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Combined Physiotherapy and Cognitive Behavioral Therapy for Functional Movement Disorders
A Randomized Clinical Trial

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IMPORTANCE Functional movement disorders (FMDs) are frequent and disabling neurological disorders with a substantial socioeconomic impact. Few randomized studies have analyzed the effectiveness of combined physiotherapy and psychotherapy in patients' quality of life.

OBJECTIVE To assess the efficacy of multidisciplinary treatment (physiotherapy plus cognitive behavioral therapy) in FMDs.

DESIGN, SETTING, AND PARTICIPANTS This was a parallel, rater-blinded, single-center, randomized clinical trial. Recruitment took place from June 2022 to April 2023, and follow-up visits were performed at months 3 and 5, concluding in October 2023. Participants were recruited from a national referral center for movement disorders: the Movement Disorders Unit from the Hospital Universitario Virgen Rocio in Seville, Spain. Patients had to be 18 years or older with a confirmed FMD diagnosis and capable of giving consent to participate. Patients who did not meet eligibility criteria or refused to participate were excluded. Any uncontrolled psychiatric disorder was considered an exclusion criterion.

INTERVENTIONS Patients were randomly assigned, in a ratio of 1:1 to multidisciplinary treatment (physiotherapy plus cognitive behavioral therapy), or a control intervention (psychological support intervention).

MAIN OUTCOMES AND MEASURES Primary outcomes: between-group differences in changes from baseline to month 3 and month 5 in patients' quality of life (EQ-5D-5L score: EQ Index and EQ visual analog scale [EQ VAS]; and 36-Item Short-Form Survey Physical Component Summary [SF-36 PCS] and SF-36 Mental Component Summary [MCS]). Linear mixed models were applied, controlling by baseline severity and applying Bonferroni correction.

RESULTS Of 70 patients screened with an FMD, 40 were enrolled (mean [SD] age, 43.5 [12.8] years; age range, 18-66 years; 32 female [80%]; mean [SD] age at FMD onset, 38.4 [12.1] years), and 38 completed all the follow-up visits and were included in the analysis for primary outcomes. Multidisciplinary treatment improved SF-36 PCS with a mean between-group difference at 3 months of 4.23 points (95% CI, −0.9 to 9.4 points; $P = .11$) and a significant mean between-group difference at 5 months of 5.62 points (95% CI, 2.3-8.9 points; $P < .001$), after multiple-comparisons adjustment. There were no significant differences in other quality-of-life outcomes such as SF-36 MCS (mean between-group difference at 3 and 5 months: 0.72 points; 95% CI, −5.5 to 7.0 points; $P = .82$ and 0.69 points; 95% CI, 2.3-8.9 points; $P = .83$, respectively), EQ VAS (9.34 points; 95% CI, −0.6 to 19.3 points; $P = .07$ and 13.7 points; 95% CI, −1.7 to 29.0 points; $P = .09$, respectively) and EQ Index (0.001 point; 95% CI, −0.1 to 0.1 point; $P = .98$ and 0.08 points; 95% CI, 0-0.2 points; $P = .13$, respectively). At months 3 and 5, 42% and 47% of patients, respectively, in the multidisciplinary group reported improved health using the EQ-5D system, compared with 26% and 16% of patients, respectively, in the control group.

CONCLUSIONS AND RELEVANCE Results show that multidisciplinary treatment (physiotherapy plus cognitive behavioral therapy) effectively improves FMD symptoms and physical aspects of patients' quality of life. Further studies must be performed to evaluate the potential cost-effectiveness of this approach in FMD.

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Functional neurological disorders (FNDs) are frequent neurological disorders manifesting in young adults with motor and/or sensory symptoms that arise from the voluntary motor or somatosensory nervous system and are experienced as involuntary.[1,2] FND is the most common cause of referral for neurology clinics after headache,[3] with a huge socioeconomic impact on health systems.[4-6] Among the FND spectrum, functional seizures and functional movement disorders (FMDs) are the most frequent manifestations. FMDs have shown a similar impact on disability and quality of life than organic movement disorders.[7,8]

The underlying etiology of FMD remains elusive, but neural mechanisms coordinating emotional processing, attention, and the sense of agency of the movement have been elucidated as key circuits altered in these patients.[2] In this context, psychological factors appear to act as risk factors and contribute to the perpetuation of symptoms.[9] Due to these advances, psychological interventions such as cognitive behavioral therapy (CBT) and specialized physiotherapy have been explored for patients with FND, showing positive results in certain groups of patients.[10-18] Despite the relative relevance of psychological therapies, their effectiveness has been scarcely explored systematically so far, and relevant methodological limitations characterize the studies carried out.[19]

Additionally, it has been pointed out that specialized physiotherapy could significantly improve FMD symptoms.[20] Cohort studies[11,21-23] and a randomized feasibility have demonstrated the beneficial effects of short physiotherapy programs. Finally, different longitudinal cohort studies[15,18,24,25] have shown the benefit of a multidisciplinary approach (lasting from 1-4 weeks) combining therapies for different phenotypes of FMD.

Given the limited availability of randomized clinical trials studying the benefit of a multidisciplinary approach for FMDs, we conducted a single-blind randomized clinical trial of combined therapy (physiotherapy and CBT) for the treatment of FMDs.

Key Points

Question What is the efficacy of a multidisciplinary treatment (combining specialized physiotherapy and cognitive behavioral therapy) for individuals with functional movement disorders, comparing its effect on patient-reported quality of life with that of a control intervention (psychological support intervention)?

