Assistive Technology
The Official Journal of RESNA

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uaty20

Effect of Fully Immersive Virtual Reality Treatment Combined with Exercise in Fibromyalgia Patients: A Randomized Controlled Trial

C Gulsen , F Soke , K Cekim , Y Apaydin , C Ozkul , A Guclu-Gunduz & DT Akcali

To cite this article: C Gulsen , F Soke , K Cekim , Y Apaydin , C Ozkul , A Guclu-Gunduz & DT Akcali (2020): Effect of Fully Immersive Virtual Reality Treatment Combined with Exercise in Fibromyalgia Patients: A Randomized Controlled Trial, Assistive Technology, DOI: 10.1080/10400435.2020.1772900

To link to this article: https://doi.org/10.1080/10400435.2020.1772900

Accepted author version posted online: 16 Jun 2020.

Publisher: Taylor & Francis & RESNA

Journal: Assistive Technology

DOI: 10.1080/10400435.2020.1772900

Effect of Fully Immersive Virtual Reality Treatment Combined with Exercise in Fibromyalgia Patients: A Randomized Controlled Trial

Gulsen C[1], Soke F[1], Eldemir K[1], Apaydin Y[1], Ozkul C[1], Guclu-Gunduz A[1], Akcali DT[2],

[1]Cagri Gulsen, PT. (fztcagri@gmail.com) Gazi University, Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0001-5830-438X

[1]Fatih Soke, PT. (fthsk_8993@hotmail.com) Gazi University, Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0002-8457-1198

[1]Kader Eldemir, PT. (fztkader2015@gmail.com) Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0002-1167-8971

[1]Yasemin Apaydin, PT. (fztyaseminaydin@hotmail.com) Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0001-6650-2632

[1]Cagla Ozkul, Ph.D., PT. (caglaozkul@hotmail.com) Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0001-9367-9910

[1]Arzu Guclu-Gunduz, Associate. Prof. (arzuguclu@hotmail.com) Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey. ORCID ID: 0000-0001-8464-1929

[2]Didem Tuba Akcali, Prof. Dr. (didemakcali@yahoo.com), Gazi University, Faculty of Medicine, Department of Algology, Ankara, Turkey. ORCID ID: 0000-0003-3590-5531

Corresponding author:

Arzu Guclu-Gunduz, Assoc. Prof.

Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Emniyet Mahallesi, Muammer Yasar Bostanci Cad. No:16 Besevler/Ankara, 06500 TURKEY.

e-mailarzuguclu@hotmail.com

Telephone number: +905326528533

Funding: None

Abstract

This trial was designed to evaluate the effects of fully immersive virtual reality (IVR) treatment combined with exercise training in fibromyalgia patients. Twenty patients were randomized into exercise group (EG) or IVR combined with exercise group (Exercise+IVR). The EG had combined exercise training consisted of 30 minutes of aerobic training and 30 minutes of Pilates training and Exercise+IVR group had the same protocol with EG plus 20 minutes of IVR, twice a week for 8 weeks. Visual analogue scale for pain, Modified Sensory Organisation Test for balance, Tampa Scale of Kinesiophobia for kinesiophobia, Fibromyalgia Impact Questionnaire for impact of fibromyalgia, Fatigue Severity Scale for fatigue, International Physical Activity Questionnaire for level of physical activity, six-minute walk test for functional capacity, and Short-Form 36 Health Survey for quality of life were used for evaluation. Pain, balance, kinesiophobia, impact of fibromyalgia, fatigue, level of physical activity, functional exercise capacity and quality of life scores improved significantly in both groups ($p<0.05$). Exercise+IVR group showed significant improvement compared to the EG regarding pain, kinesiophobia, fatigue, level of physical activity and mental component of quality of life ($p<0.05$). IVR treatment may be an effective method as an adjunctive therapy with other exercise trainings in fibromyalgia.

Keywords: Immersive Virtual Reality, Fibromyalgia, Exercise, Pilates, Aerobic Exercise

Introduction

Fibromyalgia (FM) is a debilitating syndrome characterized by chronic widespread pain and tender points in muscles and soft tissues (Wolfe et al., 2010). Other symptoms often include fatigue, somatosensory impairments and disturbances in sleep, cognition and mood. With the effect of these symptoms, patient's quality of life may decrease, and physical and psychosocial disability may occur (Kösehasanoğulları et al., 2019). Compared with healthy subjects, FM patients are less physically active, they have significantly lower perceived functional ability and they demonstrate worsened physical performance (McLoughlin et al., 2011). As a result of these impaired physical fitness, FM patients tend to have a sedentary lifestyle that worsens symptoms and increases the risks of additional morbidity (Bidonde et al., 2017). Exercise training is an effective and low-cost non-pharmacological management strategy of FM. Exercise is known to enhance feelings of “energy” and improves quality of life, cognitive function, anxiety, depression, pain, sleep quality and stress responses (Busch et al., 2011). Previous researches demonstrated that combined exercise programs have more positive effects compared to single type of exercises in FM (Okifuji et al., 2016; Sañudo et al., 2010). Exercise programs including flexibility training, strength maintenance, endurance and aerobic conditioning are accepted as a standard treatment protocol in FM ((Okifuji et al., 2016; Winkelmann et al., 2017). There is a growing evidence and strong recommendation of using aerobic and strengthening training together for FM treatment (Macfarlane et al., 2017). Studies investigating the effect of combined exercise programs consisting of aerobic, strength and flexibility training on FM patients show beneficial effects (García-Martínez et al., 2012; Rooks et al., 2007; Sañudo et al., 2011). Pilates covers a combination of muscle strengthening, flexibility and endurance training. It has been used for a long time in rehabilitation settings, but its use for FM treatment is relatively new (Parikh & Arora, 2016). Pilates studies in FM suggest favorable results (Altan et al., 2009; Ekici et al., 2017; Komatsu et al., 2016). Aerobic training in FM patients also leads improvements (Bircan et al., 2008; Hooten et al., 2012; Richards & Scott, 2002; Wigers et al., 1996). However, it is still not clear that whether the combined exercises consist of aerobic training and Pilates are effective in FM patients due to lack of evidence.

