2nd order Butterworth filter (cutoff 4Hz), followed by a moving average window of 1-second window width, and then normalized by bodyweight. The maximal torque in each contraction was identified for evaluation. The following parameters were determined; the highest peak torque of 18 contractions (PT18), average max torque of the last three contractions (PT3), average max torque of the two recovery contractions on day 1 (PR1), and average max torque of the three recovery contractions on day 2 (PR2). The following variables were calculated and used in further data analysis: peak torque reduction (ΔT_{peak}) after muscle fatigue defined as PT18 – PT3, with a bigger value representing a greater reduction in torque after fatigue; peak torque recovery at day 1 (ΔT_{r1}) defined as PT18 – PR1 with a smaller value representing better recovery at day 1; peak torque recovery at day 2 (ΔT_{r2}) defined as PT18 – PR2 with a smaller value representing better recovery at day 2.

Torque was further processed to determine a value known as the fatigue index [85]. First the starting point of each contraction was manually selected on the plot of the filtered torque data. The fatigue index was then calculated based on the method developed by Surakka et al., 2005. (Appendix D – adapted equation) The fatigue index parameters were calculated for the time periods of immediately after fatigue (FIa) (small number means fatigue occurred and is at a high level), first day recovery (Fif), and second day recovery (FIs) (both have big numbers recovery is occurring and fatigue is at a low level).

The reported values of a participant's perceived exertion and muscle pain or soreness score were gathered and compared to the torque values or fatigue index values at the time points of the 18th contraction and 3rd contraction on day 2 to determine possible correlations.

EMG was processed first by using a Root Mean Square (RMS) filter on a 1-second window, then filtered through a 2nd degree Butterworth Filter (cutoff 4Hz). The maximal value

of EMG for each of the three muscles (VM, RF, and VL): at each of the contractions was determined. The EMG parameters were calculated for the time periods of immediately after fatigue (EMG_a), first day recovery (EMG_f), and second day recovery (EMG_s). (Results same as torque bigger number for after fatigue and for recoveries small number better)

Other Measurements

Demographic and medical variables: The following demographic variables were collected at baseline phase from each participant: age, gender, height, and weight. The following medical variables were also collected for FM patients: time since diagnosis.

Feasibility Measurements: Ongoing records of recruitment and withdrawals were maintained throughout the study.

Data Analysis

Means and standard deviations were calculated for all study variables mentioned above. We conducted statistical analysis on differences between the FM patients and healthy controls. To compare differences between the two groups in measurements of muscle torque and fatigue index calculated from the time series or muscle torque and three EMG signals from three muscle groups, each measurement produced three variables: the change immediate after fatigue, first day recovery, and second day recovery. The independent t-test with Bonferroni correction for alpha level ($0.05/(5*3) = 0.003$) was used to analyze the difference in each variable between healthy controls and patients with FM. The perceived exhaustion measurement produced 12 variables. Similarly, the independent t-test with Bonferroni correction for alpha level ($0.05/12 = 0.004$) was

used. Power and sample size calculations were done using the following site:

http://www.statisticalsolutions.net/pss_calc.php.

3.4 Results

Comparison between healthy controls and patient group

No significant differences were found between healthy control participants and participants with FM in all three variables of muscle torque (Figure 3-2) and three variables of fatigue index (Figure 3-3). The peak torque recovery day 2 was -0.02 in healthy controls but 0.25 in the patient group ($p = .21$). The peak torque reduction after fatigue, however, was much larger for healthy controls (1.02) than the patient group (0.51) and was the only p value trending in the significant direction (0.05). Both fatigue indexes in the first and second day had relatively large differences between the two groups, but in the opposite direction from the first day to the second day. The healthy controls had a smaller recovery mean value (14.93) compared to the patient group (20.50) in the first day ($p = 0.14$), but a larger recovery value (18.45) than the patient group (14.28) in the second day ($p = 0.16$). Those trends may have indicated a potential significance if the study had a larger sample size: torque day 2 (power - .06/sample size 126), torque after fatigue (power - .69/sample size 28), fatigue index day 1 (power - .55/sample size 35), and fatigue index day 2 (power - .18/sample size 80).

(Figure 3-2, Figure 3-3)

There was a significant difference ($p < 0.004$) between healthy control participants and participants with FM in pain score immediately after fatigue test in the first day of the experiment (Table 3-1). Four variables showed a large difference in the mean value between the two groups along with relatively small p values ($p = 0.02 - 0.06$): Day1 – warm-up, contraction 6,

Day2 – warm-up, and pain/sore. In such cases, a trend towards significance was observed. Significant differences may have been present in those variables if the study had a larger sample size: pain on day 1 had a power of 1, with some others above .80 and the rest were one at .62 and then .19 below requiring 100 people for good power. All of the rest of the values of ratings of perceived exertion were not significant.

(Table 3-1)

There were no significant differences in EMG variables between healthy control participants and participants with FM for the VM muscle (Figure 3-4: Recovery (EMGf & EMGs) with a small number shows recovery and a large number on decrease after fatigue (EMGa) represents more fatigue. The alpha value for a significance was set at $p < .003$ Figure 3-4), RF muscle (Figure 3-5), and VL muscle (Figure 3-6). Although not statistically significant, some variables showed large differences in mean values between the two groups along with relatively small p values: VM peak recovery day 1 ($p = 0.07$), VM peak recovery day 2 ($p = 0.14$), RF peak recovery day 1 ($p = 0.10$), VL peak recovery day 1 ($p = 0.04$), and VL peak recovery day 2 ($p = 0.16$). In those cases, a trend towards significance was observed. Those trends may have been statistically significant if the study had a larger sample size: EMG had one with power .83 for VL day 1 and the rest had power .38 and lower and sample size of 33 – 180 and upwards over 1000.

(Figure 3-4, Figure 3-5, Figure 3-6)

3.5 Discussion

Evaluation of the peak torque among patients with FM has shown that recovery in the second day may be different from healthy controls. As healthy controls appeared to be able to reach a full recovery in peak torque day 2, while FM patients did not. Although the difference was only approaching significance in our data, the trend towards a significant difference was

clear and with an increased sample size in a future study, a significant difference would be expected. This finding agrees with that of a very similar study that found based on maximal torque across contractions that patients did not recover a day later to the full baseline torque [82]. The differences between healthy controls and patients brought about speculation of an altered recovery pattern in the patient population. Past studies have shown that healthy adults have decreased muscle torque measures immediately after fatiguing exercise. The muscle soreness appeared a day later, and upon becoming accustomed to exercise the amount of soreness can be reduced. [64-67] Patients with FM have been reported to have a similar response after fatiguing exercise, however patients completed fewer repetitions and achieved lower outputs that were inversely correlated with their activity levels [75, 76].

Values of the fatigue index, an indirect measure of fatigue calculated from objective measurements of muscle torque, showed no significant differences between the two groups. However, healthy controls appeared to have higher residual fatigue on day 1, while having less fatigue and thus better recovery on day 2. It seemed that a larger decrease in muscle torque was associated with a higher fatigue index. The healthy controls in the current study were those with a low activity life style. They were the most similar in the amount of physical activity as compared to patient participants, while recovering better after fatiguing exercise, just as other healthy controls in past studies [66, 67]. However, the findings of our study that patients were unable to recover to their baseline and were different from the controls suggested an altered recovery pattern.

Muscle EMG signals had different patterns between the two groups for peak EMG day 2. The RF muscle showed patterns that agreed with past findings that increases in muscle torque and fatigue index were associated with soreness in fatigue testing [66]. However, the VM and

VL muscles didn't show the same pattern, instead there was a decrease or no change in the EMG signal similar to another study [68]. We only examined the peak amplitude of the EMG signal, which may not be a good measure of the median frequency or muscle fatigue. The relationship between muscle fatigue and EMG amplitude can be rather complicated as changes could be due to varying activation strategies, non-maximal effort, or changes in the participant's motivation with higher exertion levels, making it hard to pick a specific EMG parameter to relate to fatigue [68]. In addition, there are three muscles involved in the experimental fatiguing exercise, which further complicates the problem of measuring muscle fatigue.

Participant's ratings of perceived exertion on both days after warm-up showed a trend towards elevation in patients versus the healthy controls. Patients appeared to feel higher fatigue levels after warm-up because of their FM conditions. Healthy controls were more exhausted at the time of the 6th contraction, suggesting that they might be making more effort than the patients. Pain scores after fatigue exercise were significantly higher in the patient group than the healthy controls with a similar trend on day 2. The results correlated with those of a previous study in which patients had higher mental and physical fatigue along with ratings of perceived exertion. The FM condition creates overwhelming perceptions of pain and reduced exercise tolerance [63]. Thus there might be an altered recovery pattern as pain was higher by day 2.

3.6 Conclusion

We were only able to recruit 12 healthy controls and 11 FM patients within the time frame of the current study, which lead to insufficient statistical power. The trends towards an altered recovery in torque and fatigue index measures between controls and patients may be true, but would be better confirmed with a larger population. A different evaluation of the EMG

measures may prove more beneficial in order to be compared with torque and fatigue changes, in future research. Future studies should continue on the recovery issue and evaluation of various types of exercise on the recovery process along with a participant's feelings and perceptions of fatigue and pain.

3.7 Figures and Tables



Figure 3-1: Set-up of the Biodex and EMG on a subject

Changes in Peak Torque

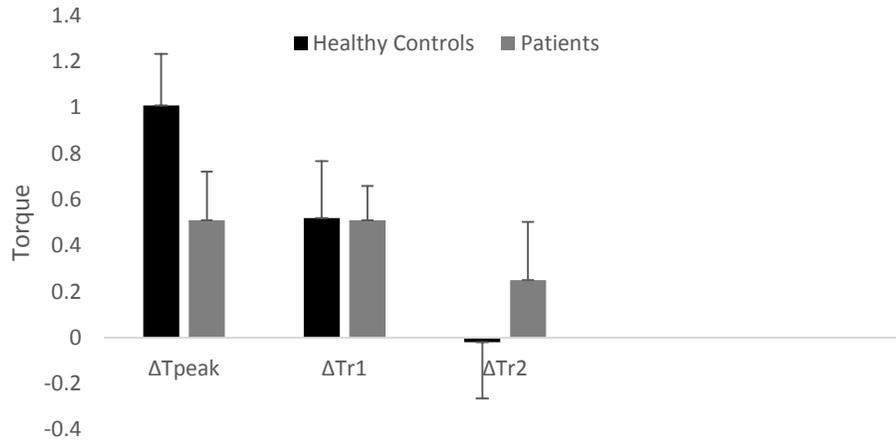


Figure 3-2: Smaller numbers on $\Delta Tr1$ and $\Delta Tr2$ show good recovery and a larger number on ΔT_{peak} shows that more fatigue occurred. The alpha value for significance was set at $p < .003$

Changes in Fatigue Index Values

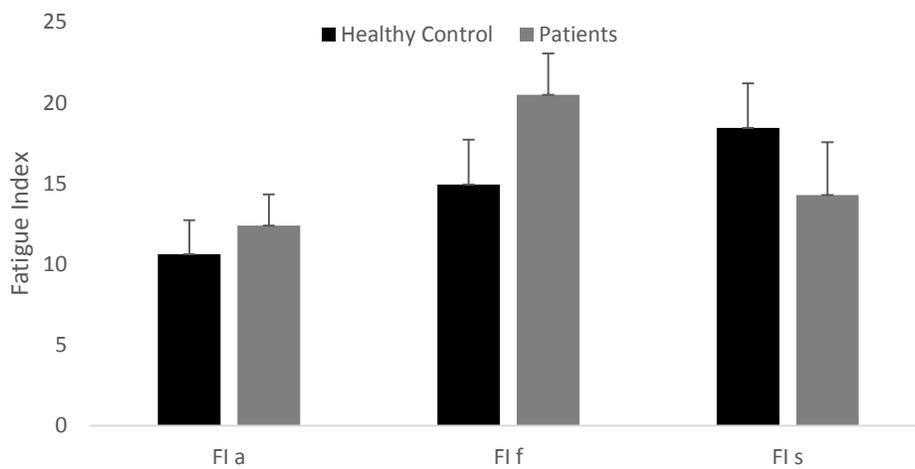


Figure 3-3: Large numbers on FI f and FI s show that recovery occurs as fatigue is reduced and a small number on FI a shows that more fatigue occurred due to the contractions. The alpha value for a significance was set at $p < .003$

Ratings of Perceived Exertion

	Healthy Control	Patients	P-value
Day 1 – Warm-up	2.38 ± 1.19	4.00 ± 2.49	.02
Contraction 6	3.75 ± 1.50	2.63 ± 1.34	.03
Contraction 12	4.42 ± 1.69	3.95 ± 2.32	.29
Contraction 18	4.75 ± 1.56	4.68 ± 2.94	.94
Recovery 5	2.17 ± 1.19	2.68 ± 2.02	.22
Recovery 30	1.0 ± 1.28	1.73 ± 2.20	.17
Pain/Sore	0.25 ± 0.62	3.32 ± 3.12	.002*
Day 2 – Warm-up	1.83 ± 1.05	2.72 ± 1.62	.06
Contraction 1	1.08 ± 1.10	1.45 ± 1.13	.22
Contraction 2	1.04 ± 0.96	1.36 ± 1.02	.73
Contraction 3	1.13 ± 0.98	1.27 ± 1.01	.73
Pain/Sore	0.58 ± 1.44	2.41 ± 2.84	.03

Table 3-1: Scores on a scale of 1-10, significant values * (p<.004)

