Effect of an interactive Pilates-based telerehabilitation intervention in people with multiple sclerosis: Protocol for a Randomized Controlled Trial.

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Abstract

Background: Multiple Sclerosis (MS) progressively worsens over time, leading to cumulative physical disability, cognitive deficits, and other symptoms that prevent people with MS (PwMS) from performing daily living activities correctly and regularly. Recently, physical activity (PA) has been recommended in MS to maintain good physical fitness and mental health, reduce symptoms severity and risk of relapse, and improve quality of life.
In this context, Pilates has been suggested as an ideal PA to manage physical, cognitive and psychological MS symptoms and a method useful to maintain and improve balance and gait.

Objective: This paper presents the protocol for a study that aims to assess the efficacy on the physical domain, specifically balance and gait, of an at-home self-managed PA intervention delivered through the MS-FIT exergame. Additionally, measures of cognitive performances, quality of life (QoL) and wellbeing will be considered.

Methods: This is a multicentre 2-arm randomized controlled trial with three assessment points (baseline, post-intervention at 12 weeks, and follow-up at 6 weeks). PwMS with mild disability, low fall risk, preserved cognitive functions and low anxiety and depression are potential eligible participants.

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The primary outcome is the Timed Up and Go, a test deputed to assess ambulation. We will also administer other tests for the motor function and for cognition, fatigue, quality of life, wellbeing, and PA. Acceptance and satisfaction towards the received intervention and the subjective impression of changes in performances will be assessed with dedicated questionnaires.

Results: Recruitment for the trial started on March 16, 2022, and the first participant was randomized on the same day. Data analysis and results are aimed to be published in early 2025.

Conclusions: Cumulative data suggest that Pilates has verified benefits in several neurological diseases and can be a PA tool for PwMS. With this study we will provide evidence for a use in the clinical practice of a digital tool for self-administration of Pilates exercises at home as a complement of rehabilitation and for the continuity-of-care of PwMS. Clinical Trial: ClinicalTrials.gov (number ID: NCT04011579)

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Trial registration: ClinicalTrials.gov (number ID: NCT04011579).

Keyword: exergame; MS-FIT; Pilates; Kinect; multiple sclerosis; exercise

Introduction

Multiple sclerosis (MS) is an inflammatory neurodegenerative chronic disease with autoimmune demyelinating lesions of the central nervous system and one of the most common causes of neurological disability in young adults. Clinically, MS progressively worsens over time, leading to cumulative physical disability, cognitive deficits, and neuropsychiatric and behavioural symptoms (Giovannoni et al., 2016). Physical impairments lead up to 85% of people with MS (PwMS) to complain ambulation impairments after generally 10-15 years of disease, and, after 20 years, more than 66% of PwMS do not retain the ability to walk (Giovannoni et al., 2016). Several factors such as weakness, spasticity, cerebellar ataxia, fatigue and impaired attention can cause imbalance and walking impairment (Cameron & Nilsagård, 2013; Cameron & Wagner, 2011). They prevent people from performing daily living activities correctly and regularly with negative effects on working status and social relationships. Rehabilitation is the main option to enhance recovery from disabling symptoms like spasticity, ataxia, sensory loss, fatigue, pain, mood and cognitive disorders (Rehabilitation in Multiple Sclerosis, RIMS). More recently, regular physical activity (PA) has been recommended for PwMS.

PA, including leisure time physical activity and exercise, comprises any bodily movement produced by skeletal muscle contraction that results in a substantial increase in energy expenditure over resting levels (Pilutti et al., 2014). In PwMS, PA maintains good physical fitness and mental health, prevents or reduces symptoms severity and risk of relapse, and improves quality of life (Dalgas et al., 2019; Motl et al., 2009; Riemenschneider et al., 2018). Based on current evidence and experts' opinion, the recent MS guidelines recommend at least 150 minutes/week of exercise and/or 150 minutes/week of lifestyle PA throughout the disease course (Kalb et al., 2020). However, Klaren et al. (2013) (Klaren et al., 2013) refer that PwMS do not engage in sufficient PA amounts, with only about 20% of PwMS meeting the recommended levels of moderate/vigorous daily activity compared to 40% in healthy subjects. Although a recent survey study reported higher percentages among PwMS, only 60% of the

total sample met the recommendations with the lowest percentage shown in the severe disability group (Pedullà et al., 2023). Moreover, although generally beneficial, the advantages of PA could be limited if not included in a personalized and supervised structured program.