Virtual reality (VR) is a novel approach in the field of pain management. While exact mechanisms remain unclear to reduce pain, it is suggested that VR can direct the individual’s attention away from the real world into the virtual environment and by diverting attention, pain reduction can be possible (White et al., 2018). With VR specific games, improvements in physical symptoms such as mobility skills, balance, fatigue etc. were also demonstrated (Martín-Martínez et al., 2019). Therefore, VR is used as an adjunctive therapy method for pain management, and it improves the physical performance (Garrett et al., 2017; Wiederhold et al., 2014).

VR technologies can be classified as non-immersive, semi-immersive and fully immersive according to the immersion level. Immersion is an objective and technology-related component of VR, and it makes its user's experience of psychological, perceptual, and "feel of being there" (Lee et al., 2020). Non-immersive systems consist of computer screens or TV monitors and platforms such as Nintendo Wii, X-box Kinect, which is low cost but have very low sense of immersion. Semi-immersive systems have same platforms but for higher sense of immersion, they use better displays such as panoramic TVs. Fully-immersive VR technologies use head-mounted displays (HMD) such as Oculus Rift and HTC Vive, which is relatively expensive but have very high sense of immersion (Lee et al., 2020; Rose et al., 2018). For the practice of the real world tasks, immersive virtual environments are more relevant than non-immersive ones as they also have the capability of providing feedback for the participants (Kozhevnikov et al., 2005). It is also thought that immersion quality is related to the quality of distraction away from pain, and high immersion level produce more pain reduction than lower ones (Shahrbanian et al., 2012).

Studies investigating the effect of VR treatment in FM used non-immersive VR technologies such as exergames (Collado-Mateo et al., 2017; Garcia-Palacios et al., 2015; Martín-Martínez et al., 2019; Villafaina et al., 2019). To the best of our knowledge, there is no study investigating the effect of fully immersive VR treatment as an adjunctive therapy on FM patients. Also we did not come across any study combining VR with Pilates and aerobic training in FM patients. Therefore, the aim of this randomized controlled trial was to evaluate the effects of IVR treatment combined with exercise training in FM patients.

Materials and Methods

Design

This study was designed as a single blinded, randomized controlled trial with two groups: an exercise group and IVR combined with exercise group (exercise+IVR). All the patients were provided with written informed consent to participate, and the study protocol was approved by the Clinical Research Ethics Committee of the Gazi University. Patients were assigned to computer-generated random code numbers, and then they were randomly allocated into one of the groups. Researchers who evaluated the patients were blinded. Participants were not blinded due to they were informed about the protocol and knew they participated in the IVR intervention or did not.

Subjects

The study took place at the Faculty of Health Sciences, Department of Physical Therapy and Rehabilitation of Gazi University in Ankara, Turkey between January 2018 and March 2019. Participants were recruited from Gazi University Hospital, Department of Algology. Inclusion criteria were: a) diagnosed with FM in accordance with the American College of Rheumatology criteria (Wolfe et al., 2010) by a specialist physician, b) accepting to participate in the study, c) being between the age of 18 and 65 years, d) not having a cardiovascular, pulmonary, hormonal or orthopedic disease, e) not having a inability to prevent doing exercise, f) being able to communicate effectively with the researchers. Exclusion criteria were: a) having any vision, hearing, perception or sensation problem that may affect research results, b) having additional rheumatological disease (rheumatoid arthritis, osteoarthritis, etc.), c)using medication other than the prescribed pharmacologic agents for FM symptoms, d) have been using opioids for longterm. Patients were removed from the study if they had injection for tender points during intervention period.

Outcome Measurements

Demographic and clinical characteristics of the patients included in the study were obtained. Patients were evaluated on baseline and post-treatment.

Pain: Pain was measured on a 10 cm visual analogue scale (VAS), on which the patients marked the pain they had experienced in last seven days (0 = no pain, 10 = the worst pain imaginable).

Balance: Modified Sensory Organisation Test (MSOT) was used to examine the effects of somatosensory, vestibular and vision sensations on balance (Arnold & Schmitz, 1998). The test was conducted by using the Biodex Balance System (Shirley, NY, USA). The test comprises four conditions: eyes open on a firm surface, eyes closed on a firm surface, eyes open on a foam surface, and eyes closed on a foam surface. Participants have to maintain their feet on the platform during the 30 s test, with a rest of 10 s between each condition. Higher sway point would mean poorer balance.

Kinesiophobia: The Turkish version of the 17-item Tampa scale for kinesiophobia (TSK) was used to measure the fear of movement and reinjury due to movement. The TSK is a self-completed four-point Likert scale, ranging from strongly dis-agree to strongly agree. Four items (i.e., items 4, 8, 12and 16) are inversely phrased and the range of scores are from 17 to 68 where the higher scores indicate an increase in the kinesiophobia degree (Roelofs et al., 2004).

Impact of Fibromyalgia: Impact of fibromyalgia was assessed by using the Turkish version of the10-item Fibromyalgia Impact Questionnaire (FIQ). FIQ is a self-administered test which measures physical function, work status, depression, anxiety, sleep, pain, stiffness, fatigue and well-being. Total scores range from 0 to 100 where higher scores indicate more severe symptoms and disability (Burckhardt et al., 1991).

Fatigue: The Turkish version of the Fatigue Severity Scale (FSS) was used to assess the perceived impact of fatigue in last 4 weeks. The FSS is a unidimensional 9-item measure that evaluates fatigue severity. Each question scores between 1 (strongly disagree) and 7 (strongly agree). The overall score is the mean of the rating from the 9 item and recorded as the FSS score. Higher scores indicate more perceived fatigue (Krupp et al., 1989).

Level of Physical Activity: The level of physical activity was assessed by the Turkish version of long form of the International Physical Activity Questionnaire (IPAQ). The questionnaire examines frequency, intensity and total time of physical activity in different situations such as; work, transportation, housework-house care-family care, recreation-sport-free time and total time of sitting in last week. Higher scores indicate higher level of activity (Kim et al., 2013).