Findings In this parallel randomized clinical trial that included 40 adults with functional movement disorders, multidisciplinary treatment significantly improved physical aspects of quality of life. There was no significant difference between interventions on mental health–related quality of life, but there was a nonsignificant improvement in general health self-perception; at months 3 and 5 after intervention, 42% and 47% of patients in the multidisciplinary-treatment group reported improved health compared with 26% and 16% in the control group, respectively.

Meaning Results show that multidisciplinary treatment (physiotherapy plus cognitive behavioral therapy) effectively improves symptoms and physical aspects of the quality of life of patients with functional movement disorders against nondirected psychological support and education; this improvement seems to be driven by changes in mobility and pain domains.

Methods

Participants

The trial protocol was approved by the regional scientific ethics committee (1633-N-21) of the University Hospital Virgen Rocio-Virgen Macarena in Seville, Spain (Supplement 1). In this trial, we focused on enrolling patients diagnosed withan FMD at the Movement Disorders Unit of the Department of Neurology, University Hospital Virgen Rocio. These diagnoses followed the phenotype-based Espay & Lang criteria,[26] consistent with the current understanding of FND (*Diagnostic and Statistical Manual of Mental Disorders* [Fifth Edition]).[27] Patients were included in the study if they had a confirmed FMD, were 18 years or older, and were able to freely give their consent to participate and attend the intervention and follow-ups. Any noncontrolled psychiatric disorder was considered exclusion criteria. Complete eligibility criteria are provided in the eMethods in Supplement 2. Due to the estimated small sample size, information on participant race and ethnicity was not included in the original trial protocol. The vast majority of the trial cohort was European White race.

Study Design

This double-arm, parallel-group, single-blind, randomized clinical trial compared multidisciplinary treatment (combining specialized physiotherapy[28] and a brief CBT program) with a control intervention (nondirected psychological support therapy) in patients diagnosed with an FMD.

The trial was performed following the principles of the Declaration of Helsinki. All patients were adequately informed and received written information regarding the study. Written informed consent was obtained from all the patients. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Randomization, Masking, and Procedures

Randomization in a 1:1 ratio of multidisciplinary treatment to the control procedure was performed with the use of a Microsoft Excel random number-generator function. Each trial-group assignment was sealed in a numbered envelope; assignments were done after the FMD diagnosis. All patients received the diagnosis of FMD identically in addition to the same supportive information based on current evidence and online resources.[29] Patients were assessed at baseline from a clinical and neuropsychological point of view, and afterward, the trial-group assignment was performed and revealed to the therapeutic team by a neurologist. The experimental group formed the first arm. The participants allocated to this arm underwent a protocolized multidisciplinary program consisting of 4 successive, weekly, 1-hour group sessions of CBT and 12 ambulatory 1-hour individualized physiotherapy sessions based on the published consensus of physiotherapy recommendations for FMD.[28] An experienced clinical psychologist (M.C.R) delivered CBT sessions in an outpatient neurologic

clinic. The sessions were delivered by a physiotherapist (M.M.D.B.) with special training in neurophysiotherapy and FMD physiotherapy.

Participants randomly assigned to the control group underwent 4 weekly 1-hour group sessions of nondirective supportive psychotherapy provided by the same clinical psychologist. These sessions included discussion about life stressors, and the therapist offered empathy.

Both groups received sessions in the neurology outpatient clinics, using identical rooms at the University Hospital Virgen Rocio. Patients were assessed at months 3 and 5 in the same neurology department. Quality-of-life questionnaires (the 5-level version of the EQ-5D questionnaire [EQ-5D-5L] and the 36-Item Short-Form Survey [SF-36]) were filled out by the patients after available instructions. Follow-up motor assessments were done by blinded neurologists with experience in movement disorders. All the details of the structure (type of sessions) and content of the interventions are described in the eMethods in Supplement 2.

Outcomes

The primary outcome in this trial was the change in patients' quality of life measured by changes (between-group differences) in the EQ-5D-5L and SF-36 at month 3 and 5 after intervention. The secondary outcomes were the change at months 3 and 5 in motor severity, Clinical Global Impressions of Severity/Improvement (CGI-S/-I), and caregiver's burden. The primary outcomes (EQ visual analog scale [EQ VAS], EQ Index, SF-36 Physical Component Summary [SF-36 PCS], and SF-36 Mental Component Summary [SF-36 MCS]) were obtained following the authors' recommendation.[30-35] The outcomes were chosen based on the currently available recommendations for outcomes measurement in FND.[36] Further details regarding questionnaires and outcomes are provided in the eMethods in Supplement 2.

Statistical Analysis

The trial assessed the superiority of a multidisciplinary approach as compared with a control intervention. Details regarding the sample size calculation are provided in the eMethods in Supplement 2. Descriptive statistics were used to summarize the baseline characteristics of the participants and for outcomes. Categorical variables are described as numbers and percentages; continuous variables are described as mean and SD. For continuous variables, linear mixed models for repeated measures were used to evaluate the magnitude of changes in primary and secondary outcomes between the 2 groups and across time, controlling by baseline severity. Bonferroni correction for multiple comparisons was applied for primary outcome analyses. The mixed modeling approach is a powerful statistical tool to evaluate group differences over time with unequal numbers of participants at follow-up because it assumes that the missingness is independent of unobserved measurements but dependent on the observed measurements (missing at random).[37] Additionally, the Paretian Classification of Health Change and the probability of superiority were applied to understand better the health change in the EQ-5D profile.[35,38] Two-sided *P* values of .05 or less were considered to indicate statistical significance. Analyses were performed with JASP software, version 0.18 (JASP), GraphPad Prism 8 (GraphPad Software), and R, version 3.31 (R Project for Statistical Computing). Further details regarding the methodology are provided in the eMethods in Supplement 2.