Changes in Peak EMG – Vastus Medialis (VM)

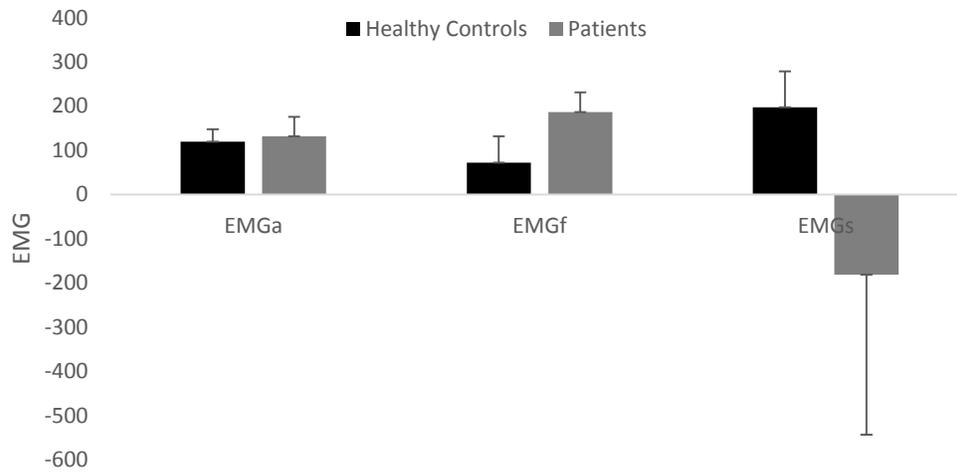


Figure 3-4: Recovery (EMG_f & EMG_s) with a small number shows recovery and a large number on decrease after fatigue (EMG_a) represents more fatigue. The alpha value for a significance was set at $p < .003$

Changes in Peak EMG – Rectus Femoris (RF)

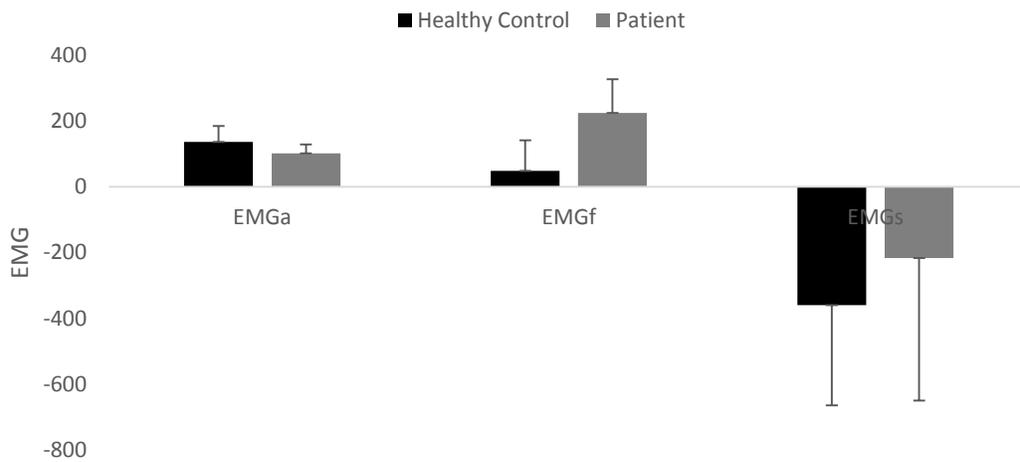


Figure 3-5: Recovery (EMG_f & EMG_s) with a small number shows recovery and a large number on decrease after fatigue (EMG_a) represents more fatigue. The alpha value for a significance was set at $p < .003$

Changes in Peak EMG – Vastus Lateralis (VL)

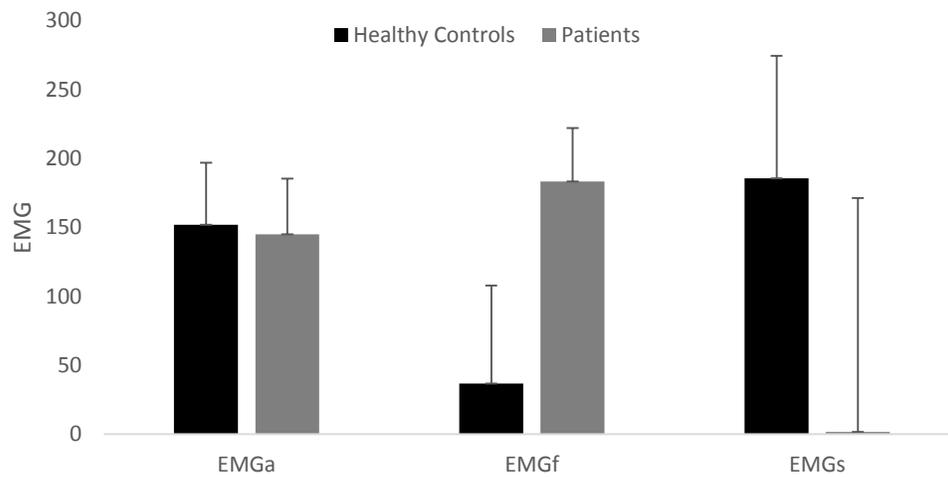


Figure 3-6: Recovery (EMGf & EMGs) with a small number shows recovery and a large number on decrease after fatigue (EMGa) represents more fatigue. The alpha value for significance was set at $p < .003$

Chapter 4. A pilot study of a mind body intervention

4.1 Introduction

Fibromyalgia (FM) is characterized by widespread chronic pain and persistent fatigue occurring across a wide spectrum of people. Approximately 6 million (2-5%) people in the US have FM. Women are more likely to have FM as 80-90% of those diagnosed are women. [4, 6-11] Pain in fibromyalgia is believed by the some clinical investigators to result from neurochemical imbalances in the central nervous system that lead to a “central amplification” of pain perceptions [18].

Animal studies have shown that animals reacted significantly to non-nociceptive stress and such reactions over time result in a higher level of pain, fatigue, and other behavioral alterations. [86-89] Chronic pain can create a higher corticosteroid level and an increased incidence of anxiety and depression among animals [90]. Meditation/relaxation has been shown to release stress, reduce anxiety, and improve psychological well-being. Qigong exercise, one type of meditation therapy rooted in traditional Chinese medicine, has been used in practicing meditation and shown benefits on psychological and physiological issues including pain, fatigue, and sleep disturbance. [91, 92] Several studies have shown promising outcomes of Qigong exercise in patients with FM alone, or combined with acupuncture and/or yoga [93-95]. A possible benefit of Qigong exercise in patients with FM may lie in restoring normal recovery patterns after fatiguing exercise, but no studies have explored this possibility.

4.2 Methods

Participants – FM Patients

Out of 13 FM patients who participated in the study mentioned in Chapter 2, six of them participated in this study (6 females; mean age 50.8 ± 10.9 years, mean body weight 103.2 ± 5.6 kg, mean FM history range 4.7 ± 4.3 years). They were all ambulatory and fulfilled established criteria for fibromyalgia [15, 16]. None of the patients had a history of severe mental illness or any other neurological disability. All participants gave their informed consent as approved by the institutional IRB.

Study participants were recruited from patients who had previously provided their contact information to our research team, were seen at the Rheumatology Clinic at the University of Kansas Medical Center (KUMC) outpatient clinics for diagnosis and treatment, or registered in the Heron Database. Patients with a diagnosis of primary FM, based on the 1990 American College of Rheumatology criteria by Wolfe *et al.*, between the ages of 18 and 63 years; willing to remain on current CNS-active therapies (medications) for non-severe depression and other issues and not add any new ones that are commonly used to treat FM; willing to discontinue treatment with transcutaneous electrical nerve stimulation, biofeedback, tender- and trigger-point injections, acupuncture, and anesthetic or narcotic patches; with a raw score ≥ 4 on physical function component of the Fibromyalgia Impact Questionnaire (FIQ), [83] and a mean visual analog scale (VAS) pain score ≥ 40 on a scale from 0 to 100 were able to be included in the study. Patients who met the criteria for any of the following were excluded from the study: severe psychiatric illness; a current history of severe depression; abuse of alcohol, benzodiazepines, or other drugs; a history of behavior that would prohibit compliance for the duration of the study; active cardiovascular, pulmonary, hepatic, renal, gastrointestinal, or autoimmune disease (except Hashimoto's or Grave's disease that had been stable for 3 months before screening); current systemic infection; active cancer (except basal cell carcinoma);

unstable endocrine disease; severe sleep apnea; prostate enlargement or other genitourinary disorder (male patients); or pregnancy or breastfeeding (female patients). (Appendix B – Phone script FM)

Measurement of Recovery after Fatiguing Exercise

There was 1-2 weeks allowed for the collection of the fatiguing exercise measures, 8 weeks for intervention of Qigong, and 1-2 weeks for end of intervention assessment including fatiguing exercise. There was a control group and an intervention group among the patients, in which both groups completed the same fatiguing exercise protocol and had different interventions (Sham Qigong or Qigong).

Fatigue testing was conducted on all patient participants in both groups (Figure 4-1). A participant came to our campus during their testing day 1 and 2 between 9-11am. The participant walked up a slight incline outdoors to our research laboratory for about 10-15 minutes as a warm-up. The participant then sat on the chair of the Biodex System 3 Pro (Biodex Medical Systems, Inc., Shirley, New York) which included a dynamometer used in the experiment. The dynamometer's axis of rotation was lined up with the flexion/extension axis of rotation for the right knee, which was set at a flexion angle of 90°. A Telemyo™ 900 EMG System (U.S.A Inc., Scottsdale, AZ) was used in the experiment. Electrodes were placed in the appropriate locations above the knee to record the EMG signal from the Vastus Medialis (VM), Rectus Femoris (RF), and Vastus Lateralis (VL) muscles, with the ground electrode placed on the styloid process of the ulna. Data of torque and EMG were recorded at a sampling frequency of 1000Hz. The participant was given instructions about how to complete the fatiguing exercise, which was similar to that of Paul et al., 1999. Briefly, participants were instructed to produce a maximal

effort on each of 18 consecutive 10-second knee extension contractions with a 10-second rest between each. Followed by two additional contractions of a 10-second duration at 5-minutes and 30-minutes of the recovery phase. Participants were also shown a ratings of perceived exertion chart (modified Borg scale) and asked to give their rating before and after warm-up, at the 6th, 12th, and 18th contractions, 5-minute recovery and 30-minute recovery.

(Figure 4-1)

On day 2 each participant produced the maximal effort contraction for three 10-second contractions with a 1-minute rest between each. Participants were also shown a ratings of perceived exertion chart (modified Borg scale) and asked to give their rating before and after warm-up, and after each of the 3 contractions. Participants were also asked to rate their pain/soreness on a scale of 0-10 (10 highest) at the end of day 1 and on day 2 before and after exercise. Verbal encouragement was given to the participants on both days during each of the contractions in order to ensure that maximum contractions were obtained. (Appendix C – step-by-step details)

Data Processing

The data of torque and EMG were processed using a lab-made program in Matlab. The raw data was first divided into each 10 second contraction plus 1 second before and after the contraction.

Torque data was filtered using a 2nd order Butterworth filter (cutoff 4Hz), followed by a moving average window of 1-second window width, and then normalized by bodyweight. The maximal torque in each contraction was identified for evaluation. The following parameters were determined; the highest peak torque of 18 contractions (PT18), average max torque of the

last three contractions (PT3), average max torque of the two recovery contractions on day 1 (PR1), and average max torque of the three recovery contractions on day 2 (PR2). The following variables were calculated and used in further data analysis: peak torque reduction (ΔT_{peak}) after muscle fatigue defined as PT18 – PT3, with a bigger value representing a greater reduction in torque after fatigue; peak torque recovery at day 1 (ΔT_{r1}) defined as PT18 – PR1 with a smaller value representing better recovery at day 1; peak torque recovery at day 2 (ΔT_{r2}) defined as PT18 – PR2 with a smaller value representing better recovery at day 2.

Torque was further processed to determine a value known as the fatigue index [85]. First the starting point of each contraction was manually selected on the plot of the filtered torque data. The fatigue index was then calculated based on the method developed by Surakka et al., 2005. (Appendix D – adapted equation) The fatigue index parameters were calculated for the time periods of immediately after fatigue (FIa) (small number means fatigue occurred and is at a high level), first day recovery (FIf), and second day recovery (FIs) (both have big numbers recovery is occurring and fatigue is at a low level).

The reported values of a participant's perceived exertion and muscle pain or soreness score were gathered and compared to the torque values or fatigue index values at the time points of the 18th contraction and 3rd contraction on day 2 to determine possible correlations.

EMG was processed first by using a Root Mean Square (RMS) filter on a 1-second window, then filtered through a 2nd degree Butterworth Filter (cutoff 4Hz). The maximal value of EMG for each of the three muscles (VM, RF, and VL): at each of the contractions was determined. The EMG parameters were calculated for the time periods of immediately after fatigue (EMGa), first day recovery (EMGf), and second day recovery (EMGs). (Results same as torque bigger number for after fatigue and for recoveries small number better)

Data Analysis

Means and standard deviations were calculated for all study variables mentioned above. We conducted statistical analysis on the differences between FM patients and healthy controls. Three variables; immediate after fatigue, first day recovery, and second day recovery, were used in data analysis for muscle torque, fatigue index, and each of the three EMG signals.