Pilates has been suggested as an ideal approach to manage physical, cognitive and psychological MS symptoms (Sánchez-Lastra et al., 2019) and a popular alternative method for balance and gait performance maintenance and improvement (Arik et al., 2022) such as in other neurological conditions (Çoban et al., 2021; Cronin et al., 2023; de Faria et al., 2023). Indeed, it is a precise controlled form of exercise using the stabilizing muscles of the body and based on the principles of concentration, control, centring, flowing movement, precision and breathing. If correctly followed, they can improve flexibility, strength, core stability, muscle control, breathing and posture, and increase body awareness with less ground impact and joint stress (Kloubec, 2010; Wells et al., 2012). Research outcomes support the therapeutic use of Pilates in MS management because it is a safe active treatment method (few adverse effects), with high adherence (low dropout rate), and can improve important meaning functions (e.g. balance, gait, physical-functional capacities, and cognition) (Rodríguez-Fuentes et al., 2022).

A possible perspective to deliver Pilates interventions could take meaningful advantage from the proliferation of exergames and new technologies for telerehabilitation (Taylor et al., 2011). Playing exergames is a form of whole-body physical exercise (Read, 2011) that requires users to complete assigned tasks aimed at improving fitness and promoting an active lifestyle (Lange et al., 2010). Moreover, exergames have been demonstrated to be comparable to traditional therapies and can be more fun and acceptable that could improve the engagement of PwMS in PA (Horne-Moyer et al., 2014). Telerehabilitation solutions based on exergames represents an alternative efficient method to overcome barriers that prevent PwMS from access to long-term regular rehabilitative interventions (i.e. transportations, working time, etc.) and to deliver effective treatments in a setting matching with patient’s circumstances (e.g., at-home), priorities (e.g., during lunch break), and abilities (e.g.,

physical impairment) (Charvet et al., 2017).

Recently, MS-FIT, a usable Kinect-based exergame implementing Pilates exercises, has been developed by an Italian network of experts in the field of MS rehabilitation for a future use in research and clinic (Tacchino et al., 2023). It has been customized for PwMS, allows to tailor the intervention in order to potentiate the effects of an ongoing program, and was intended to be developed for asynchronous telerehabilitation purposes.