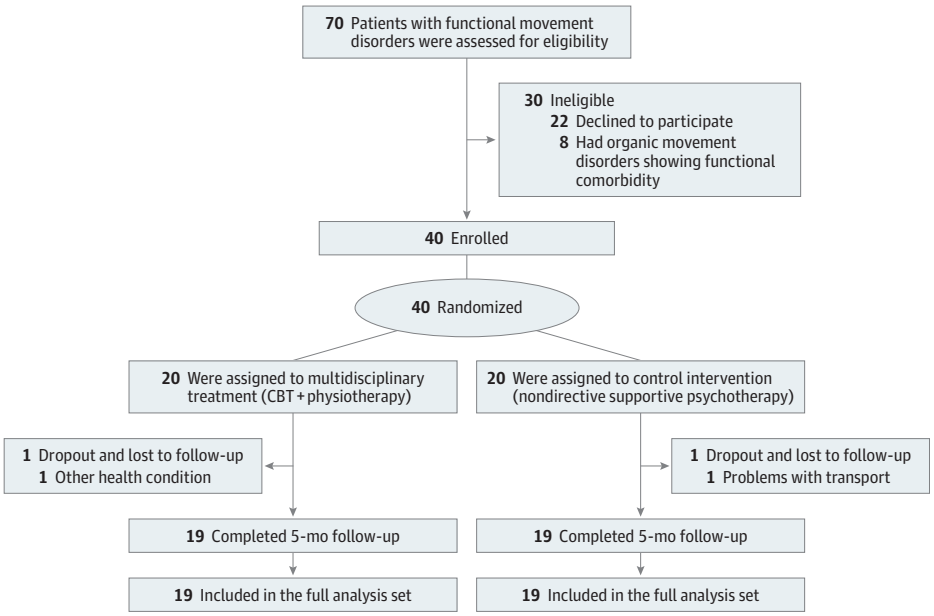
Results

A total of 70 patients were assessed for eligibility, and 40 patients (mean [SD] age, 43.5 [12.8] years; age range, 18-66 years; 32 female [80%]; 8 male [20%]; mean [SD] age at FMD onset, 38.4 [12.1] years) were enrolled from June 2022 to April 2023 (**Figure 1**). A total of 20 patients were randomly assigned to multidisciplinary treatment and 20 to the control intervention. Two patients, 1 from each study arm, were lost to follow-up, leaving a total of 38 patients who completed all the follow-up visits and were included in the analysis for primary outcomes. **Table 1** presents patient demographics and baseline characteristics. The mean (SD) health self-perception of the overall cohort was 50.4 (21.5) points, based on the EQ VAS (range, 0-100). Thirteen participants (33%) were unemployed, and 16 (40%) were not working due to ill health.

The demographic and clinical characteristics (motor, nonmotor, and self-reported quality of life) of the patients were similar in the 2 groups at baseline (Table 1 and eTable 1 in Supplement 2). Both groups exhibited moderate levels of anxiety and depression at baseline and moderate baseline levels of pain and fatigue.

Continuous clinical outcome measures for baseline and the change at follow-up visits are reported in **Table 2**. The multidisciplinary-treatment group had an increase in the mean (SD) SF-36 PCS score, from 33.3 (9.6) points at baseline to 36.9 (10.1) points at month 5 (least-squares mean difference, 3.21 points; 95% CI, 0.3-6.1 points), as compared with a change in the control group from 31.3 (9.3) points at baseline to 30.4 (8.0) points at month 5 (least-squares mean difference, −0.55 points; 95% CI, −3.4 to 2.3 points). The between-group difference in the change in SF-36 PCS score at month 3 was 4.23 points (95% CI, −0.9 to 9.4 points; $P = .11$) and at month 5 was 5.62 points (95% CI, 2.3-8.9 points; $P < .001$) (**Figure 2**A and B). The multidisciplinary-treatment group also had an increase in the mean (SD) SF-36 MCS score from 30.9 (11.8) points at baseline to 36.7 (13.9) points at month 5 (least-squares mean difference, 3.07 points; 95% CI, −2.4 to 8.6 points), as compared with a change in the control group from 32.2 (14.5) points at baseline to 37.2 (11.2) points at month 5 (least-squares mean difference, 2.94 points; 95% CI, −2.2 to 8.1 points). However, there was no significant between-group difference in the change in the SF-36 MCS score either at month 3 (0.72 points; 95% CI, −5.5 to 7.0 points; $P = .82$) or at month 5 (0.69 points; 95% CI, 2.3-8.9 points; $P = .83$) (Figure 2A and B). Regarding the EQ-5D-5L, the multidisciplinary-treatment group showed an increase in the mean (SD) EQ-VAS score from 46.6 (23.1) points at baseline to 63.7 (22.8) points at month 5 (least squares mean difference, 18.2 points; 95% CI, 5.9-30.4 points), as compared with the control group (from 54.3 [19.7] points at baseline to 55.4 [20.9] points at month 5; least-squares mean dif-

Figure 1. Trial Profile



CBT indicates cognitive behavioral therapy.

ference, 3.05 points; 95% CI, −6.8 to 12.9 points). The between-group difference in the change in the EQ VAS score at month 3 was 9.34 points (95% CI, −0.6 to 19.3; $P = .07$) and at month 5 was 13.7 points (95% CI, −1.7 to 29.0; $P = .09$). Additionally, the between-group difference in the EQ Index (range, 0-1) at months 3 and 5 was 0.001 point (95% CI, −0.1 to 0.1 point; $P = .98$) and 0.08 points (95% CI, 0-0.2 points; $P = .13$), respectively (Figure 2A and B).