Intervention

The control group of patients completed two training sessions for Sham Qigong that included the same body movements as the Qigong group, but did not include the meditation and breathing control that was associated with it. They were simply instructed to breathe in and out during the same parts of the movements, complete the exercise twice daily at home, once in the morning and in the evening, and participate in the group session once a week. The participants in the intervention group completed two training sessions for Qigong during the baseline phase, weekly group exercise sessions once per week, and daily home exercises two times each day, morning and evening, during the intervention phase. An experienced Qigong exercise instructor provided the training sessions for a specific Qigong exercise, “Six Healing Sound” Qigong, and led the group exercise sessions. (Appendix E – Steps Qigong)

The subjects were asked at weekly group meetings to turn in daily recordings of their Sham Qigong/Qigong exercise in the past week. The participants were encouraged to maintain their compliance to the program. The participants were given a list of all of the days that they were required to come to KUMC for the group sessions and instructed to call if they would be missing a session. At group sessions participants were led through their respective Sham Qigong

or Qigong and then discussions took place on articles and topics that the participants were interested in related to FM. (Appendix G – Articles for discussion intervention patients)

Other Outcome Measurements

Demographic and medical variables: The following demographic variables were collected at baseline phase from each participant: age, gender, height, and weight. The following medical variables were also collected: time since diagnosis.

Diary: Each participant in both groups were asked to keep a diary every morning. The diary recorded the morning and evening Sham Qigong/Qigong exercise completions.

Feasibility Measurements: Ongoing records of recruitment and withdrawals were maintained throughout the study. Self-reported Qigong exercise and information on the participant's attendance to group Sham Qigong/Qigong exercise was recorded daily by participants in the diary. The following measurements were conducted in the baseline phase and at the end of the 8-week intervention phase for all participants.

Clinical Pain: Measured by using the Short Form McGill Pain Questionnaire (SF-MPQ) [96]. The questionnaire has been extensively validated and contains 15 pain adjectives. A sensory score was obtained by summing 11 of the items, an affective score was obtained by summing the remaining 4 items, and a total score was obtained by summing all of the items.

Evoked Pressure Pain: Evaluated by use of dolorimetry, also known as tender point testing.

This was used before the fatiguing test and then after the intervention before the fatiguing test, as to eliminate measuring pain due to the fatiguing test. Pressure pain threshold was defined as the minimum force applied which induces pain. Mechanical pressure, determined as kilogram [97] per 1 cm² of skin on the sensitive areas, as applied by the Fisher's hand dolorimeter. The examiner places the rubber tip on the examination site and gradually increases the pressure at a rate of approximately 1 kg/cm² per second. Participants were instructed to say "yes" when the sensation of pressure changed to one of pain and the pain pressure threshold was recorded. Pain threshold was measured in the 18 points specified by the ACR [15] according to Okifuji instructions [98]. In this study, the tested points were considered as tender when a painful or unpleasant sensation was triggered with a pressure 2.6kg/cm². This value is equivalent to 4.0 kg/cm² described by Wolfe et al (1990) for the Fischer dolorimeter, as shown previously [99]. We also applied pressure to the thumbnail and measured the pressure needed for discomfort and that for pain.

Fatigue: The level of fatigue was measured using the Multidimensional Fatigue Inventory (MFI) which consisted of the following five dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Items were answered in a 5-point Likert scale, Smets et al, 1995 & 1996.

Fibromyalgia Impact Questionnaire (FIQ): Developed in the late 1980's in an attempt to capture the total spectrum of problems related to FM and the responses to therapy. It has been shown to have a credible construct, validity, reliable test-retest characteristics and a good sensitivity in

demonstrating therapeutic change. The original questionnaire was modified in 1997 and 2002, to reflect ongoing experience with the instrument and to clarify the scoring system. The latest version of the FIQ can be found at the web site of the Oregon Fibromyalgia Foundation (www.myalgia.com/FIQ/FIQ).

Health Assessment: The health pattern and its problems were assessed using the General Health section of MOS (SF-36 Questionnaire) (distributed by RAND, Santa Monica, CA). The questionnaire addressed activity and feelings.

Sleep Quality: The Pittsburgh Sleep Quality Index (PSQI) was developed by Dr. Daniel J. Buysse and coworkers at the University of Pittsburgh's Western Psychiatric Institute and Clinic in the late 1980's. It consisted on 19 individual items which were used to generate seven composite scores. The 7 categories included: subjective sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

Depression: The Geriatric Depression Scale (Short Form) was used to assess the level of depression found within a participant before and after intervention. Scores that were greater than 5 were suggestive of depression and greater than 10 considered to almost always be depression.

Anxiety: The Geriatric Anxiety Scale – Version 2.0 was used to evaluate anxiety levels [100]. Items 1-25 were scored and a sum of somatic, cognitive, and affective anxiety were found along with the total. The final five items could be used to address areas of concern for the respondent.

A comparison was done between the before and after sum of the questionnaires, adherence to exercise morning and night, and group attendance were done for the two groups of patients in the study, control and intervention. (Appendix F – FM Questionnaires)

Data Analysis

The data analysis for the study was focused on the trends between comparing mean values of changes in scores between the patient control and intervention groups. Due to a limited sample size (n=3 in each group), no statistical analysis was conducted.

4.3 Results

Comparisons between the patient control (Sham Qigong) group and the intervention (Qigong) group

Due to limited sample size, there was no statistical analysis on any variables for differences between the patient control and intervention group. We compared the two groups by examining the mean values. The intervention group showed reduced value in muscle torque on the first day of recovery, but not on the second day recovery (Figure 4-2). No reduction in the control group were found in the recovery values in both days. The decrease after fatigue saw higher values for both groups after the intervention, representing higher levels of fatigue after the intervention. The fatigue indexes during recovery were slightly improved for controls after the Sham Qigong intervention on day 1 and after the Qigong intervention for the intervention group on day 2. Participants were more fatigued in the final category decrease after fatigue (Figure 4-3). After the intervention both groups of participants showed a reduction in decrease after fatigue representing that more fatigue occurred.

(Figure 4-2, Figure 4-3)

The control and intervention group both had higher ratings of perceived exertion at all contraction time points after the intervention (Table 4-1). During warm-up controls showed reduced exertion after intervention while the intervention group had no changes. Both groups showed reduction after the intervention in the level of pain that they had on days 1 and 2.

(Table 4-1)

The first and second day recovery had a smaller difference in EMG variables over all of the muscles after the intervention for the control group, while the intervention group had a larger difference over all muscles representing reduced recovery. The decrease after fatigue had higher differences in both groups after intervention for all muscles, except the VL in the control group (Figure 4-4, Figure 4-5, Figure 4-6).

(Figure 4-4, Figure 4-5, Figure 4-6)

(See Appendix G - for plots of the three variables for torque and fatigue index for each of the participants)

Clinical Questionnaires:

The intervention group had improvements in fatigue, FM impact, sleep quality, anxiety, and SF-36 (general health) (Table 4-2). The control group had improvements within pain threshold tolerance, McGill Pain, and depression (Table 4-2). In the compliance to attendance at group sessions and to exercise the controls had higher group attendance, while the intervention group was more active on completing exercise at home day and night (Table 4-2).

(Table 4-2)

4.4 Discussion

The goal of our study was to gather pilot data for a comparison between patients in a control-Sham Qigong and intervention-Qigong group exercise. Our results found that Qigong exercise may have an effect on an FM patient's recovery patterns after fatiguing exercise. Peak torque values decreased after the intervention on day 1 recovery implying recovery improvement among the intervention group. The control group had peak torque values increasing in both days after the intervention period implying that recovery was worse. Patients were reported to not recover fully compared to healthy controls, but in the current study, after the intervention there is a trend that patients were able to recover [82]. EMG values had an opposing trend as the control group showed recovery across all three muscles and the intervention group did not. This does not match with the torque results, but matches findings in studies on healthy controls without intervention where results support both findings of matching and not matching torque results [66, 68].

Values for fatigue index in the intervention and control group showed increases in fatigue for day 1 recovery and day 2 recovery respectively, implying that recovery declined. Immediately after fatigue both groups had an increase in fatigue, which did agree with the changes in torque. Ratings of perceived exertion were about the same before and after intervention for the intervention group while the control group experienced increases after the intervention. However, pain scores were found to be reduced after the intervention in both groups on days 1 and 2, implying that both Sham Qigong and Qigong interventions may help relieve pain to some extent or that neither are clinically significant and resulted from a placebo effect. As the intervention may have helped to reduce the overwhelming perception of pain that

patients have and thus Qigong may have some effect on recovery patterns, but the issue needs to be further studied.

The benefits of Qigong exercise were further supported by the improvements of one group or the other on the questionnaires that were done before and after the intervention. The intervention group saw improvements in feelings of fatigue, FM impact of daily activities, sleep quality, feeling of anxiety, and even changes in evaluation of general health. The control group had improvements in the remaining three questionnaires of pain threshold tolerance, types of pain feelings, and feelings of depression. Qigong has been found to show benefits in psychological and physiological issues including pain, fatigue, sleep disturbance, anxiety, and stress supporting the results found in the intervention group [91, 92]. Promising outcomes have been shown in this study on many variables and found with Qigong alone or combined with acupuncture and/or yoga [93-95]. Qigong may have benefits for restoring normal recovery patterns after fatiguing exercise in FM, but further research with a larger population needs to be done.

4.5 Figures and Tables



Figure 4-1: Set-up of Biodex and EMG on a subject

Changes in Peak Torque

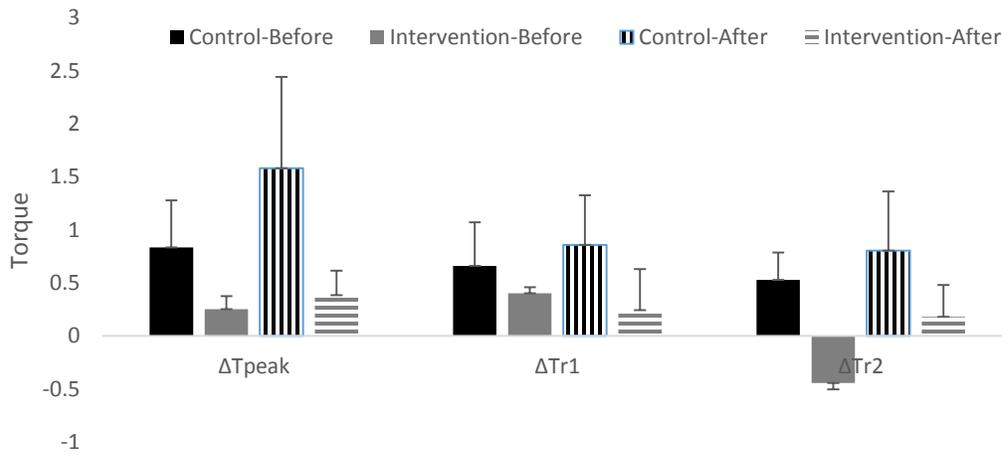


Figure 4-2: Recovery ($\Delta Tr1$ & $\Delta Tr2$) with a small number shows recovery and a large number in decrease after fatigue (ΔT_{peak}) represents more fatigue

Changes in Fatigue Index Values

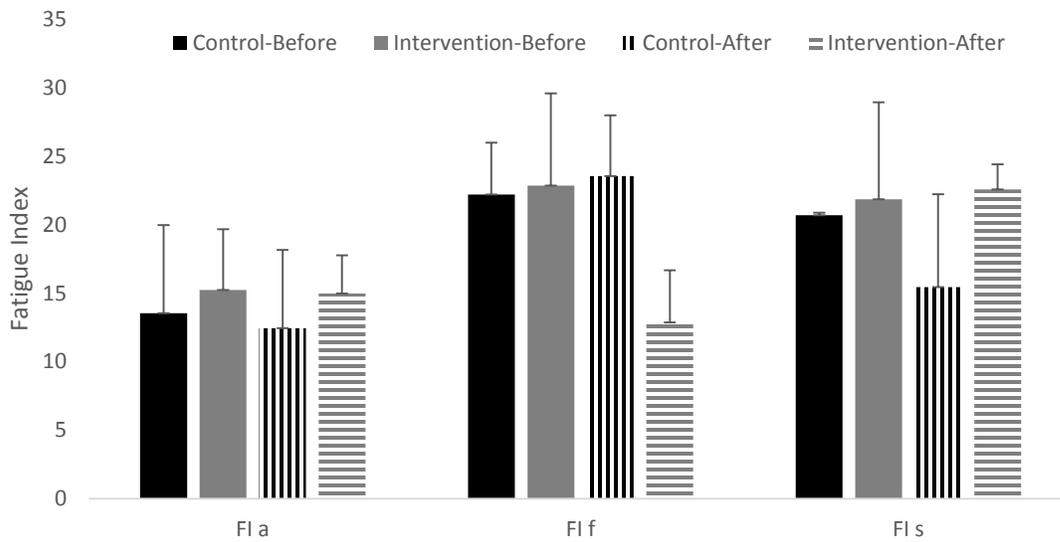


Figure 4-3: Recovery (FI f & FI s) with a large number shows that recovery occurs and a small number in decrease after fatigue (FI a) represents more fatigue

Rating of Perceived Exertion (RPE)