Functional Exercise Capacity: Functional Exercise Capacity was assessed by the Six-Minute Walk Test (6-MWT). In 6-MWT, heart rate, blood pressure and fatigue severity of the participants are recorded before and after the test. The participants are asked to walk as far as possible during 6 min in a 30 m corridor, and they are verbally encouraged every two minutes during walking. Finally the walking distance is recorded in meters (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). The heart rate was assessed by a heart rate monitor (Polar FT 100, China), and fatigue severity was assessed by modified Borg Scale during test procedure.

Quality of Life: Health-related quality of life was measured by using Turkish version of Short Form 36 (SF-36). It comprises 36 questions in 8 subscales: physical functioning, role limitations because of physical health, bodily pain, mental health, role limitations because of emotional health, social functioning, vitality and general health. All subscales range from 0 to 100, with a higher value indicating a better perceived health (Ware Jr & Sherbourne, 1992).

Intervention

Patients in both groups attended sessions monitored by an experienced physical therapist twice a week for 8 weeks. The exercise group had a combined exercise training consisting of 30 minutes of aerobic training and 30 minutes of Pilates which included strengthening and flexibility exercises. Exercise+IVR group had 20 minutes of IVR treatment in addition to the same protocol. Ten minutes of resting period was given between each training.

Aerobic Training*:* The aerobic training was given via a treadmill, and it consisted of 5 minutes warm up period, 20 minutes of training period at the level of 60-80% of maximal heart rate, and 5 minutes of cool down period.

Pilates Training: Pilates training program starting with centering in supine position for warm-up was implemented. The difficulty of the exercises was gradually increased by using different positions and elastic bands. Stretching exercises were used as a cool down period.

Immersive Virtual Reality Training: The IVR application we use was the live, direct or indirect physical appearance of the real-world environment and its contents which were enriched by computer generated audio, image, graphics and location data. Parts of the device to be used in the IVR application are listed below:

1. Computer: Consisted of system unit, monitor, keyboard, mouse and speaker.

2. Infrared Camera: Xbox Kinect sensor was used to detect body movements.

3. Head-mounted display: Oculus head-mounted display was used.

Two games were used for IVR training which were developed in our clinic with help of RAGU (Augmented Reality Applications in Rehabilitation) System and which aimed to improve balance and mobility. The first was a 10 minute football game in which the patient was asked to counter the balls from different heights by using their hands and feet. The second was a 10 minute dungeon game, the patient was asked to avoid guillotines by tilting the trunk to the right, left, forward and backward without moving his/her feet and logs by standing on single leg or jump with both legs. The level of difficulty was increased according to the patient's performance in both games. Balls speed was increased gradually in football game, and direction of ball randomly was adjusted to patient's foot or hand in order to increase the difficulty. Coming order of guillotines and logs were also randomly adjusted for the difficulty. Patients could see their scores at the end of the games. To increase the participation, they were encouraged to make better scores than previous session. A harness system was used to ensure patients safety.

Statistical Analyses

Data analysis was performed by using IBM SPSS Statistics 21.0 (IBM Corp. Armonk, NY). Descriptive data are presented as median (IQR 25% and 75%). χ2 tests used for the comparison of categorical data. A Mann-Whitney U test was used for continuous and ordinal variables to compare the change of values between before and after the intervention of the groups. A Wilcoxon signed rank test was used for the comparison between baseline and post-intervention within groups for continuous variables. A P-value of < 0.05 was considered statistically significant.

Results

The flow of participants is shown in Figure 1. 33 patients with FM were assessed for eligibility, a total of 20 patients allocated; however, 16 patients completed the study and analyzed. There were no differences between the groups at baseline in any of the demographic variables: age, BMI and disease duration, education and participation of regular physical activity ($p > 0.05$, Table 1).

Before the intervention, there were no differences between the groups in terms of pain, balance, kinesiophobia, impact of fibromyalgia, fatigue, level of physical activity, functional exercise capacity and quality of life ($p > 0.05$, Table 2). After the intervention, scores for pain, balance, kinesiophobia, impact of fibromyalgia, fatigue, level of physical activity, functional exercise capacity and quality of life improved significantly in both groups ($p < 0.05$, Table 2). When two groups were compared to each other, exercise+IVR group showed statistically more significant improvement than exercise group regarding pain, kinesiophobia, fatigue severity, level of physical activity and mental component of quality of life ($p < 0.05$, Table 3).

Discussion

This study shows that Pilates and aerobic training are more effective when combined with IVR in terms of kinesiophobia, pain, fatigue, level of physical activity and mental component of quality of life. Additionally, the results indicated that Pilates and aerobic training reduced pain, kinesiophobia, impact of fibromyalgia, fatigue and improving balance, level of physical activity, functional exercise capacity and quality of life in FM.

Changes in pain, kinesiophobia, fatigue, level of physical activity and mental component of quality of life showed that Pilates and aerobic training combined with IVR treatment were more effective than exercise without IVR in FM patients. To our knowledge this is first study investigating the effects of IVR treatment as an adjunctive therapy in FM patients. Therefore, the evidence of the effectiveness is limited. However, when we looked at the studies investigating the effects of non-immersive VR treatment on FM patients, in 2017, Collado-Mateo et al. showed eight week training of exergame designed to improve physical conditioning and increase ability to perform activities of daily living have similar results to our study regarding of balance and improvement in fear of falling. Another randomized controlled trial by Villafaina et al. in 2019, found that non-immersive VR treatment had beneficial effects on pain and quality of life in FM.

We did not come across any study investigating the effects of non-immersive VR treatment on functional exercise capacity in FM patients, but in a study in Parkinson’s disease patients, it was observed that non-immersive VR treatment had no additional improvement in terms of functional exercise capacity (de Melo et al., 2018). Another study in Parkinson's disease patients showed similar results with the previous study regarding the functional exercise capacity (Ferraz et al., 2018). These studies have similar results with our study in terms of functional exercise capacity. Therefore, it is possible to conclude that VR treatments have no additional effects on functional exercise capacity compared to combined exercise alone.