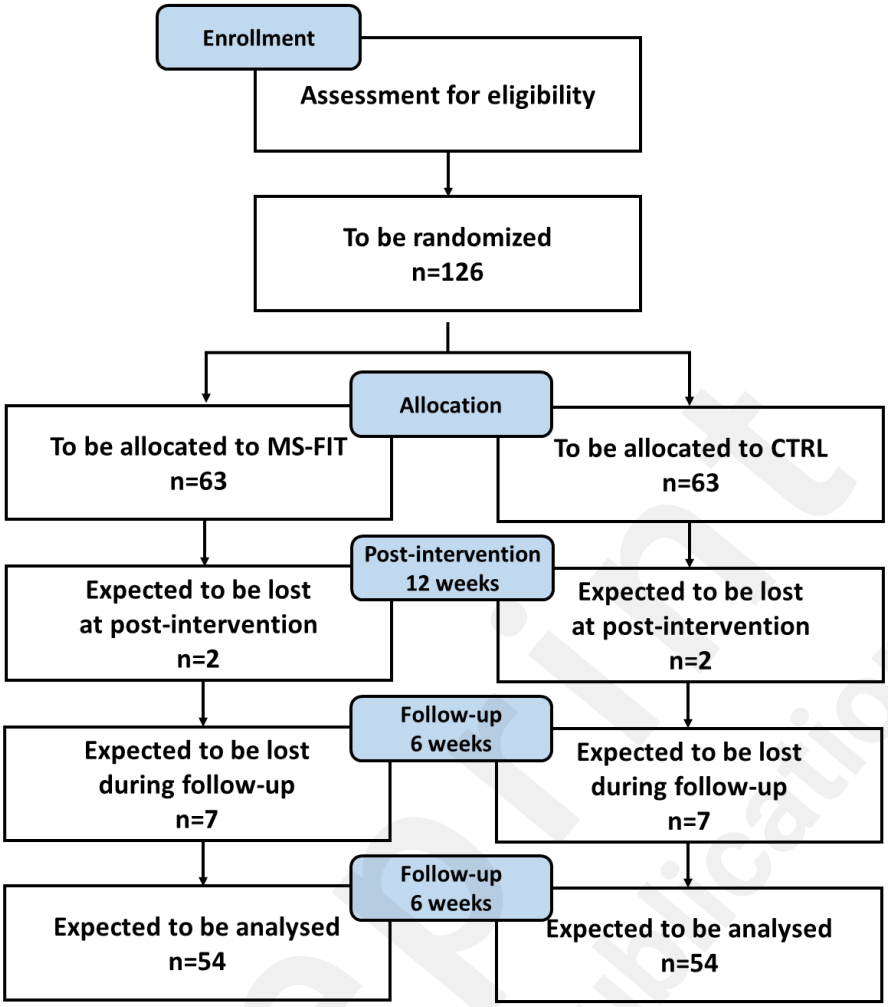
Therefore, the RCT was designed to test the efficacy on the physical domain, specifically balance and gait, of an at-home self-managed PA intervention delivered through MS-FIT. Additionally, measures of cognitive performances, quality of life (QoL) and wellbeing will be considered. If RCT results will be positive, MS-FIT could be proposed in combination with rehabilitation to potentiate the rehabilitative intervention effect and/or guarantee the continuity of care of PwMS.

Methods

Study Design

We are conducting a multicentre 2-arm randomized controlled trial with 3 assessment points (baseline, post-intervention at 12 weeks, and follow-up at 6 weeks). Participants in the intervention condition (MS-FIT group) will receive access to MS-FIT exergame for at-home self-administration (Tacchino et al., 2023) in addition to their leisure time physical activities. Participants in the control condition (CTRL group) will only have access to their leisure time physical activities. Exercise will be not admitted and rehabilitative treatments, except speech therapy, sphincter rehabilitation, and psychological support, will have to be suspended. The study design is illustrated in Figure 1.

Figure 1. Study design.



Procedures

PwMS with mild disability, low fall risk, preserved cognitive functions and low anxiety and depression are potential eligible participants and will be pre-screened at any center. They will be contacted by the center responsible who will explain the process of the study in detail to ensure that patients understand the entire clinical trial; they will receive detailed information including the purpose, procedures, contents of follow-up, data storage, benefits, and risks of the study and will be given adequate time to consider participation. They will be informed that for the entire period of participation to the study only leisure time physical activities, but not exercise and rehabilitation, will be allowed. They are also informed verbally that their participation is voluntary and that they can withdraw their consent at any point of time without giving reasons and without depriving of any treatment and care or other disadvantages.

The patients who will agree to participate will be scheduled for a first visit. They will be required to sign the written informed consent after having carefully read and understood the information about the study procedures and data security measures (including information on how to contact the study team if they had questions) provided to them. This approach is compliant with the General Data Protection Regulation (GDPR) and was approved by the ethics committees.

After consent has been given, the recruited patients will proceed to the screening evaluation, on which the inclusion and exclusion criteria are assessed and will immediately receive feedback on whether or not they can participate in the study. The enrolled patients will be administered the baseline assessment, randomized at the person level into one of the two groups (i.e. MS-FIT and CTRL) with a 1:1 allocation ratio, and notified of the results of the assignment.

The randomization sequence was generated using the website http://www.random.org. The randomization list was stored in a password-protected file with restricted access only to a researcher of FISM who prepared the list and would not be involved in the following research. The

randomization list has been implemented into a web-based, password-protected data management system/baseline electronic case record forms (eCRF) provided by Nubilaria srl (Italy).