	<i>Control</i>		<i>Intervention</i>	
	Before	After	Before	After
<i>Day 1-Warm-up</i>	3.00 ± 1.00	2.33 ± 0.58	3.00 ± 2.00	3.00 ± 1.73
<i>Contraction 6</i>	1.83 ± 1.04	4.67 ± 0.58	1.50 ± 0.50	3.17 ± 1.04
<i>Contraction 12</i>	3.17 ± 1.76	5.33 ± 0.58	2.00 ± 0.87	4.50 ± 1.50
<i>Contraction 18</i>	3.83 ± 2.84	6.00 ± 1.73	2.33 ± 1.44	5.00 ± 2.00
<i>Recovery 5</i>	1.50 ± 1.32	3.00 ± 1.00	1.50 ± 0.50	2.67 ± 1.53
<i>Recovery 30</i>	1.33 ± 1.53	2.33 ± 0.58	1.00 ± 1.00	2.33 ± 1.15
<i>Pain/Sore</i>	4.00 ± 3.61	3.33 ± 2.89	0.83 ± 1.44	0.67 ± 1.15
<i>Day 2-Warm-up</i>	3.00 ± 1.00	1.33 ± 0.58	2.00 ± 1.00	2.00 ± 1.00
<i>Contraction 1</i>	1.33 ± 0.58	4.00 ± 2.65	1.67 ± 1.15	1.67 ± 1.15
<i>Contraction 2</i>	1.33 ± 0.58	2.67 ± 1.53	1.33 ± 0.58	1.67 ± 1.15
<i>Contraction 3</i>	1.33 ± 0.58	1.33 ± 0.58	1.00 ± 0.00	1.67 ± 1.15
<i>Pain/Sore</i>	4.33 ± 2.08	0.33 ± 0.58	0.33 ± 0.58	0.00 ± 0.00

Table 4-1: Values given on a scale of 1-10

Changes in Peak EMG – Vastus Medialis - VM

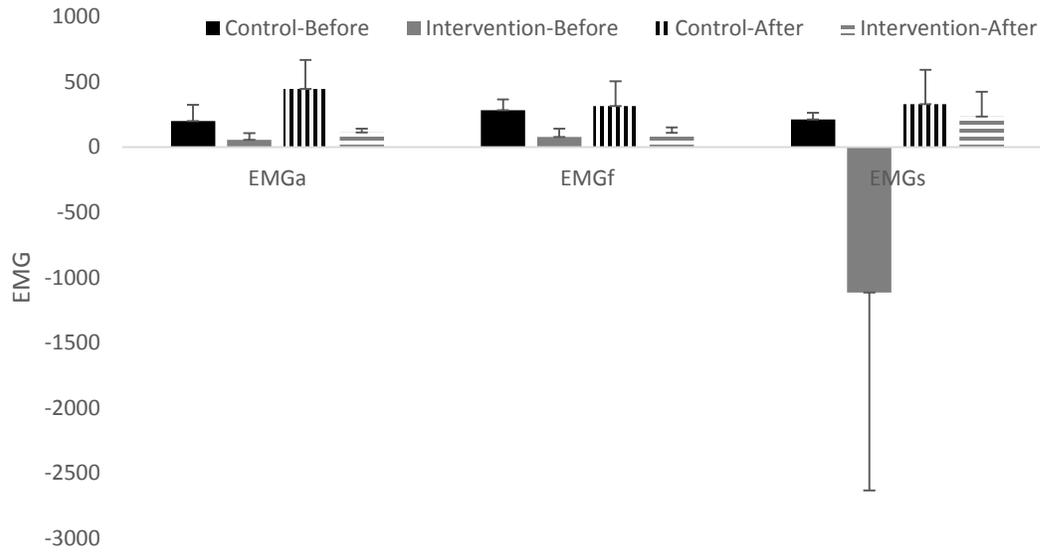


Figure 4-4: Recovery (EMGf & EMGs) with a small number shows recovery and a large number on decrease after fatigue (EMGa) represents more fatigue

Changes in Peak EMG – Rectus Femoris - RF

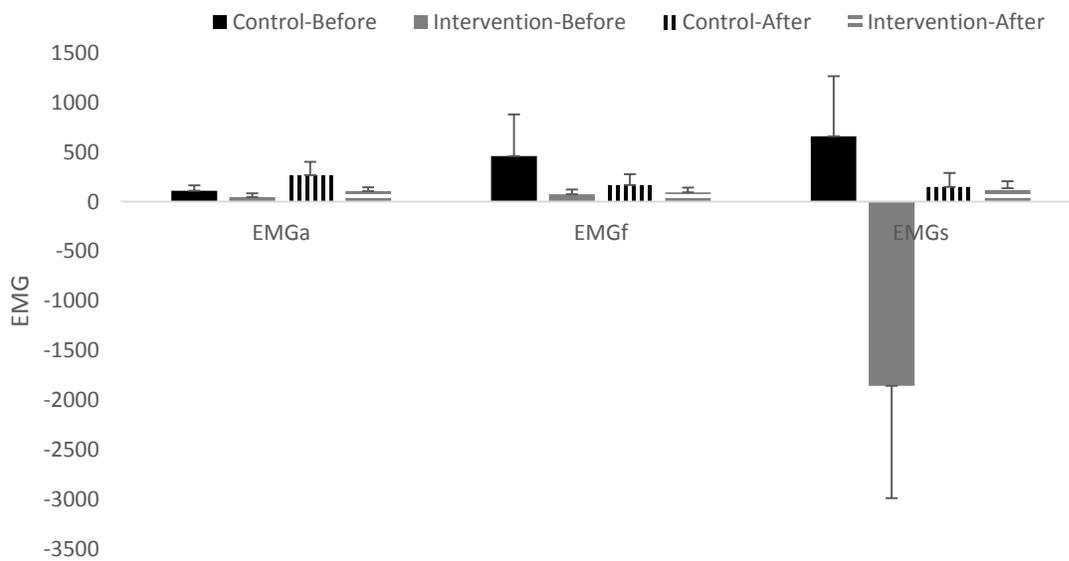


Figure 4-5: Recovery (EMGf & EMGs) with a small number shows recovery and a large number on decrease after fatigue (EMGa) represents more fatigue

Changes in Peak EMG – Vastus Lateralis - VL

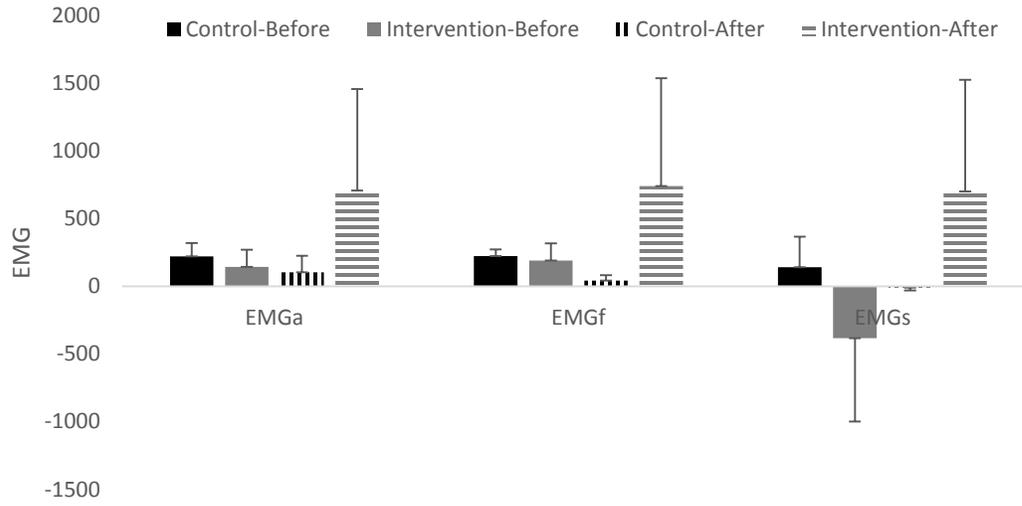


Figure 4-6: Recovery (EMGf & EMGs) with a small number shows recovery and a large number on decrease after fatigue (EMGa) represents more fatigue

Clinical Questionnaires

	Control		Intervention	
	Before	After	Before	After
1. Tender Point Pain Threshold	111.07 ± 41.95	135.42 ± 58.42	94.72 ± 41.21	94.33 ± 33.04
2. McGill Pain	16.0 ± 6.24	13.33 ± 5.86	20.0 ± 9.64	19.67 ± 2.33
3. Fatigue	81.0 ± 6.08	82.83 ± 4.25	76.0 ± 18.33	69.33 ± 15.94
4. FM Impact	65.91 ± 7.54	66.42 ± 11.92	62.48 ± 15.60	50.26 ± 10.72
5. Pittsburgh Sleep Quality Index	11.0 ± 3.0	13.0 ± 5.57	12.33 ± 3.06	11.0 ± 5.0
6. Geriatric Depression Scale	6.0 ± 1.73	3.67 ± 1.53	7.67 ± 6.50	6.0 ± 4.36
7. Geriatric Anxiety Scale 2.0	26.33 ± 7.51	27.33 ± 2.89	35.25 ± 17.05	27.67 ± 3.79
8. SF-36	95.0 ± 2.0	94.67 ± 2.08	90.83 ± 5.25	100.67 ± 6.66
9. Diary %Exercise (day/night)	Over the Intervention 43 / 42		Over the Intervention 65 / 50	
10. Diary %Attendance at Group	Over the Intervention 81		Over the Intervention 67	

Table 4-2: 1. Testing with pressure device in kg, 2. Pain experience through adjectives, 3. General – physical – mental fatigue with reduced activity and motivation, 4. Problems with FM and responses to therapy, 5. Sleep quality, 6. Above 5 suggests depression and greater 10 almost always depression, 7. Level of anxiety experienced, 8. General health, 9. Qigong exercise completed day/night, and 10. Attendance at group exercise and discussion

Chapter 5. Conclusion

5.1 Summary of Findings

Healthy controls recovered near baseline levels of muscle torque on day 2 while FM patients did not. Altered muscle forces and EMG signals recorded during the recovery phase supported trends that FM patients differ from healthy controls. Healthy controls had better recovery day 2 compared to the patients in both torque and fatigue index measures. For EMG amplitude only one muscle, the RF, showed patterns confirming findings in muscle torque and fatigue index for controls and patients. Perceived exertion scores had trends with patients being higher than controls. Pain scores after fatigue exercise were significantly higher in the patient group than the healthy controls.

For the pilot study on Qigong exercise among FM patients, results showed that there may be an effect on an FM patient's recovery patterns after fatiguing exercise. As muscle torque had reduction after intervention suggesting improvement in day 1 recovery for intervention participants. Control participants had increases in torque suggesting a lower level of recovery. However, pain scores were reduced after intervention in both groups on both day 1 and 2, implying that both the Sham Qigong and Qigong interventions might relieve pain to some extent or that neither are clinically significant and resulted from a placebo effect. Improvements by both groups were seen on the questionnaires suggesting that Qigong may have potential benefits and needs to be further studied on a larger population.

5.2 Clinical Implications

Clinicians would be able to use the knowledge of an altered recovery pattern to prescribe movements after an exercise day that could help the patient to recover. They would also be able

to relate to the patient on a more personal level and help them to cope day-to-day to enabling them to accomplish desired activities. It would open the door for suggestions from clinicians on the types of exercise that they may want done in a study to see if recovery is altered and allow them to think more about what could be causing it. For Qigong, clinicians would be able to suggest it as a relaxing exercise that could help the patient to alleviate pain, sleep better, and just be able to take time from the day to relax. The benefits of both exercise recovery and Qigong could help clinicians by giving them another way to treat patients that has shown promising results.

5.3 Limitations

We were only able to recruit 12 healthy controls and 11 patients for participation in the “Altered Fatigue Recovery in Patients with Fibromyalgia” study. In which case there may not have been enough participants for variables to be significant and so current findings may be true, but would be better supported through a bigger study population. As for the benefits of Qigong from “A pilot study of a mind body intervention” the improvements may be true, but since the groups only had three participants in each findings will need to be supported by a larger study group in the future.

5.4 Future Directions

Studies should be done evaluating throughout the exercise process how patients are recovering and the influence of other exercise or intervention on their feelings and perceptions of fatigue and pain. Another addition to consider is biomarkers and investigating if an altered pattern in the level of the biomarkers exists throughout a study with a before and after

intervention design to influence changes on the biomarkers. So future research to find more commonalities on altered recovery patterns would prove beneficial.