A possible explanation to better outcomes in pain, kinesiophobia, fatigue, level of physical activity and mental component of quality of life that IVR treatment may effectively overcome the fear of movement. Our previous study showed that kinesiophobia had a negative impact on pain, fatigue, impact of fibromyalgia and quality of life in FM patients (Gülşen et al. 2018). It is also reported that kinesiophobia negatively affects pain (Comachio et al., 2018; Demirbüken et al., 2016; Larsson et al., 2016; Luque-Suarez et al., 2019), fatigue (Celletti et al., 2013), level of physical activity (Demirbüken et al., 2016) and quality of life (Comachio et al., 2018; Larsson et al., 2016; Luque-Suarez et al., 2019) in chronic pain patients. IVR treatment has a very high sense of immersion and offers more enjoyable experience to patients (Nichols et al., 2000). In chronic fatigue patients, kinesiophobia was found to be associated with activity limitations/participation restrictions (Nijs et al., 2004). We can speculate that higher degree of enjoyment leads higher degree of participation of patients. In light of the results obtained from this study, we can conclude that increased level of participation may eliminate negative effects of kinesiophobia on pain, fatigue, level of physical activity and mental component of quality of life.

Similar to our results, studies investigating the effects of combined exercise programs consisting of aerobic, strengthening and flexibility exercises on FM patients showed improvement in pain (García-Martínez et al., 2012), impact of fibromyalgia and quality of life (Rooks et al., 2007; Sañudo et al., 2011). We cannot find any evidence for the effect of combined exercise regarding of balance, kinesiophobia, level of physical activity and functional exercise capacity in FM. When the literature is examined, it is seen that the effects of Pilates and aerobic training are examined separately. There is no study that combines Pilates and aerobic training.

When we looked at the studies investigating the effects of Pilates in FM (Altan et al., 2009; Ekici et al., 2017; Komatsu et al., 2016); we similarly found improvements in pain (Altan et al., 2009; Ekici et al., 2017; Komatsu et al., 2016), impact of fibromyalgia (Ekici et al., 2017; Komatsu et al., 2016), and quality of life (Ekici et al., 2017; Komatsu et al., 2016). Additionally, aerobic training in FM patients also leads improvements in terms of pain (Bircan et al., 2008; Hooten et al., 2012; Richards & Scott, 2002; Wigers et al., 1996), impact of fibromyalgia (Bircan et al., 2008; Richards & Scott, 2002), fatigue (Bircan et al., 2008), functional exercise capacity (Bircan et al., 2008) and quality of life (Bircan et al., 2008; Richards & Scott, 2002).

Moreover, it is still not clear that whether the combined exercises consisting of aerobic, strength and flexibility training are effective on fatigue, balance, kinesiophobia and level of physical activity in FM patients due to lack of evidence. Positive effects of Pilates regarding of balance (Cruz-Díaz et al., 2015; de Oliveira et al., 2019; Valenza et al., 2017), kinesiophobia (Cruz-Díaz et al., 2017, 2018), and level of physical activity (Ruiz-Montero et al., 2019) were shown in chronic pain patients. Aerobic training in chronic pain patients have similar results in terms of balance (Bressel et al., 2014; Irandoust et al., 2018), kinesiophobia (Mannion et al., 1999) and level of physical activity (Ilves at al., 2017). Although these results are related to chronic pain patients, it is seen that the improvements obtained are based on the same hypothesis as our study.

The present study has some limitations and strengths that should be mentioned. First, small sample size may affect the comparisons, and it is difficult to generalize the findings. Second, all analyzed patients were female, so we cannot generalize the findings to male patients. Third, the enjoyment levels of patients were not assessed, so any relationship between enjoyment and kinesiophobia could not be investigated. However, this is the first study investigating the effects of IVR treatment as an adjunctive therapy in FM patients. This is the one of very few studies examining the effects of a combined exercise method in such a wide frame on FM patients.

Conclusion

Combined exercise training had positive effects on FM patients. IVR treatment may be an effective method as an adjunctive therapy with other exercise modalities since it has elevated the positive effects of exercise on kinesiophobia, pain, fatigue, level of physical activity and mental component of quality of life.

Acknowledgments

None

Author Disclosure Statement

No competing financial interests exist.

References

Altan, L., Korkmaz, N., Bingol, U., & Gunay, B. (2009). Effect of pilates training on people with fibromyalgia syndrome: a pilot study. *Archives of Physical Medicine and Rehabilitation*, *90*(12), 1983–1988.

Arnold, B. L., & Schmitz, R. J. (1998). Examination of balance measures produced by the biodex stability system. *Journal of athletic training*, *33*(4), 323–327.

ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. (2002). ATS statement: guidelines for the six-minute walk test. *American Journal of Respiratory and Critical Care Medicine*, *166*(1), 111-117.

Bidonde, J., Busch, A. J., Schachter, C. L., Overend, T. J., Kim, S. Y., Góes, S. M., Boden, C., & Foulds, H. J. (2017). Aerobic exercise training for adults with fibromyalgia. *The Cochrane database of systematic reviews*, *6*(6), CD012700.

Bircan, Ç., Karasel, S.A., Akgün, B., El, O., & Alper, S. (2008). Effects of muscle strengthening versus aerobic exercise program in fibromyalgia. *Rheumatology International*, *28*(6), 527–532.

Bressel, E., Wing, J. E., Miller, A. I., & Dolny, D. G. (2014). High-intensity interval training on an aquatic treadmill in adults with osteoarthritis: effect on pain, balance, function, and mobility. *The Journal of Strength & Conditioning Research*, *28*(8), 2088-2096.

Burckhardt, C. S., Clark, S. R., & Bennett, R. M. (1991). The fibromyalgia impact questionnaire: development and validation. *The Journal of Rheumatology*, *18*(5), 728-733.