For each centre, authorized trained personnel will edit/audit the trial data into the eCRF. Paper copies of eCRFs and any (anonymized) supporting documentation will be stored securely at each centre, with identifying contact details and signed consent forms stored separately, for seven years. Data quality will be ensured by database validation checks, which include missing data, out-of-range values, illogical entries and invalid responses. Data entered by sites into the trial database will be subject to monitoring and review by dedicated staff, and data queries will be raised as necessary.

Population

Participants will be recruited among those followed by Italian Multiple Sclerosis Society (AISM) Rehabilitation Services of Genoa and Padua, the Multiple Sclerosis Center of IRCCS Foundation "Carlo Besta" Neurological Institute (Milan), Vita-Salute San Raffaele University (Milan), the Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI) of the University of Genoa, the Neurology Unit of IRCCS Neuromed (Pozzilli), the Department of Medical Science and Public health of the University of Cagliari, Department of Traslational Biomedicine and Neurosciences (DiBraiN) of the University A. Moro (Bari), the IRCCS Fondazione Don Carlo Gnocchi ONLUS (Milan), the Uosi Multiple Sclerosis Rehabilitation of the IRCCS Istituto delle Scienze Neurologiche of Bologna, Department of Advanced Medical and Surgical Sciences (DAMSS) of the University of Campania Luigi Vanvitelli (Naples), the Department of Neurosciences of the S. Camillo-Forlanini Hospital (Rome), the Department of Medical and Surgical Sciences and Advanced Technologies "G.F. Ingrassia" (DGFI) of the University of Catania, and the IRCCS Centro Neurolesi "Bonino-Pulejo" (Messina).

Eligibility Criteria

Eligibility criteria were selected to ensure an optimal fit of the study sample with respect to the subsequent implementation of the MS-FIT intervention in the health care setting, to minimize the impact of confounding variables (e.g. rehabilitation outcomes), and to ensure comparability with other studies on similar interventions.

Inclusion Criteria

The study includes PwMS with a diagnosis of MS following the McDonald criteria (Thompson et al., 2017) and age ≥18; all disease courses (relapsing-remitting, primary progressive, secondary progressive) are admitted (Lublin et al., 2014). Patients will be included if their level of disability based on the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) is from 2 to 4. Indeed, we expect that in PwMS with a lower EDSS the proposed intervention could be not effective and other forms of PA mainly based on exercise should be considered. For PwMS with higher EDSS Pilates could be recommended as a complement but not as a replacement of rehabilitation; also for this reason, we considered unethical to include patients that should suspend their treatments for the aims of the study. Moreover, asynchronous tele-rehabilitative tools for balance self-administered training should be proposed when patient's ability to safely balance is preserved. In any case, we included patients with preserved balance as evaluated with the Berg Balance Scale (BBS) > 46 (Cattaneo et al., 2006).

A normal cognitive functioning determined by a Mini-Mental Status Examination (MMSE) > 24 (Beatty, 1990) is considered in order to warrant the ability to use the MS-FIT exergame; a Hospital Anxiety and Depression Scale (HADS) < 10 in the two subset of anxiety and depression (Honarmand & Feinstein, 2009) could prevent a loss of adherence due to mood disorders.

Exclusion Criteria

The study excludes individuals who have received a rehabilitative treatment in the last month before

being contacted. Other exclusion criteria are: visual deficits that could compromise the use of the MS-FIT exergame and relapses in the last 3 months. Participants with relapses during the period of their involvement in the study will be considered as drop-out.

Intervention

Subjects in the MS-FIT group will receive the MS-FIT exergame (Tacchino et al., 2023). MS-FIT is a tool for an individual interactive game-based training using Microsoft Kinect Sensor V2. It implements Pilates exercises appropriately adapted to MS requirements. The usability of the tool has been successfully tested in a previous work (Tacchino et al., 2023). The Microsoft Kinect Sensor V2 allows the user to interact through gestures and spoken commands that warrant better access, participation and benefit to people with impairment such as PwMS.