Bibliography

1. Meeus, M., et al., *Symptom fluctuations and daily physical activity in patients with chronic fatigue syndrome: a case-control study*. Arch Phys Med Rehabil, 2011. **92**: p. 1820-1826.
2. Ruiz, J., et al., *Objectively measured sedentary time and physical activity in women with fibromyalgia: a cross-sectional study*. BMJ Open, 2013. **3**: p. 1-9.
3. Jones, K. and G. Liptan, *Exercise interventions in fibromyalgia: clinical applications from the evidence*. Rheum Dis Clin N Am, 2009. **35**: p. 373-391.
4. Bates, D., et al., *Prevalence of fatigue and chronic fatigue syndrome in a primary care practice*. Arch Intern Med, 1993. **153**: p. 2759-2765.
5. Fukuda, K., et al., *The chronic fatigue syndrome: a comprehensive approach to its definition and study*. Ann Intern Med, 1994. **121**: p. 953-959.
6. Komaroff, A. and D. Buchwald, *Chronic fatigue syndrome: an update*. Annu Rev Med, 1998. **49**: p. 1-13.
7. Kroenke, K., et al., *Chronic fatigue in primary care. Prevalence, patient characteristics and outcome*. JAMA, 1988. **206**(929-934).
8. Price, R., et al., *Estimating the prevalence of chronic fatigue syndrome and associated symptoms in the community*. Public Health Rep, 1992. **107**: p. 514-522.
9. Sharpe, M., et al., *Follow up of patients presenting with fatigue to an infectious diseases clinic*. BMJ, 1992. **305**: p. 147-152.
10. Walker, E., W. Katon, and R. Jemelka, *Psychiatric disorders and medical care utilization among people in the general population who report fatigue*. J Gen Intern Med, 1993. **8**: p. 436-440.
11. Jones, K., S. Clark, and R. Bennett, *Prescribing exercise for people with fibromyalgia*. AACN Clinical Issues, 2002. **13**(2): p. 277-293.
12. Christley, Y., T. Duffy, and C. Martin, *A review of the definitional criteria for chronic fatigue syndrome*. Journal of Evaluation in Clinical Practice, 2012. **18**: p. 25-31.
13. Sharpe, M., et al., *A report - chronic fatigue syndrome: guidelines for research*. Journal of the Royal Society of Medicine, 1991. **84**: p. 118-121.
14. Macrae, H., et al., *Effects of training on lactate production and removal during progressive exercise in humans*. Journal of Applied Physiology, 1992. **72**(5): p. 1649-56.
15. Wolfe, F., et al., *The american college of rheumatology 1990 criteria for the classification of fibromyalgia*. Arthritis and Rheumatism, 1990. **33**(2): p. 160-172.
16. Wolfe, F., et al., *The american college of rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity*. Arthritis Care & Research, 2010. **62**(5): p. 600-610.
17. Ablin, J., D. Buskila, and D. Clauw, *Biomarkers in fibromyalgia*. Current Pain & Headache Reports, 2009. **13**: p. 343-349.
18. Clauw, D., L. Arnold, and B. McCarberg, *The Science of Fibromyalgia*. Mayo clinic Proc., 2011. **86**(9): p. 907-911.
19. Arnold, L., D. Clauw, and B. McCarberg, *Improving the recognition and diagnosis of fibromyalgia*. Mayo Clinic Proc., 2011. **86**(5): p. 457-464.
20. Pedersen, B. and B. Saltin, *Evidence for prescribing exercise as therapy in chronic disease*. Scand J Med Sci Sports, 2006. **16**(1): p. 3-63.

21. Sanudo, B., et al., *Aerobic exercise versus combined exercise therapy in women with fibromyalgia syndrome: a randomized controlled trial*. Arch Phys Med Rehabil, 2010. **91**: p. 1838-1843.
22. Busch, A., et al., *Best practice: E-model-prescribing physical activity and exercise for individuals with fibromyalgia*. Physiotherapy Theory and Practice, 2008. **24**(3): p. 151-166.
23. Hurley, B., E. Hanson, and A. Sheaff, *Strength training as a countermeasure to aging muscle and chronic disease*. Sports Med, 2011. **41**(4): p. 289-306.
24. Carvalho, R., S. Uehara, and G. Rosa, *Microencapsulated conjugated linoleic acid associated with hypocaloric diet reduces body fat in sedentary women with metabolic syndrome*. Vasc Health Risk Manag, 2012. **8**: p. 661-7.
25. Daenen, L., et al., *Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice*. Clin J Pain, 2015. **31**: p. 108-114.
26. Gowans, S. and A. DeHueck, *Effectiveness of exercise in management of fibromyalgia*. Curr Opin Rheumatol, 2004. **16**: p. 138-142.
27. Gowans, S.E., et al., *Six-month and one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia*. Arthritis Rheum, 2004. **51**(6): p. 890-8.
28. Newcomb, L., et al., *Influence of Preferred versus prescribed exercise on pain in fibromyalgia*. Medicine & Science in Sports & Exercise, 2011: p. 1106-1113.
29. Bennett, R.M., et al., *Group treatment of fibromyalgia: a 6 month outpatient program*. J Rheumatol, 1996. **23**(3): p. 521-8.
30. Gowans, S., et al., *A randomized controlled clinical trial of education and physical training for individuals with fibromyalgia*. Arthritis Care & Research, 1999. **12**: p. 120-128.
31. Gowans, S., et al., *Six-month & one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia*. Arthritis and Rheumatism, 2004. **51**(6): p. 890-898.
32. Ramsay, C., et al., *An observer-blinded comparison of supervised and unsupervised aerobic exercise regimens in fibromyalgia*. Rheumatology (Oxford), 2000. **39**(5): p. 501-5.
33. Wigers, S., T. Stiles, and P. Vogel, *Effects of aerobic exercise versus stress management treatment in fibromyalgia: a 4.5 year prospective study*. Scand J Rheumatol, 1996. **25**: p. 77-86.
34. Ayan, C., et al., *Health education home-based program in females with fibromyalgia: a pilot study*. Journal of Back and Musculoskeletal Rehabilitation, 2009. **22**: p. 99-105.
35. Pantou, L., et al., *Effects of resistance training and chiropractic treatment in women with fibromyalgia*. The Journal of Alternative and Complementary Medicine, 2009. **15**(3): p. 321-328.
36. Richards, S. and D. Scott, *Prescribed exercise in people with fibromyalgia: parallel group randomised controlled trial*. BMJ, 2002. **325**(185): p. 1-4.
37. Busch, A.J., et al., *Resistance exercise training for fibromyalgia*. Cochrane Database Syst Rev, 2013. **12**: p. CD010884.
38. Gowans, S.E., et al., *A randomized, controlled trial of exercise and education for individuals with fibromyalgia*. Arthritis Care Res, 1999. **12**(2): p. 120-8.
39. De Becker, P., et al., *Exercise capacity in chronic fatigue syndrome*. Arch Intern Med, 2000. **160**(21): p. 3270-3277.

40. Farquhar, W., et al., *Blood volume and its relation to peak O₂ consumption and physical activity in patients with chronic fatigue*. Am J Physiol Heart Circ Physiol, 2002. **282**(1): p. H66-71.
41. Sisto, S., et al., *Metabolic and cardiovascular effects of a progressive exercise test in patients with chronic fatigue syndrome*. Am J Med, 1996. **100**(6): p. 634-640.
42. Snell, C., et al., *Exercise capacity and immune function in male and female patients with chronic fatigue syndrome (CFS)*. In Vivo, 2005. **19**(2): p. 387-390.
43. Dobkin, P., et al., *Maintenance of exercise in women with fibromyalgia*. Arthritis and Rheumatism, 2005. **53**(5): p. 724-731.
44. Nijs, J., et al., *Can exercise limits prevent post-exertional malaise in chronic fatigue syndrome? An uncontrolled clinical trial*. Clin Rehabil, 2008. **22**(5): p. 426-435.
45. Dailey, D., V. Keffala, and K. Sluka, *Do cognitive and physical fatigue tasks enhance pain, cognitive fatigue, and physical fatigue in people with fibromyalgia?* Arthritis Care Res (Hoboken), 2015. **67**(2): p. 288-296.
46. Nijs, J., et al., *Fear of movement and avoidance behaviour toward physical activity in chronic-fatigue syndrome and fibromyalgia: state of the art and implications for clinical practice*. Clin Rheumatol, 2013. **32**(8): p. 1121-1129.
47. Peckerman, A., et al., *Abnormal impedance cardiography predicts symptom severity in chronic fatigue syndrome*. Am J Med Sci, 2003. **326**(2): p. 55-60.
48. VanNess, J., et al., *Postexertional malaise in women with chronic fatigue syndrome*. J Womens Health (Larchmt), 2010. **19**(2): p. 239-244.
49. Black, C., P. O'Connor, and K. McCully, *Increased daily physical activity and fatigue symptoms in chronic fatigue syndrome*. Dyn Med, 2005. **4**(1).
50. Busch, A.J., et al., *Exercise therapy for fibromyalgia*. Curr Pain Headache Rep, 2011. **15**(5): p. 358-67.
51. Hauser, W., et al., *Efficacy of different types of aerobic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomised controlled trials*. Arthritis Res Ther, 2010. **12**(3): p. R79.
52. Caseras, X., et al., *Probing the working memory system in chronic fatigue syndrome: a functional magnetic resonance imaging study using the n-back task*. Psychosom Med, 2006. **68**(6): p. 947-955.
53. Lange, G., et al., *Objective evidence of cognitive complaints in chronic fatigue syndrome: a bold fmri study of verbal working memory*. Neuroimage, 2005. **26**(2): p. 513-524.
54. Majer, M., et al., *Neuropsychological performance in persons with chronic fatigue syndrome: results from a population-based study*. Psychosom Med, 2008. **70**(7): p. 829-836.
55. Wicksell, R., et al., *Acceptance and commitment therapy for fibromyalgia: a randomized controlled trial*. Eur J Pain, 2013: p. 599-611.
56. Williams, D., *Psychological and behavioural therapies in FM and related syndromes*. Best practice and research in clinical rheumatology, 2003. **17**(4): p. 649-665.
57. Glombiewski, J., et al., *Psychological treatments for FM: A meta-analysis*. Pain, 2010. **151**(2): p. 280-295.
58. Redondo, J., et al., *Long-term efficacy of therapy in patients with fibromyalgia: A physical exercise-based program and a cognitive-behavioural approach*. Arthritis and rheumatism-arthritis care and research, 2004. **51**(2): p. 184-192.

59. White, K. and W. Nielson, *Cognitive Behavioural treatment of FM syndrome - a follow-up assessment*. Journal of rheumatology, 1995. **22**(4): p. 717-721.
60. Williams, D., et al., *Improving physical function status in patients with fibromyalgia: a brief cognitive behavioural intervention*. Journal of rheumatology, 2002. **29**(6): p. 1280-1286.
61. Edinger, J., et al., *Behavioral insomnia therapy for FM patients - a randomized clinical trial*. Archives of internal medicine, 2005. **165**(21): p. 2527-2535.
62. Dishman, R., A. Jackson, and M. Bray, *Self-regulation of exercise behavior in the TIGER study*. Ann Behav Med, 2014. **48**: p. 80-91.
63. Wallman, K., et al., *Physiological responses during a submaximal cycle test in chronic fatigue syndrome*. Medicine and Science in Sports and Exercise, 2004: p. 1682-1688.
64. Aminian-Far, A., et al., *Whole-Body vibration and the prevention and treatment of Delayed-Onset muscle soreness*. Journal of Athletic Training, 2011. **46**(1): p. 43-49.
65. Evangelista, R., et al., *Rest interval between resistance exercise sets: length affects volume but not creatine kinase activity or muscle soreness*. International Journal of Sports Physiology and Performance, 2011. **6**: p. 118-127.
66. Vaczi, M., et al., *Mechanical, biochemical, and electromyographic responses to short-term eccentric knee extensor training in humans*. Journal of Strength and Conditioning Research, 2011. **25**(4): p. 922-932.
67. Willoughby, D., B. McFarlin, and C. Bois, *Interleukin-6 expression after repeated bouts of eccentric exercise*. Int J Sports Med, 2003. **24**: p. 15-21.
68. Ebersole, K., K. O'Connor, and A. Wier, *Mechanomyographic and electromyographic responses to repeated concentric muscle actions of the quadriceps femoris*. Journal of Electromyography and Kinesiology, 2006. **16**(2): p. 149-57.
69. Finsterer, J., *Biomarkers of peripheral muscle fatigue during exercise*. BMC Musculoskeletal Disorders, 2012. **13**: p. 218-230.
70. Rosendal, L., et al., *Increase in interstitial interleukin-6 of human skeletal muscle with repetitive low-force exercise*. American Physiological Society, 2005. **98**: p. 477-481.
71. Steinberg, J., et al., *Cytokine and Oxidative responses to maximal cycling exercise in sedentary subjects*. Medicine and Science in Sports and Exercise, 2007: p. 964-968.
72. Croft, L., et al., *High-intensity interval training attenuates the exercise-induced increase in plasma IL-6 in response to acute exercise*. Appl Physiol Nutr Metab, 2009. **34**: p. 1098-1107.
73. Libardi, C., et al., *Effect of resistance, endurance, and concurrent training on TNF-alpha, IL-6, and CRP*. American College of Sports Medicine, 2012: p. 50-56.
74. Vollestad, N., *Measurement of human muscle fatigue*. Journal of Neuroscience Methods, 1997. **74**: p. 219-227.
75. Norregaard, J., et al., *Biochemical changes in relation to a maximal exercise test in patients with fibromyalgia*. Clinical Physiology, 1994. **14**: p. 159-167.
76. Umeda, M., L. Corbin, and K. Maluf, *Examination of contraction-induced muscle pain as a behavioral correlate of physical activity in women with and without fibromyalgia*. Disabil Rehabil, Early Online, 2014: p. 1-6.
77. Klimas, N., G. Broderick, and M. Fletcher, *Biomarkers for chronic fatigue*. Brain, Behavior, and Immunity, 2012. **26**: p. 1202-1210.
78. Cannon, J., et al., *Acute phase responses and cytokine secretion in chronic fatigue syndrome*. Journal of Clinical Immunology, 1999. **19**(6): p. 414-421.