Regarding SF-36 subdomains (eTable 2 in Supplement 2), there was a significant between-group difference in bodily pain and self-reported change health status (eFigure 1 in Supplement 2) and a nonsignificant improvement in physical and social functioning. Other SF-36 domains, such as general health, physical and emotional role limitations, and emotional well-being, showed improvement in both groups at months 3 and 5 (eTable 2 in Supplement 2).

Regarding the EQ-5D descriptive system (eTables 4-5 in Supplement 2), 42% and 47% of patients from the active-treatment group reported an improvement in their health state at month 3 and 5, respectively, compared with 26% and 16% from the control group (Figure 2C). On the other hand, 42% and 32% of patients from the control group reported a worsened health state at month 3 and 5, respectively (compared with baseline). However, 37% and 16% of patients treated with the multidisciplinary approach experienced a worsening at months 3 and 5, respectively. The patients in the multidisciplinary treatment group improved in mobility and pain/discomfort (EQ-5D-5L) by 42% (8 of 19) and 26% (5 of 19), respectively, compared with 21% (4 of 19) and 5% (1 of 19) in the control group. Considering the probability of superiority within each EQ-5D dimension, most patients in the active-treatment group improved in mobility and pain/discomfort both at months 3 and 5 (eFigure 2 in Supplement 2). Meanwhile, at months 3 and 5, patients from the control group did not change or experienced worse mobility and pain/discomfort, respectively. Both groups showed an improvement in anxiety-depression dimension by month 5. These results from the EQ-5D-5L are consistent with those obtained with SF-36 (eFigures 1 and 5 and eTable 2 in Supplement 2).

Regarding secondary outcomes, the multidisciplinary-treatment group significantly improved in FMD severity at months 3 and 5, showing a decrease in scores greater than 50% at month 5 (**Figure 3**). However, no improvement in the caregivers' burden was observed compared with the control group.

One adverse incident was reported during the study (suicidal attempt) in a patient from the control group with a previous history of controlled major depressive disorder during the patient's fifth month of follow-up. Although an additional psychiatric assessment was offered by the research team as soon as the team was notified of the event, the patient was already receiving care from a local mental health team. No other serious adverse events were reported (eTable 6 in Supplement 2). Three patients from the active-treatment group (20% of those unemployed or with incapacity at baseline) returned to their work or studies, but none of the control group patients returned to work (eTables 7-9 in Supplement 2).

Discussion

This rater-blinded randomized clinical trial showed that multidisciplinary treatment for FMD improved physical aspects of the quality of life of patients with an FMD compared with a control intervention (which included an adequate diagnosis with an empathic approach by a neurologist plus a nondirected psychological intervention). During the follow-up visits,

Table 1. Baseline Demographic and Clinical Characteristics of the Study Groups

Characteristic	Multidisciplinary treatment (n = 20)	Control intervention (n = 20)
Age, mean (SD) [range], y	42.3 (14.0) [18-66]	44.7 (11.6) [21-64]
Sex, No. (%)		
Male	4 (20)	4 (20)
Female	16 (80)	16 (80)
Social support, No. (%)		
Negative influence/absence	1 (5)	1 (5)
Exists but daily absent	0	2 (10)
Inconstant	4 (20)	6 (30)
Constant	10 (50)	7 (35)
Constant and social life	4 (20)	3 (15)
Constant and excellent social life	1 (5)	1 (5)
Educational level, No.		
Basic	2 (10)	3 (15)
Elementary school	5 (25)	5 (25)
High school	7 (35)	7 (35)
Bachelor or higher	6 (30)	5 (25)
Employment status, No. (%)		
Active (working or studying)	4 (20)	5 (25)
Unemployed	7 (35)	6 (30)
Retired	1 (5)	1 (5)
Temporal incapacity	5 (25)	2 (10)
Permanent incapacity	3 (15)	6 (30)
Age at FMD onset, mean (SD) [range], y	36.7 (12.6) [15-60]	40.2 (11.4) [18-61]
Disease duration, mean (SD) [range], y	5.6 (5.5) [0-23]	4.6 (4.4) [0-20]
Age at FMD diagnosis, mean (SD) [range], y	39.9 (12.9) [18-62]	42.7 (11.3) [20-62]
Diagnosis delay, mean (SD) [range], y	3.2 (3.5) [0-14]	2.6 (3.3) [0-15]
FMD motor severity (sFMDRS[a] total score), mean (SD)	13.5 (5.5)	12.8 (7.7)
Activities of daily living functioning (SEADL[b] total score), mean (SD)	71.5 (16.6)	77.5 (15.5)
FMD global severity (CGI-S[c]), mean (SD)	4.6 (0.8)	4.0 (1.2)
FMD main phenotype, No. (%)		
Tremor	11 (55)	5 (25)
Gait disorders	3 (15)	9 (45)
Dystonia	5 (25)	3 (15)
Myoclonus/jerks	1 (5)	2 (10)
Tics	0 (0)	1 (5)

(continued)

Table 1. Baseline Demographic and Clinical Characteristics of the Study Groups (continued)