Busch, A. J., Webber, S. C., Brachaniec, M., Bidonde, J., Bello-Haas, V. D., Danyliw, A. D., Overend, T. J., Richards, R. S., Sawant, A., & Schachter, C. L. (2011). Exercise therapy for fibromyalgia. *Current pain and headache reports*, *15*(5), 358–367.

Celletti, C., Castori, M., La Torre, G., & Camerota, F. (2013). Evaluation of kinesiophobia and its correlations with pain and fatigue in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type. *BioMed research international*, 2013, 580460.

Collado-Mateo, D., Domínguez-Muñoz, F. J., Adsuar, J. C., Merellano-Navarro, E., & Gusi, N. (2017). Exergames for women with fibromyalgia: a randomised controlled trial to evaluate the effects on mobility skills, balance and fear of falling. *PeerJ*, *5*, e3211.

Comachio, J., Magalhães, M. O., Silva, A. P. D. M. C., & Marques, A. P. (2018). A cross-sectional study of associations between kinesiophobia, pain, disability, and quality of life in patients with chronic low back pain. *Advances in Rheumatology*, *58*(1),8.

Cruz-Díaz, D., Bergamin, M., Gobbo, S., Martínez-Amat, A., & Hita-Contreras, F. (2017). Comparative effects of 12 weeks of equipment based and mat Pilates in patients with Chronic Low Back Pain on pain, function and transversus abdominis activation. A randomized controlled trial. *Complementary therapies in medicine*, *33*, 72-77.

Cruz-Díaz, D., Martínez-Amat, A., Manuel, J., Casuso, R. A., de Guevara, N. M. L., & Hita-Contreras, F. (2015). Effects of a six-week Pilates intervention on balance and fear of falling in women aged over 65 with chronic low-back pain: A randomized controlled trial. *Maturitas*, *82*(4), 371-376.

Cruz-Díaz, D., Romeu, M., Velasco-González, C., Martínez-Amat, A., & Hita-Contreras, F. (2018). The effectiveness of 12 weeks of Pilates intervention on disability, pain and kinesiophobia in patients with chronic low back pain: a randomized controlled trial. *Clinical rehabilitation*, *32*(9), 1249-1257.

de Melo, G. E. L., Kleiner, A. F. R., Lopes, J. B. P., Dumont, A. J. L., Lazzari, R. D., Galli, M., & Oliveira, C. S. (2018). Effect of virtual reality training on walking distance and physical fitness in individuals with Parkinson's disease. *NeuroRehabilitation*, *42*(4), 473-480.

de Oliveira, N. T. B., Ricci, N. A., dos Santos Franco, Y. R., Santo Salvador, E. M. E., Almeida, I. C. B., & Cabral, C. M. N. (2019). Effectiveness of the Pilates method versus aerobic exercises in the treatment of older adults with chronic low back pain: a randomized controlled trial protocol. *BMC musculoskeletal disorders*, *20*(1), 250.

Demirbüken, İ., Özgül, B., Kuru Çolak, T., Aydoğdu, O., Sarı, Z., & Yurdalan, S. U. (2016). Kinesiophobia in relation to physical activity in chronic neck pain. *Journal of back and musculoskeletal rehabilitation*, *29*(1), 41-47.

Ekici, G., Unal, E., Akbayrak, T., Vardar-Yagli, N., Yakut, Y., & Karabulut, E. (2017). Effects of active/passive interventions on pain, anxiety, and quality of life in women with fibromyalgia: randomized controlled pilot trial. *Women & Health, 57*(1), 88–107.

Ferraz, D. D., Trippo, K. V., Duarte, G. P., Neto, M. G., Santos, K. O. B., & Oliveira Filho, J. (2018). The effects of functional training, bicycle exercise, and exergaming on walking capacity of elderly patients with Parkinson disease: a pilot randomized controlled single-blinded trial. *Archives of physical medicine and rehabilitation*, *99*(5), 826-833.

García-Martínez, A.M., De Paz, J.A. & Márquez, S. (2012). Effects of an exercise programme on self-esteem, self-concept and quality of life in women with fibromyalgia: a randomized controlled trial. *Rheumatology International*, *32*, 1869–1876.

Garcia-Palacios, A., Herrero, R., Vizcaíno, Y., Belmonte, M.A., Castilla, D., Molinari, G., Baños, R.M., & Botella, C. (2015). Integrating virtual reality with activity management for the treatment of fibromyalgia: acceptability and preliminary efficacy. *The Clinical Journal of Pain, 31*(6), 564–572.

Garrett, B., Taverner, T., & McDade, P. (2017). Virtual Reality as an Adjunct Home Therapy in Chronic Pain Management: An Exploratory Study. *JMIR medical informatics*, *5*(2), e11.

Gülşen, Ç., GÜNDÜZ, A. G., SÖKE, F., ÇEKİM, K., AYDIN, Y., & AKÇALI, D. (2018). AB1398-HPR The effects of kinesiophobia on pain, fatigue severity, functional exercise capacity, functional status and quality of life in fibromyalgia. *Annals of the Rheumatic Diseases, 77*(Suppl 2), 1835.

Hooten, W.M., Qu, W., Townsend, C.O., & Judd, J.W. (2012). Effects of strength vs aerobic exercise on pain severity in adults with fibromyalgia: a randomized equivalence trial. *Pain*, *153*(4), 915–923.

Ilves, O., Häkkinen, A., Dekker, J., Wahlman, M., Tarnanen, S., Pekkanen, L., Ylinen, J., Kautiainen, H., & Neva, M. (2017). Effectiveness of postoperative home-exercise compared with usual care on kinesiophobia and physical activity in spondylolisthesis: A randomized controlled trial. *Journal of Rehabilitation Medicine*, 49(9), 751-757.

Irandoust, K., Taheri, M., & Shavikloo, J. (2018). The effect of water-based aerobic training on the dynamic balance and walking speed of obese elderly men with low back pain. *Sleep Hypn*, *20*, 233-40.

Kim, Y., Park, I., & Kang, M. (2013). Convergent validity of the international physical activity questionnaire (IPAQ): meta-analysis. *Public Health Nutrition*, *16*(3), 440-52.