MS-FIT implements Pilates exercises identified for a safe execution through a digital tool; the exercises aimed to train breathing, posture, and balance. To ensure that the exergame is appropriate for each potential MS user, different levels of accessibility are considered (e.g. some exercises are executed while seated). A teacher-avatar verbally explains and visually shows the exercise the user will have to execute. The Kinect will record the user' movements and, accordingly, will show the user-avatar on the screen. The level of accuracy in movements' performances will determine the rewards to the user and, finally, the access to new levels of difficulty.

MS-FIT is thought to be used without the synchronous supervision of the therapist.

Subjects in the MS-FIT group will train at home with MS-FIT for 12 weeks and they will be required to perform the exercises for a total of 30 minutes/day for at least 3 days/week. Before starting the intervention, each subject will be trained to the use of the tool by a physical therapist, not necessarily certified for Pilates; however, the therapist will be trained to the principles of Pilates.

Subjects in the CTRL group will not receive the MS-FIT tool but they will be offered the MS-FIT intervention at the end of their participation to the study.

All the participants will be assessed at the baseline (T0), after 12 weeks (T1) and at a 6-week follow-up (T2).

Measures

Primary outcome

The primary outcome of the study is the Timed Up and Go (TUG) test (Podsiadlo & Richardson, 1991), a commonly used outcome measure of dynamic balance that can assess activity limitations by examining the patient's ability to ambulate and perform transfers. The TUG was originally created to predict fall risk in geriatric patients. The focus of the test has been shown to be a relevant outcome measure when assessing balance and general mobility for patients with various disabilities across the lifespan.

At the "go" signal, the subject has to stand up from a chair, walk 3 m, turn around, walk back to the chair, and sit down as quickly as possible, but safely. The subject starts with the back against the chair and the arms resting on the armrests and is timed from the moment he/she lifts the pelvis from the chair until he returns with the pelvis in the chair (Cattaneo et al., 2006). The subject wears his/her regular footwear and uses his/her customary walking aid (none, cane, walker). No physical assistance is given.

Secondary outcomes

Secondary outcomes will evaluate the effects of the intervention on:

- motor function: Visual Analogue Scale (VAS) (0-10) for balance subjective disability improvement (Price et al., 1983), Timed 25-Foot Walk (T25FW) (Motl et al., 2017), Ambulation Index (AI) (Hauser et al., 1983), 2-Minutes Walking Test (2WT) (Gijbels et al., 2012), Twelve Item MS Walking Scale (MSWS-12) (Hobart et al., 2003), Nine-Hole Peg Test (9HPT) (Rudick et al., 2001);

- cognition: Brief International Cognitive Assessment for MS (BICAMS) (Goretti et al., 2014);
- fatigue: Modified Fatigue Impact Scale (MFIS) (Flachenecker et al., 2002);
- quality of life: Multiple Sclerosis Quality of Life-54 (MSQoL54) (Solari et al., 1999; Vickrey et al., 1995);
- wellbeing: Psychological Well-Being Scales (PWB) (Ryff & Keyes, 1995);
- physical activity: International Physical Activity Questionnaire (IPAQ) (Hagströmer et al., 2006).

Moreover, the acceptance of the used technology will be evaluated with an ad-hoc questionnaire on the patient's expectations; the satisfaction towards the intervention will be evaluated with the Client Satisfaction Questionnaire (CSQ-8) (Attkisson & Zwick, 1982) and looking at the of technology with the Tele-healthcare Satisfaction Questionnaire (TSQ) (Ambrosini et al., 2014); the general subjective impression of change will be assessed with the 7-points scale Patients' Global Impression of Change (PGIC) (from 1: 'no change or worse' to 7: 'a great deal better').

A general evaluation of the total energy expenditure in leisure time physical activity will be obtained through the Minnesota Leisure-Time Physical Activity Questionnaire (Richardson et al., 1994).

Blood sample

If the participant consents, a blood sample will be collected at T0 to investigate if genetic polymorphisms of candidate regulators of neural plasticity could be correlated to the response to the proposed intervention. According to previous studies (Choi et al., 2011) the participants could be subdivided in subgroups with respect to the polymorphism. For example, for the CNR1 gene the subdivision could be based on the number of AAT repetitions (short AAT: homozygous or heterozygous for allele with ≤11 repeats of AAT triplets; long AAT: homozygous for allele with ≥12 repeats of AAT triplets).