Characteristic	Multidisciplinary treatment (n = 20)	Control intervention (n = 20)
Combined FMD phenotype, No. (%)	15 (75)	16 (80)
Coexistence of other FND, No. (%)		
Dissociative seizures	2 (10)	2 (10)
Functional sensitive disorders	4 (20)	7 (35)
Functional cognitive disorders	6 (30)	3 (15)
Cognition (MoCA[d] total score), mean (SD)	25.8 (2.8)	26.1 (2.6)
Depression (BDI-II[e] total score), mean (SD)	21.8 (12.2)	22.4 (10.8)
Anxiety (HAMA[f] total score), mean (SD)	20.6 (9.4)	20.2 (7.5)
Pain (VAS[g]), mean (SD)	39.7 (32.5)	49.6 (24.8)
Fatigue (VAS), mean (SD)		
Physical	56.1 (30.7)	57.2 (31.4)
Mental	70.3 (29.2)	55.3 (28.8)
Zarit Caregiver Burden Interview, mean (SD)[h]	46.8 (15.4)	42.5 (14.9)
EQ VAS-EQ-5D-5L[i] (VAS: 0-100), mean (SD)	46.6 (23.1)	54.3 (19.7)
EQ-5D-5L descriptive system		
Mobility, No. (%)		
No problems	7 (35)	4 (20)
Slight to severe	11 (55)	13(65)
Extreme problems	2 (10)	3 (15)
Self-care, No. (%)		
No problems	10 (50)	9 (45)
Slight to severe	10 (50)	11 (55)
Extreme problems	0	0
Usual activities, No. (%)		
No problems	3 (15)	3 (15)
Slight to severe	15 (75)	15 (75)
Extreme problems	2 (10)	2 (10)
Pain/discomfort, No. (%)		
No problems	5 (25)	1 (5)
Slight to severe	13 (65)	19 (95)
Extreme problems	2 (10)	0 (0)
Anxiety/depression, No. (%)		
No problems	3 (15)	3 (15)
Slight to severe	14 (70)	16 (80)
Extreme problems	3 (15)	1 (5)

(continued)

Table 1. Baseline Demographic and Clinical Characteristics of the Study Groups (continued)

Characteristic	Multidisciplinary treatment (n = 20)	Control intervention (n = 20)
SF-36[j] PCS mean (SD)	33.32 (9.58)	31.33 (9.30)
SF-36 MCS, mean (SD)	30.85 (11.84)	32.19 (14.52)
SF-36 domains, mean (SD)		
General health perceptions	39.80 (18.78)	36.63 (23.82)
Physical functioning	43.25 (28.86)	36.75 (27.88)
Social functioning	33.13 (28.18)	37.50 (26.35)
Role limitations due to physical problems	25.94 (27.68)	28.75 (27.31)
Role limitations due to emotional problems	47.08 (34.86)	50.00 (25.88)
Mental health	44.50 (20.71)	46.75 (25.15)
Bodily pain	35.65 (33.40)	32.21 (20.53)
Vitality	31.25 (23.39)	37.17 (27.36)

Abbreviations: BDI-II, Beck Depression Inventory-II; CGI-S, Clinical Global Impressions-Severity; EQ-5D-5L, 5-level EQ-5D; FMD, functional movement disorder; FND, functional neurological disorder; HAMA, Hamilton Anxiety Rating Scale; MCS, Mental Component Summary; MoCA, Montreal Cognitive Assessment; PCS, Physical Component Summary; SEADL, Schwab & England Activities of Daily Living Scale; SF-36, 36-Item Short Form Survey; sFMDRS, simplified Functional Movement Disorders Rating Scale; VAS, visual analog scale.

[a] sFMDRS ranges from 0 to 54; higher scores show higher motor severity of the FMD.

[b] SEADL ranges from 0 to 100; 100 = completely independent and 0 = totally dependent, bedridden.

[c] CGI-S ranges from 1 to 7, with higher scores indicating higher severity.

[d] MoCA ranges from 0 to 30.

[e] BDI-II ranges from 0 to 63.

[f] HAMA ranges from 0 to 56.

[g] VAS ranges from 0 to 100 with higher scores indicating higher intensity of the symptoms/perception.

[h] A total of 38 caregivers completed the Zarit Caregiver Burden Interview at baseline.

[i] EQ-5D-5L consists of 2 pages: the EQ-5D descriptive system and the EQ VAS. The descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems (1), slight problems (2), moderate problems (3), severe problems (4), and extreme problems (5). The EQ VAS records the patient's self-rated health on a vertical visual analogue scale, where the end points are labeled "the best health you can imagine" and "the worst health you can imagine."

[j] Higher scores represent better health in the SF-36.

patients included in the active-treatment group had a significant improvement in SF-36 PCS score, and they specifically experienced a significant change in pain and their perception of change in health status compared with the previous year (eFigure 1 in Supplement 2). The multidisciplinary treatment did not specifically impact the mental health component of quality of life, as both groups reported similar improvements. However, the change in physical quality of life may be also partially related to nonsignificant improvements in physical and social functioning (eFigure 1 and eTable 2 in Supplement 2). Although the active-treatment group showed a 39% and 11% improvement in the self-perception of their state of health at month 5 (EQ VAS and EQI Index, respectively) (Table 2), there was no significant difference compared with the control intervention (Figure 2B).