Komatsu, M., Avila, M.A., Colombo, M.M., Gramani-Say, K., & Driusso, P. (2016). Pilates training improves pain and quality of life of women with fibromyalgia syndrome. *Revista Dor*, *17*(4), 274-278.

Kösehasanoğulları, M., Erdinç-Gündüz, N., & Akalın, E. (2019). Is fibromyalgia syndrome a neuropathic pain syndrome? *Archives of Rheumatology*, *34*(2), 196-203.

Kozhevnikov, M., Kosslyn, S., & Shephard, J. (2005). Spatial versus object visualizers: A new characterization of visual cognitive style. *Memory & Cognition*, *33*(4), 710–726.

Krupp, L. B., LaRocca, N. G., Muir-Nash, J., & Steinberg, A. D. (1989). The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of neurology*, *46*(10), 1121-1123.

Larsson, C., Hansson, E. E., Sundquist, K., & Jakobsson, U. (2016). Kinesiophobia and its relation to pain characteristics and cognitive affective variables in older adults with chronic pain. *BMC geriatrics*, *16*(1), 128.

Lee, S.H., Jung, H.Y., Yun, S.J., Oh, B.M., & Seo, H.G. (2020). Upper extremity rehabilitation using fully ımmersive virtual reality games with a head mount display: a feasibility study. *PM & R*, *12*(3), 257-262.

Luque-Suarez, A., Martinez-Calderon, J., & Falla, D. (2019). Role of kinesiophobia on pain, disability and quality of life in people suffering from chronic musculoskeletal pain: a systematic review. *Br J Sports Med*, *53*(9), 554-559.

Macfarlane, G.J., Kronisch, C., Dean, L.E., Atzeni, F., Häuser, W., Fluß, E., Choy, E., Kosek, E., Amris, K., Branco, J., Dincer, F., Leino-Arjas, P., Longley, K., McCarthy, G.M., Makri, S., Perrot, S., Sarzi-Puttini, P., Taylor, A., & Jones, G.T. (2017). EULAR revised recommendations for the management of fibromyalgia. *Annals of the Rheumatic Diseases*, *76*(2), 318-328.

Mannion, A. F., Müntener, M., Taimela, S., & Dvorak, J. (1999). A randomized clinical trial of three active therapies for chronic low back pain. *Spine (Phila Pa 1976)*, *24*, 2435–48.

Martín-Martínez, J.P., Villafaina, S., Collado-Mateo, D., Pérez-Gómez, J., & Gusi N. (2019). Effects of 24-week exergame intervention on physical function under single- and dual-task conditions in fibromyalgia: A randomized controlled trial. *Scandinavian Journal of Medicine & Science in Sports*, *29*(10), 1610-1617.

McLoughlin, M. J., Colbert, L. H., Stegner, A. J., & Cook, D. B. (2011). Are women with fibromyalgia less physically active than healthy women?. *Medicine and science in sports and exercise*, *43*(5), 905–912.

Nichols, S., Haldane, C., & Wilson, J. R. (2000). Measurement of presence and its consequences in virtual environments. *International Journal of Human-Computer Studies*, *52*(3), 471-491.

Nijs, J., De Meirleir, K., & Duquet, W. (2004). Kinesiophobia in chronic fatigue syndrome: assessment and associations with disability. *Archives of physical medicine and rehabilitation*, *85*(10), 1586-1592.

Okifuji, A., Gao, J., Bokat, C., & Hare, B. D. (2016). Management of fibromyalgia syndrome in 2016. *Pain management*, *6*(4), 383–400.

Parikh, C.M., & Arora, M. (2016). Role of Pilates in rehabilitation: A literature review. *International Journal of Therapies and Rehabilitation Research*, *5*(4), 77-83.

Richards, S. C., & Scott, D. L. (2002). Prescribed exercise in people with fibromyalgia: parallel group randomised controlled trial. *BMJ (Clinical research ed.)*, *325*(7357), 185.

Roelofs, J., Goubert, L., Peters, M.L., Vlaeyen, J.W., & Crombez, G. (2004). The Tampa Scale for Kinesiophobia: further examination of psychometric properties in patients with chronic low back pain and fibromyalgia. *European Journal of Pain, 8*(5), 495-502.

Rooks, D.S., Gautam, S., Romeling, M., Cross, M.L., Stratigakis, D., Evans, B., Goldenberg, D.L., Iversen, M.D., & Katz, J.N. (2007). Group exercise, education, and combination self-management in women with fibromyalgia: a randomized trial. *Archives of Internal Medicine*, *167*(20), 2192-2200.

Rose, T., Nam, C. S., & Chen, K. B. (2018). Immersion of virtual reality for rehabilitation-Review. *Applied ergonomics*, *69*, 153-161.

Ruiz-Montero, P. J., Ruiz-Rico Ruiz, G. J., Martín-Moya, R., & González-Matarín, P. J. (2019). Do Health-Related Quality of Life and Pain-Coping Strategies Explain the Relationship between Older Women Participants in a Pilates-Aerobic Program and Bodily Pain? A Multiple Mediation Model. *International journal of environmental research and public health*, *16*(18), 3249.

Sañudo, B., Galiano, D., Carrasco, L., Blagojevic, M., de Hoyo, M., & Saxton, J. (2010). Aerobic exercise versus combined exercise therapy in women with fibromyalgia syndrome: a randomized controlled trial. *Archives of physical medicine and rehabilitation*, *91*(12), 1838-43.

Sañudo, B., Galiano, D., Carrasco, L., de Hoyo, M., & McVeigh, J.G. (2011). Effects of a prolonged exercise program on key health outcomes in women with fibromyalgia: a randomized controlled trial. *Journal of Rehabilitation Medicine*, *43*(6), 521-526.

Shahrbanian, S., Ma, X., Aghaei, N., Korner-Bitensky, N., Moshiri, K., & Simmonds, M.J. (2012). Use of virtual reality (immersive vs. non immersive) for pain management in children and adults: A systematic review of evidence from randomized controlled trials. *European Journal of Experimental Biology*, *2*(5):1408-1422.