All blood samples will be genotyped for a total of 55 genetic polymorphisms of 23 potential regulators, like: Homer1; AKT1; RAPTOR; D2R; GAPD; CHAT; p53; BRCA2; LIG4; XRCC5; CYP3A4; NBS1; MDM2; CNR1, ATTn; CNR2; GRIN1; GRIN2B; TRPV1; FAAH, COMPT; BDNF.

Blood sample will be collected early in the morning after awakening (8:00 am). To synchronize the sample for lifestyle variables, subjects were requested to avoid excessive physical activity the last three days before the blood sampling, sleep for 7–8h the night before study, avoid starving, and eat a usual breakfast in the morning (Choi et al., 2011). The samples will be analysed in the centre of DC.

Other measures

The adherence to the intervention will be provided by the number of sessions actually performed with the MS-FIT tool and the number of dropouts. The safety will be assessed with the number of any potential issues (i.e. number of falls).

We will also collect information about the pharmacological treatment followed by the participants and the type of PA practiced during the participation to the study.

Criteria for the premature withdrawal

In addition to the withdrawal of consent at any time, the responsible of each center could consider criteria for premature withdrawal also any medical conditions that could jeopardize the patient's safety if she/he continues the study and/or study results, disease treatment changes during the study, and no compliance of the participants to the study procedures.

Sample size

The sample size has been calculated by referring to the TUG change after a Pilates intervention found by Karlon et al. (Kalron et al., 2017) in a group of PwMS. The authors did not find any

differences between the group receiving the Pilates intervention and the control group receiving an intervention of physical therapy. Pilates group improved the performance in TUG of about 1.8 s that is clinically relevant for PwMS. By considering a variability of about 3.4 s, a power of 80%, a level of significance (two sided) of 5% and a potential loss of 15% of patients at follow-up, the estimation of the necessary sample size consists of approximately 63 subjects for the experimental group (a total of 126).

Data collection and management

Data entry, including quality checks and validation by double entry, will be performed through the eCRF. Missing unit record data will be compared with the matching handwriting CRF and corrected accordingly.

Statistical analysis

Descriptive statistics will be used to evaluate differences between the two groups of participants. Study hypotheses will be tested using an intention-to-treat analysis, whereby all consenting patients who were randomized during the accrual period will be included in the analysis.

Continuous data will be summarized using count, mean, median, standard deviation, interquartile ranges whereas categorical measures will be described using frequencies. Normality assumption will be tested with the Shapiro-Wilk test. Pre-post effects within groups will be investigated using t test for paired data or Wilcoxon matched-pairs signed-rank test.

Between group proportions will be compared by χ^2 or Fisher's exact test, while between-group comparisons for continuous variables will be done using either the two-sided unpaired t-test or the Wilcoxon two-sided two-sample test for non-normal data. Correlations will be computed using Pearson’s or Spearman’s coefficients.

Primary analysis will be performed comparing mean changes from T0 to T1 in primary and

secondary study outcomes. In particular, the MS-FIT group will be compared with the CTRL group with the analyses of covariance (ANCOVA). The model includes the change as dependent variable, with intervention group as a main effect and the baseline value as an additional covariate. Finally, to evaluate the effect's persistence of intervention will be performed generalized estimating equation models, here the average effect of the intervention across the time points T0, T1 and T2 on all outcomes, adjusted for the baseline outcome value, will be evaluated between the two groups.

Differences among subgroups in polymorphisms will be analyzed using the analyses of variance (ANOVA) or Kruskal-Wallis test, as appropriate.

Statistical analysis will be performed using STATISTICA 7.1 software (StatSoft GmbH). Significance will be recognized for $p<0.05$.

Ethical Considerations

This trial is conducted in compliance with the protocol, the Declaration of Helsinki and good clinical practice. It has been approved by the Ethics Committee at San Martino Hospital (No.134/2018) and registered prior to patient enrolment at ClinicalTrials.gov (number ID: NCT04011579).