These results are in line with those of previous studies.[12,13,16,22,24,25] In our study, 63% and 79% of the patients in the active-treatment group showed some degree of improvement in their quality of life by months 3 and 5 (EQ-5D-5L), respectively, and up to 47% experienced an improvement in 1 or more aspects of their life without worsening (Figure 2C) compared with 16% in the control group at month 5. The probability of superiority index helps to better understand this change and shows that patients from the active-treatment group improved since month 3 in mobility and pain/discomfort, whereas patients from the control group experienced no change (eFigures 2 and 5 in Supplement 2). The secondary outcomes may also shed light on these results because a significant change in motor state was observed through follow-up visits (Figure 3 and eFigure 3 in Supplement 2), with little impact on caregiver burden. Additionally, 58% of patients from the multidisciplinary-treatment group reported at month 5 "very much improved" or "much improved" compared with 5% in the control group (Figure 3C and eTable 3 and eFigure 4 in Supplement 2). Further, previous noncontrolled cohort studies evaluating the long-term effect of a multidisciplinary approach in FMD showed that up to 66% of patients reported a sustained improvement in their self-perception of symptom severity.[24] The improvements in the current cohort seem to be driven by a significant improvement in pain and nonsignificant improvements in physical functioning and social functioning. Interestingly, a randomized feasibility study showed that specialized physiotherapy for FMD significantly improved SF-36 PCS score, physical function, and social function in FMD compared with standard physiotherapy, but a nonsignificant improvement was shown for pain and general health.[22] These discrepancies could be related to some differential aspects of our selected cohorts and approaches. First, we did not exclude patients with significant pain and/or fatigue symptoms at baseline in order to explore the effect of this intervention in a study sample with high external validity. However, this could have limited our power to improve physical function because these comorbidities could restrict the physiotherapy effectiveness. Second, the inclusion of a CBT intervention might explain the reported difference in other aspects, such as pain (EQ-5D, SF-36), especially because CBT has proven efficacy in chronic pain disorders.[39,40] Interestingly, similar results regarding summarized EQ profile values were appreciated among studies, although the increment in the EQ Index did not reach statistical significance in our study (between-group mean difference at month 5: 0.08 points; 95% CI, 0-0.2 points; $P = .13$). Further studies need to clarify the promising cost-effectiveness of a multidisciplinary intervention for FMD.

A previous randomized clinical trial[12] evaluating physical rehabilitation for functional gait disorders vs waiting list and a 4-week delayed-onset showed an improvement in independence and motor aspects of quality of life, similar to our

Table 2. Primary and Secondary Efficacy Outcomes, Assessed From Baseline to 3 Months and From Baseline to 5 Months (Intention-to-Treat Population)

Outcome	Baseline		Within-group change from baseline to 3 mo				Between-group difference in change month 3		Within-group change from baseline to 5 mo				Between-group difference in change month 5	
	Multidisciplinary treatment (n = 20), mean (SD)	Control intervention (n = 20), mean (SD)	Multidisciplinary treatment (n = 19)		Control intervention (n = 19)				Multidisciplinary treatment (n = 19)		Control intervention (n = 19)			
			Mean (95% CI)	Percentage of change	Mean (95% CI)	Percentage of change	Mean (95% CI)	*P* value[a]	Mean (95% CI)	Percentage of change	Mean (95% CI)	Percentage of change	Mean (95% CI)	*P* value[a]
Primary outcomes														
EQ VAS[b]	46.55 (23.09)	54.25 (19.69)	6.53 (−3.7 to 16.7)	14	−5.53 (−12.8 to 1.7)	−10	9.34 (−0.6 to 19.3)	.07	18.16 (5.9 to 30.4)	39	3.05 (−6.8 to 12.9)	6	13.67 (−1.7 to 29.0)	.09
EQ Index[c]	0.51 (0.34)	0.50 (0.24)	−0.01 (−0.1 to 0.1)	0	−0.05 (−0.2 to 0.1)	−10	0.001 (−0.1 to 0.1)	.98	0.06 (−0.1 to 0.2)	11	−0.01 (−0.1 to 0.1)	−2	0.08 (0 to 0.2)	.13
SF-36 PCS score[d]	33.32 (9.58)	31.33 (9.30)	2.35 (−0.6 to 5.3)	7	−1.11 (−4.6 to 2.4)	−4	4.23 (−0.9 to 9.4)	.11	3.21 (0.3 to 6.1)	10	−0.55 (−3.4 to 2.3)	−2	5.62 (2.3 to 8.9)[e]	<.001
SF-36 MCS score[f]	30.85 (11.84)	32.19 (14.52)	1.19 (−3.9 to 6.4)	4	0.76 (−3.0 to 4.6)	2	0.72 (−5.5 to 7.0)	.82	3.07 (−2.4 to 8.6)	10	2.94 (−2.2 to 8.1)	9	0.69 (−5.5 to 6.9)	.83
Secondary outcomes														
sFMDRS[g]	13.25 (5.61)	12.55 (7.58)	−7.11 (−9.6 to −4.6)	−53	0.26 (−1.3 to 1.9)	2	−7.15 (−9.7 to −4.6)[c]	<.001	−7.42 (−10-4 to −4.4)	−56	2.16 (0.6 to 3.8)	17	−9.41 (−12.6 to −6.2)[h]	<.001
CGI-S[i]	4.55 (0.76)	3.95 (1.15)	−1.32 (−1.8 to −0.8)	−29	0.21 (−0.1 to 0.5)	5	−1.53 (−2.0 to −1.1)[c]	<.001	−1.53 (−2.0 to −1.1)	−34	0.32 (−0.1 to 0.7)	8	−1.70 (−2.2 to −1.2)[h]	<.001
Zarit Caregiver Burden Interview	46.80 (15.40)	42.50 (14.94)	−2.88 (−9.8 to 4.0)	−6	4 (−2.7 to 10.7)	9	−0.38 (−10.3 to 9.6)	.94	−0.29 (−7.1 to 6.5)	−1	4.79 (−2.4 to 11.9)	11	−2.37 (−12.3 to 7.6)	.64

Abbreviations: CGI-S, Clinical Global Impressions-Severity; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, 36-Item Short Form Survey; sFMDRS, simplified Functional Movement Disorders Rating Scale; VAS, visual analog scale.

[a] *P* value was obtained from interaction between study group × visit in the linear mixed model with repeated measured.