Valenza, M. C., Rodríguez-Torres, J., Cabrera-Martos, I., Díaz-Pelegrina, A., Aguilar-Ferrándiz, M. E., & Castellote-Caballero, Y. (2017). Results of a Pilates exercise program in patients with chronic non-specific low back pain: a randomized controlled trial. *Clinical rehabilitation*, *31*(6), 753-760.

Villafaina, S., Collado-Mateo, D., Domínguez-Muñoz, F.J., Fuentes-García, J.P., & Gusi, N. (2019). Benefits of 24-Week Exergame Intervention on Health-Related Quality of Life and Pain in Women with Fibromyalgia: A Single-Blind, Randomized Controlled Trial. *Games for Health Journal*, 8(6), 380-386.

Ware Jr, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical care*, 473-483.

White, M.P., Yeo, N.L., Vassiljev, P., Lundstedt, R., Wallergård, M., Albin, M., & Lõhmus, M. (2018). A prescription for "nature" - the potential of using virtual nature in therapeutics. *Neuropsychiatric Disease and Treatment, 14*, 3001-3013.

Wiederhold, B. K., Gao, K., Kong, L., & Wiederhold, M. D. (2014). Mobile devices as adjunctive pain management tools. *Cyberpsychology, behavior and social networking*, *17*(6), 385–389.

Wigers, S.H., Stiles, T.C., & Vogel, P.A. (1996) Effects of aerobic exercise versus stress management treatment in fibromyalgia. *Scandinavian Journal of Rheumatology*, *25*(2), 77-86.

Winkelmann, A., Bork, H., Brückle, W., Dexl, C., Heldmann, P., Henningsen, P., Krumbein, L., Pullwitt, V., Schiltenwolf, M., & Häuser, W. (2017). Physiotherapie, Ergotherapie und physikalische Verfahren beim Fibromyalgiesyndrom: Aktualisierte Leitlinie 2017 und Übersicht von systematischen Übersichtsarbeiten [Physiotherapy, occupational therapy and physical therapy in fibromyalgia syndrome: Updated guidelines 2017 and overview of systematic review articles]. *Der Schmerz, 31*(3), 255-265.

Wolfe, F., Clauw, D.J., Fitzcharles, M.A., Goldenberg, D.L., Katz, R.S., Mease, P., Russell, A.S., Russell, I.J., Winfield, J.B., & Yunus, M.B. (2010). The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care & Research, 62*(5), 600-610.

Table 1. Baseline characteristics of groups

	Exercise Group (n = 8)	Exercise+IVR Group (n = 8)	
	Median (IQR 25-75) n(%)	Median (IQR 25-75) n(%)	p
Age (years)	38.50 (29.50-50.00)	46.50 (36.50-49.50)	0.636[a]
BMI	22.85 (20.52-28.56)	26.81 (23.74-30.69)	0.328[a]
Disease Duration (years)	4 (2-7.5)	4 (2.5-8)	0.830[a]
Sex			n/a
Female	8 (100)	8 (100)	
Male	0 (0)	0 (0)	
Education Level			0.788[b]
Primary Education	3 (37.5)	4 (50)	
Secondary Education	2 (25)	1 (12.5)	
Higher Education	3 (37.5)	3 (37.5)	
Participation of Regular Physical Activity			n/a
Yes	0 (0)	0 (0)	
No	8 (100)	8 (100)	

Data were given median (25^{th}-75^{th}IQR) or n (%), [a]Mann-Whitney U Test, [b] Chi-square Test

Table 2. Comparison of groups before and after the interventions

	Exercise Group (n = 8) Before	Exercise Group (n = 8) After	Within-group comparison	Exercise+IVR Group (n = 8) Before	Exercise+IVR Group (n = 8) After	Within-group comparison	Between group comparison on the baseline
	Median (IQR)	Median (IQR)	p[a]	Median (IQR)	Median (IQR)	p[a]	p[b]
VAS, cm	7.40 (5.92-8.35)	4.50 (3.47-5.72)	0.012*	8.00 (7.55-8.95)	3.95 (3.32-4.5)	0.012*	0.225
MSOT, sway point							
-Eyes open Firm surface	0.42 (0.35-0.49)	0.34 (0.25-0.38)	0.018*	0.48 (0.42-0.80)	0.42 (0.29-0.67)	0.012*	0.066
-Eyes closed Firm surface	0.70 (0.52-1.01)	0.61 (0.47-0.80)	0.012*	1.01 (0.72-1.74)	0.85 (0.63-1.02)	0.012*	0.115
-Eyes open Foam surface	0.78 (0.66-0.95)	0.63 (0.58-0.72)	0.021*	1.08 (0.81-1.69)	0.79 (0.56-1.20)	0.012*	0.093
-Eyes closed Foam surface	1.72 (1.51-2.16)	1.64 (1.34-1.98)	0.012*	2.23 (1.71-2.87)	1.79 (1.27-2.62)	0.012*	0.834
TSK, score	47.00 (43.75-53.50)	40.00 (36.25-43.50)	0.017*	49.00 (45.00-51.00)	35.00 (27.50-37.50)	0.011*	0.598
FIQ, score	67.84 (58.78-74.88)	43.16 (30.30-54.48)	0.012*	66.96 (62.10-84.9[illegible])	4[illegible].94 (33.71-49.40)	0.012*	0.529
FSS, score	6.00 (5.00-7.00)	5.11 (3.55-5.41)	0.012*	6.00 (5.72-6.80)	3.03 (2.69-4.24)	0.012*	0.958
IPAQ, score	919.00 (102.37-1298.25)	1430.25 (942.00-1778.25)	0.012*	[illegible]095.[illegible]5 (81[illegible].75-16[illegible]6.50)	2742.00 (2298.00-5735.25)	0.012*	0.226
6MWT, m	573.50 (527.75-604.75)	634.00 (583.75-641.50)	0.012*	567.50 (523.75-588.60)	621.00 (583.65-670.87)	0.012*	0.713
Sf-36, score							
Mental	91.00 (32.25-181.75)	158.50 (146.37-208.50)	0.012*	91.00 (62.00-103.25)	232.00 (187.50-250.75)	0.012*	0.958
Physical	86.50 (58.75-121.50)	19[illegible].00 (12[illegible]-219.[illegible])	0.012*	69.00 (52.50-93.25)	194.00 (163.75-261.75)	0.012*	0.227

VAS, Visual Analog Scale; MSOT, Modified Sensory Organisation Test; TSK, Tampa Scale for Kinesiophobia; FIQ, Fibromyalgia Impact Questionnaire; FSS, Fatigue Severity Scale; IPAQ, International Physical Activity Questionnaire; 6MWT, The Six-Minute Walk Test; Sf-36, Short form-36; IQR; Interquartile Range.