Any change in this protocol must be agreed to by all the study investigators. Each amendment must be signed by the principal investigator of each centre and the amendment forms will be submitted to the local Ethics Committee for approval. After that, the amendment will be updated in the clinical trial registry.

Participants will not receive compensation for participating in the study.

A formal auditing process at the end of the study is proposed for this trial.

Patient and Public Involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of our research, although the patient feedback was an important source for the development and

improvement of the MS-FIT tool investigated in this trial (Tacchino et al., 2023). Published results will be disseminated to the study participants on request.

Dissemination

The outcomes of this RCT study will be disseminated. The dissemination includes communication and promotion of the project activities and achieved results to the participants, the PwMS, people involved in the life and healthcare chain of PwMS (e.g. caregivers and healthcare professionals), and the scientific community. Dissemination activities will start with the launch and will continue for all the duration of the study. Specific activities include dissemination through material such as leaflet and videos for distribution through Internet, social networks, forum or during local, national and international events and specific meetings with end-users; dissemination through presentation of results on national and international peer-reviewed scientific journals; dissemination through presentation of research results in major conferences and annual national and international meetings of the healthcare; dissemination through the ClinicalTrials.gov registry.

Results

Trial Status

Recruitment for the trial started on March 16, 2022, and the first participant was randomized on the same day. Data analysis and results will be published in early 2025.

Discussion

Summary

Cumulative data suggest that the Pilates method has verified benefits in several neurological diseases and can be a PA tool for PwMS. A recent review (Rodríguez-Fuentes et al., 2022) in MS showed that

Pilates improves balance, gait, physical-functional conditions (muscular strength, core stability, aerobic capacity, and body composition), and cognitive functions; on the contrary, fatigue, QoL, and psychological function did not show clear improvement. Furthermore, high adherence (average adherence ≥ 80%) and few adverse effects were reported. For these reasons, future research is needed to develop clinical protocols that could maximize therapeutic effects of Pilates for PwMS. In this context, new devices and technologies for at-home interventions could provide solutions to overcome limitations due to urban barriers (e.g. transportations), daily activities (e.g. working time), and clinical conditions (e.g. level of disability) and to guarantee the continuity of care. Thus, practicing Pilates at-home through e-Health tools could help PwMS to perform regular PA and to successfully maintain own physical, cognitive and emotional status.

Here, we describe the RCT protocol designed to test the efficacy on balance and gait, of an at-home PA intervention delivered through the MS-FIT exergame. In addition, we will also assess the effects on cognition, QoL and wellbeing.

The present RCT protocol has been designed by taking into account previous studies in the MS scientific literature in terms of number of weeks of intervention, weekly frequency, session duration, outcomes, setting and control group (Rodríguez-Fuentes et al., 2022). Because only one study evaluated long-term monitoring after the intervention (Arntzen et al., 2019) and it is unclear whether the outcomes attained are maintained, as further element of novelty, we propose to schedule a follow-up assessment in order to define whether the effects of the Pilates persist.

Limitations

The first limitation of the present study is that we will have evidence of the efficacy of an exergame for Pilates only for PwMS with mild disability. However, also PwMS at more advanced disease stages benefit from regular PA to maintain fitness, to prevent pain and secondary complications of inactivity, and to treat or reduce symptoms. Thus, because specific prescriptions should be tailored

on the clinical condition, a dedicated trial should be considered for patients with higher level of disability. Secondly, owing to the discontinuation of the Kinect Sensor V2 adopted in MS-FIT, for the successful translation of the exergame into clinical practice, a new compatible commercial sensor will be identified and the app will be adapted; the Microsoft AzureKinect and MentorAge are valid and comparable systems already taken into account by other researchers (Koontz et al., 2022; Petsani et al., 2022; Tacchino et al., 2023). Thirdly, although the MS-FIT tool has not been developed to pursue rehabilitative purposes, it would be helpful to analyse the MS-FIT intervention as a complement to the work of healthcare professionals and assess if it is able to potentiate the effect of a rehabilitative intervention, eventually also in PwMS with higher level of disability. Lastly, no direct evidence, such as MRI acquisition, to reveal what microstructural changes due to the MS-FIT intervention will be considered.