[b] The EQ VAS records the patient's self-rated health on a vertical VAS, where the end points are labeled "the best health you can imagine" and "the worst health you can imagine."

[c] The EQ Index summarizes the overall severity of EQ-5D health states by generating weighted scores such as values. An EQ Index score of 1.0 represents full health.

[d] SF-36 PCS higher scores represent better health in the SF-36.

[e] *P* value <.01 after Bonferroni correction.

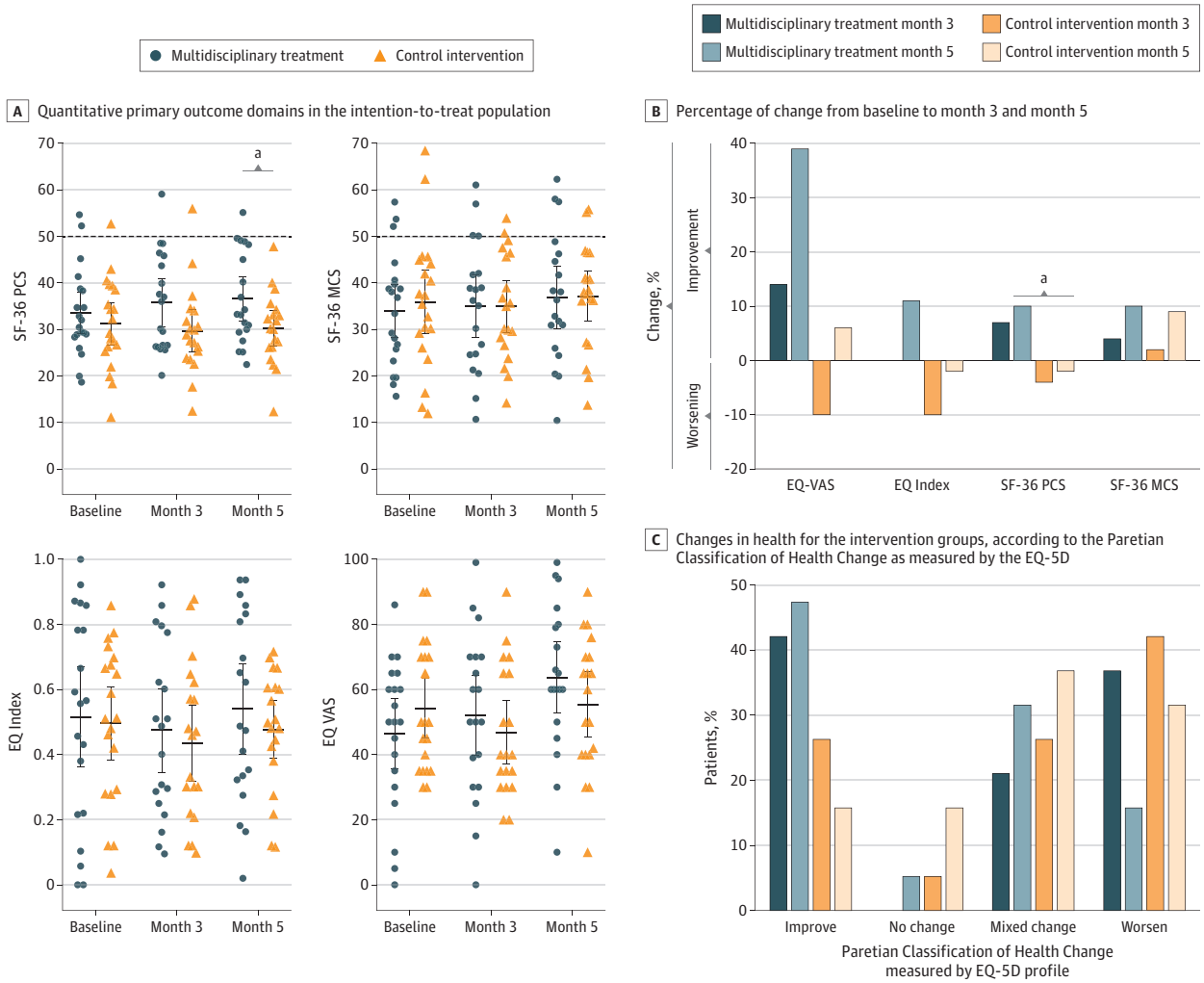
[f] SF-36 MCS higher scores represent better health in the SF-36.

[g] sFMDRS ranges from 0 to 54; higher scores show higher motor severity of the functional movement disorder.

[h] *P* value <.05.

[i] CGI-S ranges from 1 to 7, with higher scores indicating higher severity.

Figure 2. Primary Outcomes of Multidisciplinary Treatment for Functional Movement Disorders, as Compared With Control Intervention