79. Torgrimson-Ojerio, B., et al., *Preliminary evidence of a blunted anti-inflammatory response to exhaustive exercise in fibromyalgia*. Journal of Neuroimmunology, 2014. **277**: p. 160-167.
80. Ortega, E., et al., *Aquatic Exercise improves the monocyte pro- and anti-inflammatory cytokine production balance in fibromyalgia patients*. Scand J Med Sci Sports, 2012. **22**: p. 104-112.
81. Gibson, H., et al., *Exercise performance and fatiguability in patients with chronic fatigue syndrome*. J Neurol Neurosurg Psychiatry, 1993. **56**: p. 993-998.
82. Paul, L., et al., *Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome*. European Journal of Neurology, 1999. **6**(1): p. 63-9.
83. Burckhardt, C., S. Clark, and R. Bennett, *The Fibromyalgia Impact Questionnaire: Development and validation*. J Rheumatol, 1991. **18**: p. 728-733.
84. Ainsworth, B., et al., *Compendium of Physical Activities: a second update of codes and MET values*. Med Sci Sports Exerc, 2011. **43**(8): p. 1575-81.
85. Surakka, J., et al., *Reliability of knee muscle strength and fatigue measurements*. Biology of Sport, 2005. **22**(4): p. 301-313.
86. Bradesi, S., et al., *Repeated exposure to water avoidance stress in rats: a new model for sustained visceral hyperalgesia*. AM J Physiol Gastrointest Liver Physiol, 2005. **289**: p. G42-G53.
87. Gameiro, G., et al., *Nociception- and anxiety-like behavior in rats submitted to different periods of restraint stress*. Physiol Behav, 2006. **87**: p. 643-649.
88. Marcinkiewicz, C., et al., *Social defeat stress potentiates thermal sensitivity in operant models of pain processing*. Brain Research, 2009. **1251**: p. 112-120.
89. Rivat, C., et al., *Non-Nociceptive environmental stress induces hyperalgesia, not analgesia, in pain and opioid-experienced rats*. Neuropsychopharmacology, 2007. **32**: p. 2217-2228.
90. Ulrich-Lai, Y., et al., *Limbic and HPA axis function in an animal model of chronic neuropathic pain*. Physiol Behav, 2006. **88**: p. 67-76.
91. Carlson, L., et al., *Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients*. Psychoneuroendocrinology, 2004. **29**: p. 448-474.
92. Manzanque, J., et al., *Serum cytokines, mood and sleep after a qigong program: is qigong an effective psychobiological tool?* J Health Psychol, 2009. **14**(1): p. 60-67.
93. Creamer, P., et al., *Sustained improvement produced by nonpharmacologic intervention in fibromyalgia: results of a pilot study*. Arthritis Care Res, 2000. **13**(4): p. 198-204.
94. Da Silva, G., G. Lorenzi-Filho, and L. Lage, *Effects of yoga and the addition of Tui Na in patients with fibromyalgia*. J Altern Complement Med, 2007. **13**(10): p. 1107-1113.
95. Singh, B., et al., *Effectiveness of acupuncture in the treatment of fibromyalgia*. Altern Ther Health Med, 2006. **12**(2): p. 34-41.
96. Melzck, R., *The short-form McGill Pain Questionnaire*. Pain, 1987. **30**: p. 191-7.
97. Wolfe, F., et al., *Fibromyalgia and disability. Report of the Moss International Working Group on medicolegal aspects of chronic widespread musculoskeletal pain complaints and fibromyalgia*. Scand J Rheumatol, 1995. **24**(2): p. 112-118.

98. Okifuji, A., et al., *A standardized manual tender point survey. I. Development and determination of a threshold point for identification of positive tender points in Fibromyalgia Syndrome.* J Rheumatol, 1997. **24**: p. 377-383.
99. Marques, A., et al., *Quantifying pain threshold and quality of life of fibromyalgia patients.* Clin Rheumatol, 2005. **24**: p. 266-271.
100. Segal, D., et al., *Development and initial validation of a self-reported assessment tool for anxiety among other adults: The Geriatric Anxiety Scale.* Journal of Anxiety Disorders, 2010. **24**: p. 709-714.

Appendices

Appendix A – Phone Script Healthy

Study of fatiguing exercise

Hi is this (name). My name is Mariad Cocke. I am contacting you in regards to the Fatiguing exercise study that you said you were interested in participating in.

Are you still interested?

Do you have about 15 – 20 min to answer some questions to confirm your eligibility?

Subject identification number _____

Date ___ / ___ / ___

Subject name _____

1. Is the individual available for a telephone interview? YES NO

If **YES**, proceed with telephone script

If **NO**, answer the following:

Subject is not available for telephone interview because;

1. Unable to reach - number of times attempted _____
2. Subject is busy / not at home (**specify** the time to call again) _____

2. Are you able to participate in a study which requires fatiguing exercise (isometric contractions) and a blood draw during **2 visits** for one of **2 hours** and one of **1 hour**

YES - move on to question #3

NO - thank them for their time and let them know they are not eligible for this study at this time

3. What is your age? (between 30-63)

Are you considered non-obese? YES NO

Have you been diagnosed with any diseases? YES NO

Do you have any cardiovascular diseases? YES NO

Do you have any neurological disorders? YES NO

Do you have any neuromuscular disorders? YES NO

Do you have a normal sleep pattern? YES NO

Do you experience any pain that you regularly take medication for? YES NO

If yes what do you take?

Do you have high blood pressure? YES NO

If yes, what was the most recent reading?

If yes, do you take a medication? YES NO if YES what?

Do you take any medications for your blood specifically? YES NO

Do you take any sleep medications? YES NO if YES what?

Do you take any medications at all? YES NO if YES what?

Do you have any medical or surgical conditions that preclude participation in the study?

YES NO

Activity Level Evaluation Form

Name: _____

	Walking			Moderate					Vigorous		
	Work (3.3MET)	Transportation (3.3MET)	Leisure (3.3MET)	Work (4.0MET)	Vig Garden (5.5MET)	Mod Yard (4.0MET)	Mod Inside (4.0MET)	Leisure (4.0MET)	Cycle (6.0MET)	Work (8.0MET)	Leisure (8.0MET)
Time (min/day)											
Days/Week											
Total in 1 day within respective category (>180 then =180) and record the number of days that are 180 MET-min/week (MET*min/day*days/wk) sum min each day all sub category times MET times 1 day or more if same											
Total Physical Activity Sum MET-min/wk each category (answer to above that shows steps to calculate) sum walk/mod/vig for accurate total activity											
Selection:	Low (not in Mod or Vig)			Moderate: A) 3 or 3+ days MOD activity at least 20 min/day B) 5 or 5+ days MOD activity and/or WALKING at least 30 min/day C) 5 or 5+ days any combo WALKING, MOD, VIG activity with minimum total physical activity at least 600 MET-min/wk Meet at least one and moderate level					High: A) VIG at least 3 days min total phys act 1500MET-min/wk B) 7 or + combo all with min 3000MET-min/wk		

ASSUMPTION: In the **WALKING** category – **WORK AND TRANSPORTATION** occur during the 5 work days first and **LEISURE** begins on the 2 weekend days.
 In the **MODERATE** category – **WORK AND CYCLE** occur during the 5 work days first and **LEISURE** begins on the 2 weekend days. **MAKE A NOTE** under moderate on days per week for **VIG GARDEN, MOD YARD, AND MOD INSIDE** if occurred during the 5 work days or weekend.
 In the **VIGOROUS** category – **WORK** occurs during the 5 work days first and **LEISURE** begins on the 2 weekend days.

Appendix B – Phone Script Fibromyalgia
Study of mild exercise

Subject identification number _____

Date ____ / ____ / ____

Subject name _____

1. Is the individual available for a telephone interview? YES NO

If **YES**, proceed with telephone script

If **NO**, answer the following:

Subject is not available for telephone interview because;

1. Unable to reach - number of times attempted _____
2. Subject is busy / not at home (**specify** the time to call again) _____

If the candidate information comes from Heron, go through the following Heron script
Heron (FRONTIERS REGISTRY) script:

“We are contacting you because at some point you signed up for the Frontiers research participant registry through a clinic at KU Medical Center. This means that you agreed to be contacted if there are any studies for which you might qualify.

Our research team includes Dr. Wen Liu from the Physical Therapy and Rehabilitation Sciences Department at the University of Kansas Medical Center and myself (Mariad Cocke) from the Bioengineering Graduate Program at the University of Kansas.

May we tell you about a study that we are conducting on how Qigong Exercise may benefit Patients with Fibromyalgia? You are free to say “no” if you do not want to participate in the study.

Would you like to hear more about what the study is?”

If yes: provide overview of study.

“Would you mind answering some questions over the phone to confirm your eligibility or would you prefer for them to be sent via email for completion?”

If NO: “Is it ok if your information is kept in the registry, for contact about future studies?”

NO: to provide name and contact information to Jo Denton so that the name can be removed from Frontiers Registry.

2. Are you able to participate in a study which requires the practice of mild, daily exercise and **about 10** visits for assessment and group exercise sessions?

YES - move on to question #3

NO - thank them for their time and let them know they are not eligible for this study at this time

3. Are you able to participate in the required fatigue test prior to the mild exercise in **two visits** before and two visits after the mild exercise. The fatigue test involves a blood draw and some muscle contractions?

YES – move on to inclusion/exclusion criteria for FM study

NO – thank them for their time and let them know that if they are still interested they could participate in the intervention portion of the study

Phone screening for qualification in FM study based on inclusion/exclusion criteria

Inclusion criteria

Yes **No**

{ } { } A diagnosis of primary FM

{ } { } Between the ages of 18 and 70 years: DOB_____

{ } { } Willing to withdraw from CNS-active therapies
The CNS-active therapies include all drugs for depression and anxiety. Patients with severe depression or anxiety will be excluded. For patients with mild/moderate depression or anxiety, if they have been on those meds for 1 month or longer, they will be asked to be on stable doses during the study period. If they just start their meds within a month, they will have two options of either being off those meds during the study or being screened again after one month on stable dose.

{ } { } Not adding new drugs for pain or sleep during study period
Patients can keep their regular pain or sleeping medicine on stable doses during the study period if they have been taking those meds for 1 month or longer. If they just start their meds within a month, they will have two options of either being off those meds during the study or waiting until one month on stable dose. Patients should not add any new pain or sleep medicine during the study period. Patients are willing to withdraw any pain medicine during the days of baseline and end-intervention assessment.

{ } { } Willing to discontinue treatment with transcutaneous electrical nerve stimulation, biofeedback, tender- and trigger-point injections, acupuncture, and anesthetic or narcotic patches;

{ } { } A raw score ≥ 4 on the physical function component of the Fibromyalgia Impact Questionnaire (FIQ)

{ } { } A mean visual analog scale (VAS) pain score ≥ 40 on a scale from 0 to 100.

If the answer to any of above items is “**No**”, the patient is not qualified for the study.

Exclusion criteria

Yes No

- | | | |
|-----|-----|---|
| { } | { } | Severe depression, anxiety, psychosis, stroke, schizophrenia, or delusional disorder |
| { } | { } | Abuse of alcohol, benzodiazepines, or other drugs |
| { } | { } | A history of behavior that would prohibit compliance for the duration of the study.
(Ask about travel plans, review number of visits, length of study) |
| { } | { } | Active cardiovascular, pulmonary, hepatic, renal, gastrointestinal, or autoimmune disease (except Hashimoto's or Graves' disease that had been stable for 3 months before screening); |
| { } | { } | Current systemic infection; active cancer (except basal cell carcinoma) |
| { } | { } | Unstable endocrine disease |
| { } | { } | Severe sleep apnea |
| { } | { } | Prostate enlargement or other genitourinary disorder (male patients) |
| { } | { } | Pregnancy or breastfeeding (female patients) |
| { } | { } | Plan to start up a new exercise program during study period. |

If the answer to any of above items is “**Yes**”, the patient is not qualified for the study.

4. Any current exercise programs or activity? YES/NO

If YES, what currently doing and description.

5. Can you be contacted for participation in the study within two weeks?

YES - move on to question #12

NO – When will you be available for the study _____

12. What is the phone # to contact you? _____

Appendix C – Step-by-Step – Setup for Fatigue Testing

- 1) Participants arrived at the Kansas University Medical Center and were met at the designated parking area between 9-11 am to do the fatigue testing and they also returned 24 hours later to complete day 2. (This process and all the following were again repeated after the intervention was completed, with controls only doing the fatigue test at the beginning) The testing on day 1 had one and half hours allowed and day 2 had one hour.
- 2) Participants were asked to put on shorts, pants, or a dress that could be pulled about 1-2 inches above the knee in order to make the area of the quad where the EMG markers would be placed visible.
- 3) Participants were shown a Rating of Perceived Exertion (RPE) Scale and gave their current rating before and after warm-up, once seated in the biodex, followed by ratings after the 6th, 12th, and 18th (end of exercise) maximal isometric contractions, after 5 minutes recovery, and finally at the end of the 30 minutes recovery (at 24 hours they gave before, after warm-up, after each of three max effort contractions). Participants were shown a pain/soreness scale going from 0-10 (10 highest) on day 2 before the warm-up was conducted to see how they were feeling and how they had recovered after day 1.
- 4) Warm-up: a standardized walking warm-up was completed for the study for both the controls and the patients. The warm-up was about 10-15 minutes walking up a slight incline from the KUMC Center on Aging to the entrance at Murphy and then to the elevator by Robinson and up to the Neuromuscular Research Lab to complete the contractions. If the participant was at a 1.5-2 at minimum on the Rating of Perceived Exertion Scale (modified Borg Scale) then the elevator was taken to the 5th floor to the Neuromuscular Lab. If the participant was not at the proper warm-up level then they

would walk around in the lab for a bit as we did not want to aggravate symptoms greatly prior to fatigue testing.