Future directions and Conclusions

MS-FIT is a usable and accepted digital health tool for telerehabilitation implementing Pilates exercises and aimed at supporting the self-administration of a Pilates training at-home. This study will provide evidence for a use of the MS-FIT tool in the clinical practice as a complement of rehabilitation and for the continuity-of-care of PwMS. However, a feasibility protocol involving patients with moderate disability (EDSS between 4 and 6) should be designed and tested, followed by a multicentre trial that assess the effectiveness of the tool and pave the way for a more extensive use in MS.

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Conflicts of Interest

AT, MP, EC, PG, MR, LS, FP, ES, EP, MAB, and GB have no conflicts of interest to disclose. PC has received honoraria for speaking or consultation fees from Novartis, Bristol Myers and Biogen; has received funding for travel to attend scientific events or speaker honoraria from Merck Serono, Biogen Idec, Mylan and Roche; he has also received institutional research support from Merk-Serono, Novartis and Roche; he is also principal investigator in clinical trials for Novartis and Roche. LL has received honoraria for consultancy over the past 3 years from Merck, Bristol-Myers, Squibb, Janssen Cilag, and Roche. MI is co-Editor for MSJ; she has received honoraria for participation in advisory boards from Biogen, Bristol Meyer Squibb, Merck, Novartis, Roche, Sanofi, Janssen. DC is an Advisory Board member of Almirall, Bayer Schering, Biogen, GW Pharmaceuticals, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva and received honoraria for speaking or consultation fees from Almirall, Bayer Schering, Biogen, GW Pharmaceuticals, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva; he is also the principal investigator in clinical trials for Bayer Schering, Biogen, Merck Serono, Mitsubishi, Novartis, Roche, Sanofi-Genzyme, and Teva; his preclinical and clinical research was supported by grants from Bayer Schering, Biogen Idec, Celgene, Merck Serono, Novartis, Roche, Sanofi-Genzyme and Teva. DP received advisory board membership, speaker’s honoraria, travel support, research grants, consulting fees, or clinical trial support from, Almirall, Biogen, BMS-Celgene, Sanofi-Genzyme, Merck-Serono, Novartis, Roche, Alexion. GT is an Advisory Board member of Almirall, Lilly, Lundbeck, Roche and received honoraria for speaking or consultation fees from Almirall, Biogen, GW Pharmaceuticals, Merck Serono, Novartis, Roche, Sanofi-Genzyme. LP has received personal fees and non-financial support from Biogen, Bristol-Mayer, Squibb, Merck, Novartis, Roche, Sanofi, Viatris.

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Abbreviations

Ambulation Index (AI)

Analyses of covariance (ANCOVA)

Analyses of variance (ANOVA)

Berg Balance Scale (BBS)

Brief International Cognitive Assessment for MS (BICAMS)

Client Satisfaction Questionnaire (CSQ-8)

Electronic case record forms (eCRF)

Expanded Disability Status Scale (EDSS)

General Data Protection Regulation (GDPR)

Hospital Anxiety and Depression Scale (HADS)

International Physical Activity Questionnaire (IPAQ)

Mini-Mental Status Examination (MMSE)

Modified Fatigue Impact Scale (MFIS)

Multiple sclerosis (MS)

Nine-Hole Peg Test (9HPT)

Patients' Global Impression of Change (PGIC)

People with MS (PwMS)

Physical activity (PA)

Psychological Well-Being Scales (PWB)

Quality of life (QoL)

Quality of life: Multiple Sclerosis Quality of Life-54 (MSQoL54)

Tele-healthcare Satisfaction Questionnaire (TSQ)

Timed 25-Foot Walk (T25FW)

Timed Up and Go (TUG)

Twelve Item MS Walking Scale (MSWS-12)

2-Minutes Walking Test (2WT)

Visual Analogue Scale (VAS)

Supplementary Files

Figures

Study design.