[a]Wilcoxon test

[b]Mann-Whitney U test, *p<0.05

Table 3. Comparison of changes between groups (baseline-8th week)

	Exercise Group (n = 8)	Exercise + IVR Group (n = 8)	
	Median (IQR)	Median (IQR)	p[a]
VAS, cm	-2.05 (-3.75; -1.65)	-4.00 (-4.97; -2.90)	0.021*
MSOT, sway point			
-Eyes open Firm surface	-0.09 (-0.34; 0.00)	-0.12 (-0.19; -0.07)	0.461
-Eyes closed Firm surface	-0.09 (-0.18; -0.03)	-0.35 (-0.72; -0.03)	0.[illegible]1
-Eyes open Foam surface	-0.13 (-0.30; -0.06)	-0.31 (-0.56; -0.10)	0.1[illegible]2
-Eyes closed Foam surface	-0.22 (-1.01; -0.01)	-0.39 (-0.61; -0.29)	[illegible]
TSK, score	-10.00 (-11.75; -5.25)	-12.00 (-21.25; -[illegible]5)	0.034*
FIQ, score	-21.83 (-30.98; -13.34)	-27.87 (-45.70; [illegible]9.36)	0.294
FSS, score	-1.16 (-1.64; -1.00)	-2.81 ([illegible].63; [illegible].42)	0.013*
IPAQ, score	528.50 (353.62; 929.00)	1797.25 ([illegible]408.00; [illegible]093.00)	0.001*
6MWT, m	50.00 (34.00; 65.00)	[illegible].00 (3[illegible]20; 85.02)	0.344
Sf-36, score			
Mental	70.25 (19.00; 110.00)	148.00 (98.75; 168.00)	0.016*
Physical	85.00 (65.25; 122.5[illegible])	139.00 (84.25; 189.25)	0.189

VAS, Visual Analog Scale; MSOT, Modified Sensory Organization Test; TSK, Tampa Scale for Kinesiophobia; FIQ, Fibromyalgia Impact Questionnaire; FSS, Fatigue Severity Scale; IPAQ, International Physical Activity Questionnaire; 6MWT, The Six-Minute Walk Test; Sf-36, Short form-36; IQR, Interquartile Range.
[a]Mann-Whitney U test, *p<0.05.

Figure 1. Flowchart

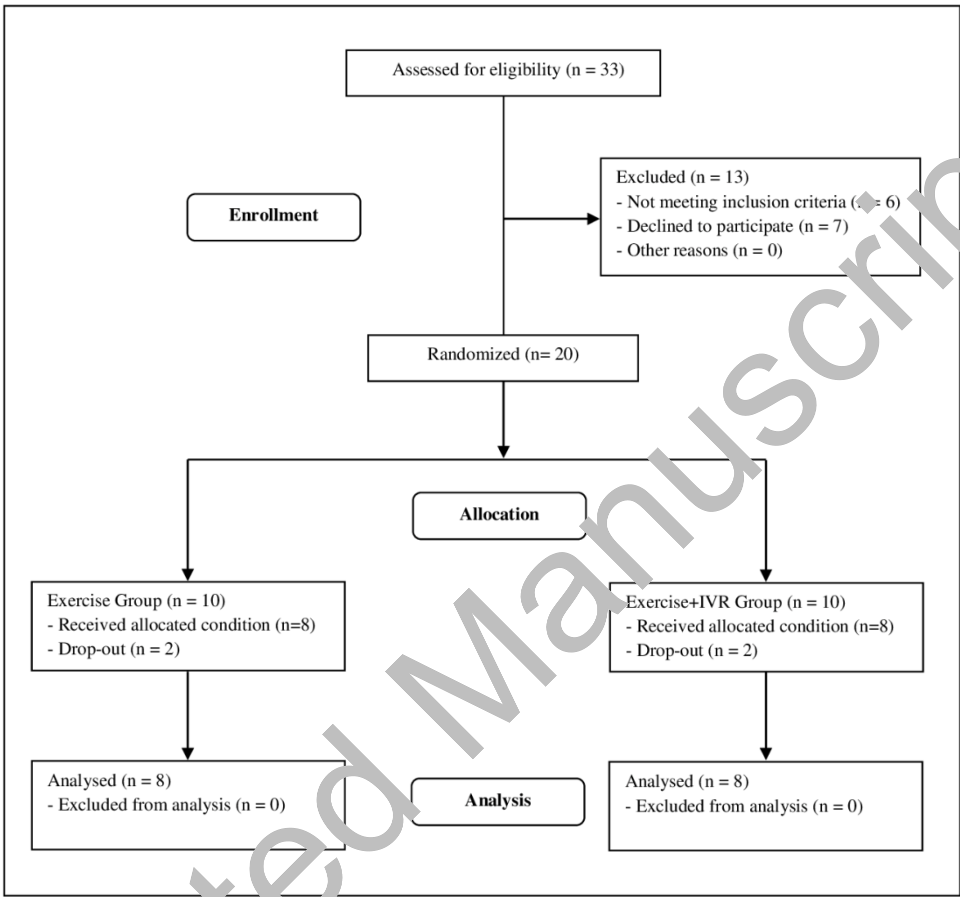

Figure 1. Flowchart