- 5) Participants were then seated in a comfortable position with the knee joint aligned with the axis of rotation of the dynamometer.
- 6) The participant's lower leg was secured to the dynamometer arm using a padded bar attachment that was firmly fixed to the load cell of the dynamometer.
- 7) The participant was then restrained in the seated position by a lap-strap and thigh strap placed over the right leg.
- 8) The knee joint was then positioned at an angle of 90° reference so that the machine could position it there automatically once testing began.
- 9) The skin of the right quadriceps was then wiped with an alcohol wipe in the spots where electrodes were placed.
- 10) EMG electrode spots were marked with an X with permanent marker and electrodes were then placed along the longitudinal axis of the quadriceps on the vastus medialis (VM), rectus femoris (RF), and vastus lateralis (VL) of the right leg.

Electrode placement on the VM was approximately at a distance of 12.7cm above the medial aspect of the patella, RF was placed at a distance of 11.3cm above the superior border of the patella, and the VL electrode was placed at a distance 12.3cm above the lateral aspect of the patella.

Each electrode was placed adjacent to one another to minimize the inter-electrode distance within each muscle, with the reference (ground) electrode being placed over the head or styloid process of the ulna. [68]

11) The participant was then given the instructions about the isometric exercise with the number of reps, contraction time, and rest time after which they then completed the following: 18 maximum quadriceps isometric voluntary contractions (MVC's) using a 50% duty cycle (10s contraction, 10s rest). After completion the participant remained in the Biodex till the 5 min recovery was completed and then the participant was allowed to get up and move a bit and sit in a more comfortable chair until 5 min prior to the 30 min recovery contraction in which they were set-up in the chair and the final contraction was completed and during both they made a 10s contraction.

12) Participants were then unhooked and told to relax and to come back for the testing at 24 hours which included:

Performing the same procedures given above, except the exercise on the Biodex was different, the subject completed 3 isometric MVC's (10s duration) with a 1 min rest period between each contraction.

13) Verbal encouragement was given to the participants on both days during each of the contractions in order to ensure that maximum contractions were obtained.

Appendix D – Adapted Equation for Fatigue Index

A contraction of 30 seconds was adjusted to a contraction of 10 seconds:

FATI: $100\% \times \{1 - (\text{AUFC}_{0-30} / (\text{Fmax}_{0.5} \times 30))\}$ was the equation adjusted for 0-10 with the max between 0-3, FATI: $100\% \times \{1 - (\text{AUFC}_{0-10} / (\text{Fmax}_{0-3} \times 10))\}$ [85]

Appendix E – Steps in Detail of Qigong Exercise

First Training Session – Participants learned a unique standing posture in which one needs to stand with knees slightly bent and have a general sense of bodily awareness, relaxed and comfortable. The distance between two feet is about shoulder width. This is the preferred standing posture during the qigong exercise. The participants also learned the way of qigong exercise in a sitting and lying posture. This specific form of qigong exercise allowed the subjects to perform the exercise in standing, sitting, or lying posture. We intended not to exclude any participant even if he/she has difficulty in a standing posture, unless the participant rejected to participate or withdrew from the study.

The participants then learned a technique to control deep breathing through a diaphragmatic breathing technique, which is different from normal breathing. In normal breathing the diaphragm contracts and the chest expands during inhalation. Diaphragmatic breathing would minimize the role of the upper chest and neck muscles in breathing and promote the use of the diaphragm. The diaphragmatic breathing used in “six healing sound” qigong exercise is focused on slow, controlled exhalation. To perform “six healing sound” breathing, one started with contracting the diaphragm slowly to exhale with the mouth slightly opened. At the end of exhalation, one simply relaxed the diaphragm muscles and inhaled through the nose naturally. Usually the exhale takes longer than the inhale.

The participants also learned how to pronounce each of the six healing sounds correctly. In a set of “six healing sound” qigong exercise, the subject would repeat six times each of the six healing sounds. When pronouncing a healing sound, one was always exhaling while quietly chanting the sound. The participant was instructed to take 3-4 deep breaths without pronouncing

any sound before the qigong exercise and between every two sounds. Those breaths were meant to facilitate the quiet meditation status before qigong exercise and make a transition between sounds.

Second Training Session – Participants first reviewed the previously learned breathing technique and six healing sounds, and were then taught the body movements associated with the first three healing sounds. The focus of the qigong exercise was to breathe slowly and coordinate breathing patterns with smooth arm movements to increase calmness and well-being while the participant's mind was merely empty with only a feeling of diaphragmatic contraction during exhalation and expansion during inhalation. This was based on an assumption that self-healing begins with a quiet and empty state of mind. The body movements associated with the first three sounds involved only upper extremity including smooth arm/hand movement up and down, extending to the front and then back towards the body. They were then taught the body movements associated with the next three healing sounds. Again, all body movements were movement in the upper extremity except for the fifth sound during which a squat with knee flexion was involved.

After the second training session, the participants were instructed to continue the qigong exercise in their homes every day, at least twice per day in the morning immediately after getting up and in the evening right before going to bed. Each set of the qigong exercise took up to 15-20 minutes. Each participant was given a diary to record the home qigong sessions and general physical activity level during the day. The participants were educated on the importance of adherence to qigong exercise. During this 6-week treatment period, the participants met with the instructor once per week in weekly group exercise. During the group exercise, the instructor evaluated and corrected the performance of each participant, answered his/her questions, and

discussed any relevant issues. The participants turned in their daily diary that recorded their qigong exercise in the past week. The participants were encouraged to maintain their compliance to the program. The participants were given a list of all of the days that they were required to come to KUMC for the group sessions and instructed to call if they would be missing a session.

Form B

MULTIDIMENSIONAL FATIGUE INVENTORY

Name initial _____

Date _____

By means of the following statements we would like to get an idea of how you have been feeling ***in the past 7 days***. Here is, for example, the statement: "I FEEL RELAXED". If you think that this is entirely true, that indeed you have been feeling relaxed in the past 7 days, please, place an X in the extreme left box; like this:

Yes, that is true

<input type="checkbox"/>				
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

No, that is not true

The more you disagree with the statement, the more you can place an X in the direction of "No, that is not true". Please, do not miss out a statement and place one X next to each statement.

	True					Not
1. I feel fit	<input type="checkbox"/>					
2. Physically I feel only able to do a little	<input type="checkbox"/>					
3. I feel very active	<input type="checkbox"/>					
4. I feel like doing all sorts of nice things	<input type="checkbox"/>					
5. I feel tired	<input type="checkbox"/>					
6. I think I do a lot in a day	<input type="checkbox"/>					
7. When I am doing something, I can keep my thoughts on	<input type="checkbox"/>					
8. Physically I can take on a lot	<input type="checkbox"/>					
9. I dread having to do things	<input type="checkbox"/>					
10. I think I do very little in a day	<input type="checkbox"/>					
11. I can concentrate well	<input type="checkbox"/>					
12. I am rested	<input type="checkbox"/>					
13. It takes a lot of effort to concentrate on things	<input type="checkbox"/>					
14. Physically I feel I am in a bad condition	<input type="checkbox"/>					
15. I have a lot of plans	<input type="checkbox"/>					
16. I tire easily	<input type="checkbox"/>					
17. I get little done	<input type="checkbox"/>					
18. I don't feel like doing anything	<input type="checkbox"/>					
19. My thoughts easily wander	<input type="checkbox"/>					
20. Physically I feel I am in an excellent condition	<input type="checkbox"/>					

FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQ)

Name initial _____

Date _____

Directions: For questions 1 through 11, please circle the number that best describes how you did overall for the *past week*. If you don't normally do something that is asked, cross the question out.

	Always	Most	Occasionally	Never				
Were you able to:								
1. Do shopping?	0	1	2	3				
2. Do laundry with a washer and dryer?	0		1	2 3				
3. Prepare meals?	0	1	2	3				
4. Wash dishes/cooking utensils by hand?.....	0	1	2	3				
5. Vacuum a rug?.....	0	1	2	3				
6. Make beds?	0	1	2	3				
7. Walk several blocks?	0	1	2	3				
8. Visit friends or relatives?	0	1	2	3				
9. Do yard work?.....	0	1	2	3				
10. Drive a car?	0	1	2	3				
11. Climb stairs?	0	1	2	3				
12. Of the 7 days in the past week, how many days did you feel good?	0	1	2	3	4	5	6	7
13. How many days last week did you miss work, including housework, because of fibromyalgia?	0	1	2	3	4	5	6	7

Directions: For the remaining items, mark the point on the line that best indicates how you felt overall for the past week.

14. When you worked, how much did pain or other symptoms of your fibromyalgia interfere with your ability to do your work, including housework?

● — I — I — I — I — I — I — I — I — I — I — ●

No problem with work Great difficulty with work

15. How bad has your pain been?

● — I — I — I — I — I — I — I — I — I — I — ●

No pain Very severe

pain

16. *How tired have you been?*

No tiredness ● ___ I ___ ● Very tired

17. *How have you felt when you get up in the morning?*

Awoke well rested ● ___ I ___ ● Awoke very
tired

18. *How bad has your stiffness been?*

No stiffness ● ___ I ___ ● Very stiff

19. *How nervous or anxious have you felt?*

Not anxious ● ___ I ___ ● Very anxious

20. *How depressed or blue have you felt?*

Not depressed ● ___ I ___ ● Very depressed

PITTSBURGH SLEEP QUALITY INDEX

Name initial _____

Date _____

The following questions relate to your usual sleep habits during the past two weeks only. Your answers should indicate the most accurate reply for the majority of days and nights in the past two weeks. Please answer all questions.

1. During the past two weeks, what time have you usually gone to bed at night?
BED TIME _____
2. During the past two weeks, how long (in minutes) has it usually taken you to fall asleep at night?
NUMBER OF MINUTES _____
3. During the past two weeks, what time have you usually gotten up in the morning?
GETTING UP TIME _____
4. During the past two weeks, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)
HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past two weeks, how often have you had trouble sleeping because you...
 - a) Cannot get to sleep within 30 minutes
Not during the past two weeks____ Less than once a week____ Once or twice a week____ Three or more times a week____
 - b) Wake up in the middle of the night or early morning
Not during the past two weeks____ Less than once a week____ Once or twice a week____ Three or more times a week____
 - c) Have to get up to use the bathroom
Not during the past two weeks____ Less than once a week____ Once or twice a week____ Three of more times a week____
 - d) Cannot breathe comfortably
Not during the past two weeks____ Less than once a week____ Once or twice a week____ Three or more times a week____
 - e) Cough or snore loudly
Not during the past two weeks____ Less than once a week____ Once or twice a week____ Three or more times a week____
 - f) Feel too cold

- | | | | | |
|---|-------------------------------------|-----------------------------|----------------------------|----------------------------------|
| | Not during the
past two weeks___ | Less than
once a week___ | Once or twice
a week___ | Three or more
times a week___ |
| g) Feel too hot | Not during the
past two weeks___ | Less than
once a week___ | Once or twice
a week___ | Three or more
times a week___ |
| h) Had bad dreams | Not during the
past two weeks___ | Less than
once a week___ | Once or twice
a week___ | Three or more
times a week___ |
| i) Have pain | Not during the
past two weeks___ | Less than
once a week___ | Once or twice
a week___ | Three or more
times a week___ |
| j) Other reason(s), please describe _____ | | | | |
-

How often during the past two weeks have you had trouble sleeping because of this?

Not during the past two weeks___	Less than once a week___	Once or twice a week___	Three or more times a week___
-------------------------------------	-----------------------------	----------------------------	----------------------------------

6. During the past two weeks, how would you rate your sleep quality overall?

Very good _____

Fairly good_____

Fairly bad_____

Very bad_____

7. During the past two weeks, how often have you taken medicine to help you sleep (prescribed or 'over the counter'?)

Not during the past two weeks___	Less than once a week___	Once or twice a week___	Three or more times a week___
-------------------------------------	-----------------------------	----------------------------	----------------------------------

8. During the past two weeks, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past two weeks___	Less than once a week___	Once or twice a week___	Three or more times a week___
-------------------------------------	-----------------------------	----------------------------	----------------------------------

9. During the past two weeks, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or roommate?

No bed partner or room mate _____

Partner/roommate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a roommate or bed partner, ask him/her how often in the past two weeks you have had...

a) Loud snoring
Not during the past two weeks _____
week _____

Less than once a week _____	Once or twice a week _____	Three or more times a _____
-----------------------------	----------------------------	-----------------------------

b) Long pauses between breaths while asleep
Not during the past two weeks _____
week _____

Less than once a week _____	Once or twice a week _____	Three or more times a _____
-----------------------------	----------------------------	-----------------------------

c) Legs twitching or jerking while you sleep
Not during the past two weeks _____
week _____

Less than once a week _____	Once or twice a week _____	Three or more times a _____
-----------------------------	----------------------------	-----------------------------

d) Episodes of disorientation or confusion during sleep
Not during the past two weeks _____
week _____

Less than once a week _____	Once or twice a week _____	Three or more times a _____
-----------------------------	----------------------------	-----------------------------

e) Other restlessness while you sleep: please describe _____

Not during the past two weeks _____ week _____	Less than once a week _____	Once or twice a week _____	Three or more times a _____
---	-----------------------------	----------------------------	-----------------------------

**GERIATRIC DEPRESSION SCALE
(Short Form)**

DIRECTIONS: To reflect over the *last week* and to choose the best answer for how you have felt.

- | | | | |
|-----|--|-----|----|
| 1. | Are you basically satisfied with your life? | Yes | No |
| 2. | Have you dropped many of your activities and interests? | Yes | No |
| 3. | Do you feel that your life is empty? | Yes | No |
| 4. | Do you often get bored? | Yes | No |
| 5. | Are you in good spirits most of the time? | Yes | No |
| 6. | Are you afraid that something bad is going to happen to you? | Yes | No |
| 7. | Do you feel happy most of the time? | Yes | No |
| 8. | Do you often feel helpless? | Yes | No |
| 9. | Do you prefer to stay at home, rather than going out and doing new things? | Yes | No |
| 10. | Do you feel you have more problems with memory than most? | Yes | No |
| 11. | Do you think it is wonderful to be alive now? | Yes | No |
| 12. | Do you feel pretty worthless the way you are now? | Yes | No |
| 13. | Do you feel full of energy? | Yes | No |
| 14. | Do you feel that your situation is hopeless? | Yes | No |
| 15. | Do you think that most people are better off than you are? | Yes | No |

Form F

Geriatric Anxiety Scale (GAS) – Version 2.0

Below is a list of common symptoms of anxiety or stress. Please read each item in the list carefully.

Indicate how often you have experienced each symptom during the PAST WEEK, INCLUDING TODAY by checking under the corresponding answer.

	Not at all	Sometimes	Most of the time	All of the time
1. My heart raced or beat strongly.	0	1	2	3
2. My breath was short.	0	1	2	3
3. I had an upset stomach.	0	1	2	3
4. I felt like things were not real or like I was outside of myself.	0	1	2	3
5. I felt like I was losing control.	0	1	2	3
6. I was afraid of being judged by others.	0	1	2	3
7. I was afraid of being humiliated or embarrassed.	0	1	2	3
8. I had difficulty falling asleep.	0	1	2	3
9. I had difficulty staying asleep.	0	1	2	3
10. I was irritable.	0	1	2	3
11. I had outbursts of anger.	0	1	2	3
12. I had difficulty concentrating.	0	1	2	3
13. I was easily startled or upset.	0	1	2	3
14. I was less interested in doing something I typically enjoy.	0	1	2	3

15. I felt detached or isolated from others.	0	1	2	3
16. I felt like I was in a daze.	0	1	2	3
17. I had a hard time sitting still.	0	1	2	3
18. I worried too much.	0	1	2	3
	Not at all	Sometimes	Most of the time	All of the time
19. I could not control my worry.	0	1	2	3
20. I felt restless, keyed up, or on edge.	0	1	2	3
21. I felt tired.	0	1	2	3
22. My muscles were tense.	0	1	2	3
23. I had back pain, neck pain, or muscle cramps.	0	1	2	3
24. I felt like I had no control over my life.	0	1	2	3
25. I felt like something terrible was going to happen to me.	0	1	2	3
26. I was concerned about my finances.	0	1	2	3
27. I was concerned about my health.	0	1	2	3
28. I was concerned about my children.	0	1	2	3
29. I was afraid of dying.	0	1	2	3
30. I was afraid of becoming a burden to my family or children.	0	1	2	3

SF-36 QUESTIONNAIRE ITEMS

Name initial: _____

Date: _____

1. In general, would you say your health is:

- Excellent 1
- Very good..... 2
- Good..... 3
- Fair 4
- Poor 5

2. **Compared to one year ago**, how would you rate your health in general **now**?

- Much better now than one year ago 1
- Somewhat better now than one year ago 2
- About the same 3
- Somewhat worse now than one year ago 4
- Much worse now than one year ago 5

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, Limited a Lot	Yes, Limited a Little	No, Not Limited at All
3. Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	1	2	3
4. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.....	1	2	3
5. Lifting or carrying groceries	1	2	3
6. Climbing several flights of stairs	1	2	3
7. Climbing one flight of stairs.....	1	2	3
8. Bending, kneeling, or stooping	1	2	3
9. Walking more than a mile	1	2	3
10. Walking several blocks	1	2	3
11. Walking one block	1	2	3

12. Bathing or dressing yourself 1 2 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	<u>Yes</u>	<u>No</u>
13. Cut down the amount of time you spent on work or other activities	1	2
14. Accomplished less than you would like.....	1	2
15. Were limited in the kind of work or other activities	1	2
16. Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	<u>Yes</u>	<u>No</u>
17. Cut down the amount of time you spent on work or other activities	1	2
18. Accomplished less than you would like.....	1	2
19. Didn't do work or other activities as carefully as usual	1	2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all.....	1
Slightly	2
Moderately	3
Quite a bit.....	4
Extremely	5

21. How much **bodily** pain have you had during the **past 4 weeks**?

None.....	1
Very mild	2
Mild.....	3

- Moderate 4
- Severe..... 5
- Very severe 6

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- Not at all..... 1
- A little bit 2
- Moderately 3
- Quite a bit..... 4
- Extremely..... 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks** . . .

	<u>All of the Time</u>	<u>Most of the Time</u>	<u>A Good Bit of the Time</u>	<u>Some of the Time</u>	<u>A Little of the Time</u>	<u>None of the Time</u>
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?.	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?...	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?.....	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- All of the time 1
- Most of the time 2
- Some of the time 3
- A little of the time 4
- None of the time..... 5

How TRUE or FALSE is each of the following statements for you.

	<u>Definitely</u> <u>True</u>	<u>Mostly</u> <u>True</u>	<u>Don't</u> <u>Know</u>	<u>Mostly</u> <u>False</u>	<u>Definitely</u> <u>False</u>
33. I seem to get sick a little easier than other people.....	1	2	3	4	5
34. I am as healthy as anybody I know.....	1	2	3	4	5
35. I expect my health to get worse.	1	2	3	4	5
36. My health is excellent.	1	2	3	4	5

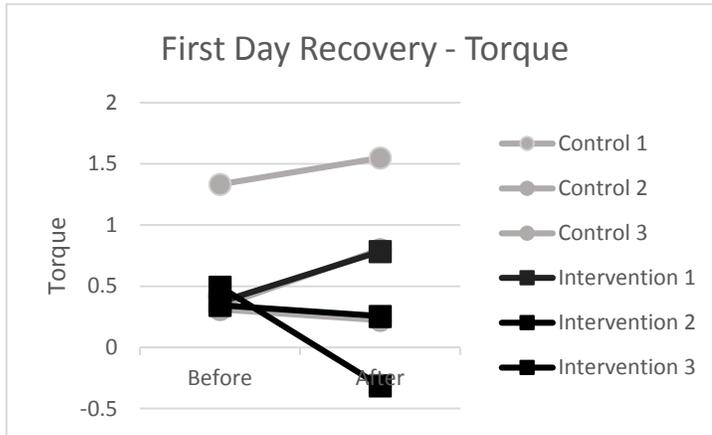
Appendix G – Articles for reading and discussion in Intervention for Patients

List of the titles and first author of articles given to participants for reading and discussion (in no particular order).

- A Mechanism-Based Approach to Prevention of and Therapy for Fibromyalgia – Charles J. Veirck
- Fibromyalgia and nutrition, what do we know? – Laura-Isabel Arranz
- Dietary aspects in fibromyalgia patients: results of a survey on food awareness, allergies and nutritional supplementation – Laura-Isabel Arranz
- Reduced Hypothalamic-Pituitary and Sympathoadrenal Responses to Hypoglycemia in Women with Fibromyalgia Syndrome – Gail K. Alder
- Group Exercise, Education, and Combination Self-management in Women with Fibromyalgia – Daniel S. Rooks
- Cognitive Impairment in Fibromyalgia – Paulo Henrique Ferreira Bertolucci
- Part 1: Clinical Characteristics and Pathophysiology of Fibromyalgia – Lesley M. Arnold
- Part 2: Treatment of Fibromyalgia – Melinda Ring
- Exercise for treating fibromyalgia syndrome (Review) – AJ Busch
- Influence of Weather Conditions on Rheumatic Pain – Ingrid Strusberg

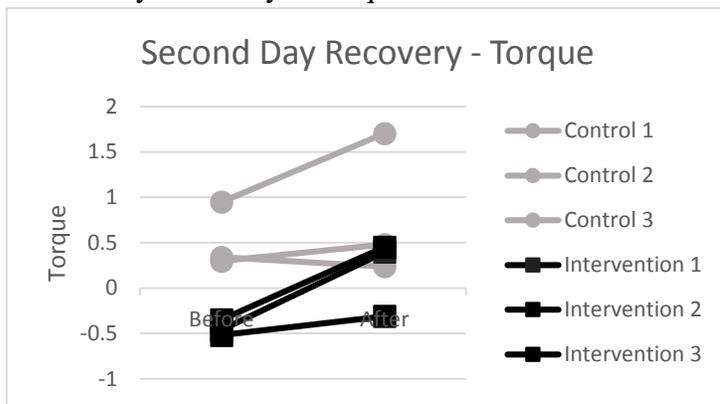
Appendix H – Graphs before/after Qigong Intervention

H – 1: First Day Recovery – Torque



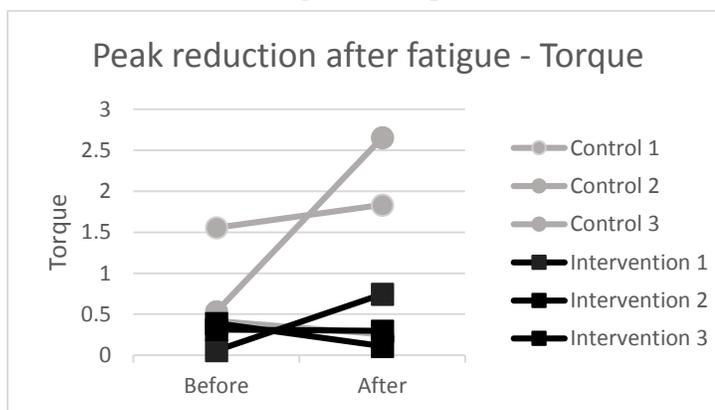
Note: Small number = improved recovery

H – 2: Second Day Recovery – Torque



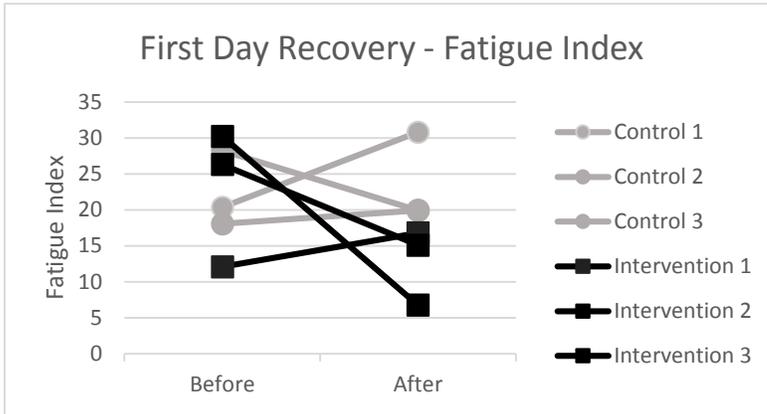
Note: Small number = improved recovery

H – 3: Peak reduction after fatigue – Torque



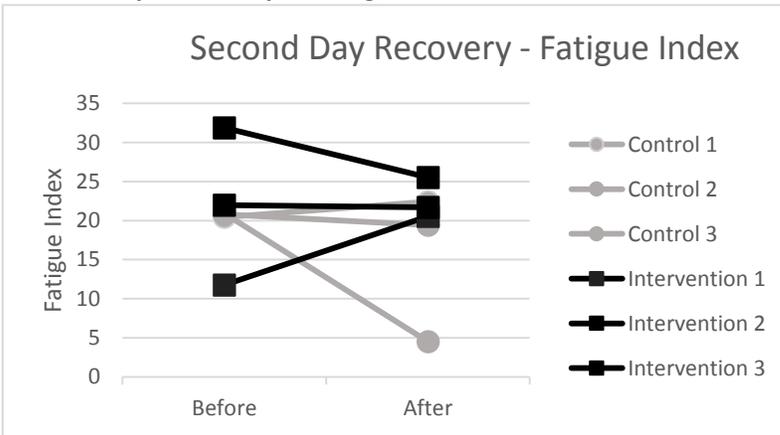
Note: Large number = more fatigue

H – 4: First Day Recovery – Fatigue Index



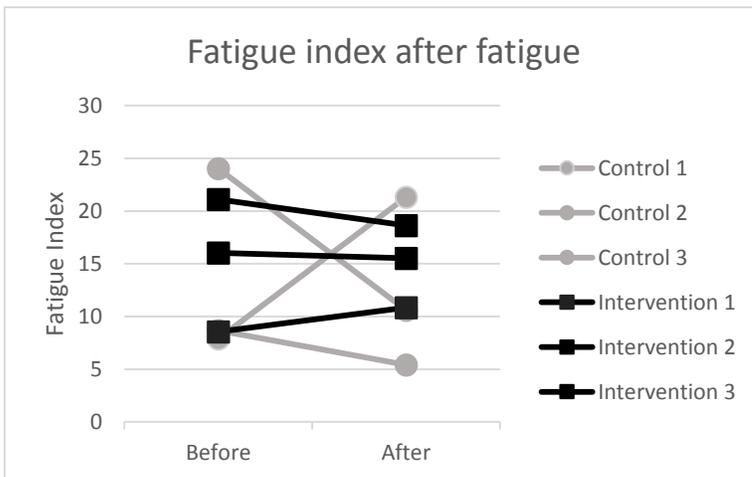
Note: Small number = improved recovery

H – 5: Second Day Recovery – Fatigue Index



Note: Small number = improved recovery

H – 6: Fatigue index after fatigue



Note: Large number = more fatigue