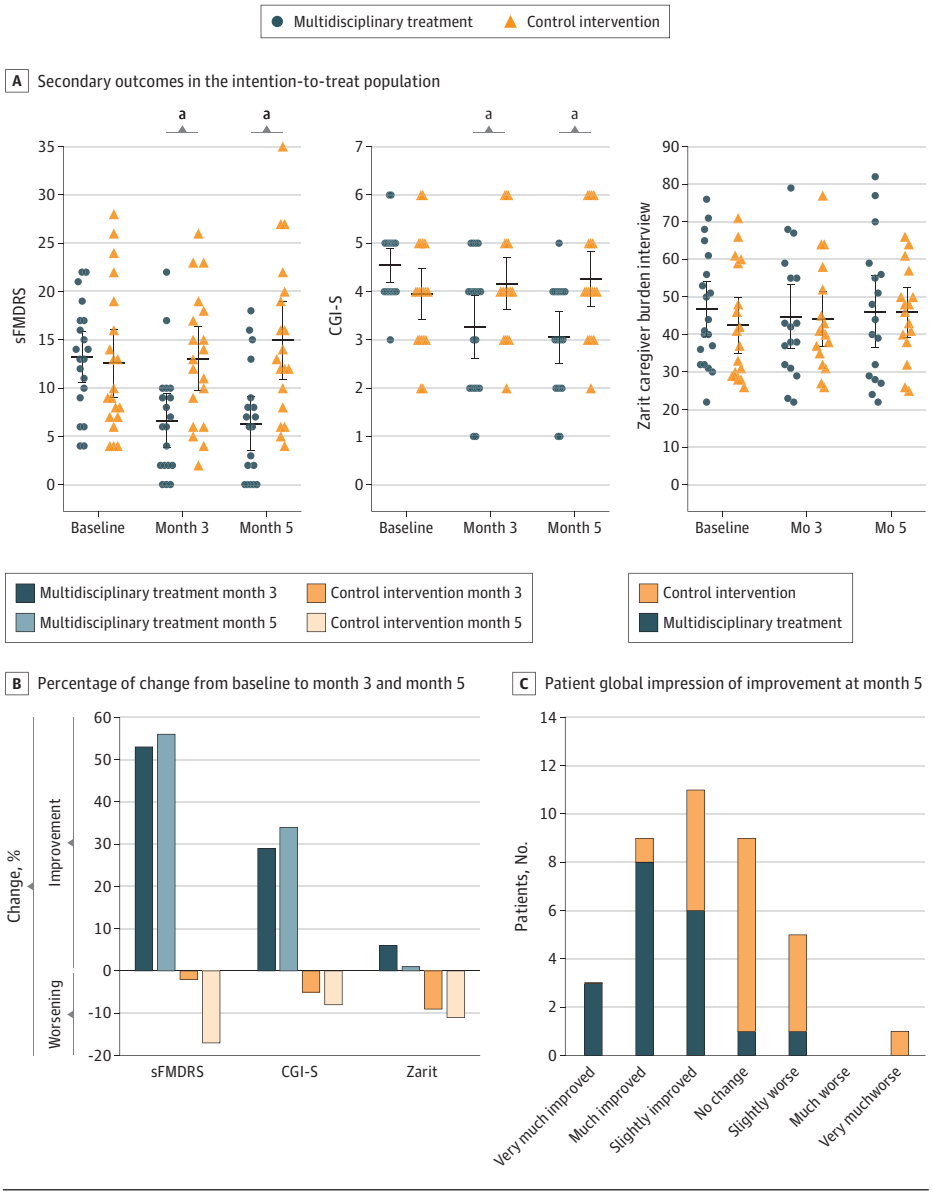


A, Quantitative primary outcome domains in the intention-to-treat population. The primary outcomes (36-Item Short-Form Survey [SF-36] Physical Component Summary [PCS] and SF-36 Mental Component Summary [MCS]) are assessed through norm-based scoring to obtain a normalized value compared with the reference population, which exhibits a mean (SD) of 50 (10) points. Higher scores of PCS and MCS indicate better state of the quality of life domain. Scores of 50 (grid line) represent mean value in the reference population. EQ visual analog scale (EQ VAS) exhibits the patient's self-perception of quality of health and is assessed on a scale from 0 to 100, with higher scores indicating better state of the quality of life. Values represent mean with 95% CI. B, Percentage of change from baseline to month 3 and month 5 in each domain of the continuous primary outcomes in both study groups. C, Changes in health for the intervention groups, according to the Paretian Classification of Health Change as measured by the EQ-5D (no change = the health profiles are the same; there has been no change in health as measured by the EQ-5D; improve = the second profile is better than the first; there has been an unequivocal improvement in health as measured by the EQ-5D; worsen = the second profile is worse than the first; there has been an unequivocal worsening in health as measured by the EQ-5D; mixed change = the first and second health profiles are noncomparable; there has been a change in health as measured by the EQ-5D but without further information we cannot say if it is an improvement or worsening).

[a]$P < .01$.

results (Table 2 and eFigure 6 in Supplement 2). There was an improvement in the physical function (SF-12) in the intervention group compared with the waiting list (mean difference: 11.7 points) during the follow-up,[12] in line with our nonsignificant change in SF-36 physical functioning (between-group difference at month 3: 17.31 points; 95% CI, 3.2-31.5 points; $P = .02$ and at month 5: 11.4 points; 95% CI, −2.3 to 25.2 points; $P = .10$) (eTable 2 in Supplement2). Interestingly, the physical rehabilitation included a cognitive behavioral frame of reference where education in the symptoms' nature played a key role. This aspect is in line with our diagnosis approach received by both groups, based on published recommendations for diagnosis and physiotherapy in FMD.[28,29] Another randomized clinical trial[13] assessed the impact of brief psychodynamics interventions against standard medical care and showed improvement in the severity of functional symptoms and CGI scales at 12-month follow-up. A nonsignificant positive impact was shown (SF-36 general health) in the treated group. However, there was a significantly quicker increase in their work ability.[13] This result is in line with our work (eTables 7-9

Figure 3. Secondary Outcomes of Multidisciplinary Treatment for Functional Movement Disorders, as Compared With Control Intervention



A, Secondary outcomes in the intention-to-treat population. The simplified Functional Movement Disorders (sFMDRS) ranges from 0 to 54, with higher scores indicating worse motor state of the FMD. Clinical Global Impression-Severity (CGI-S) ranges from 1 to 7, with higher scores indicating higher severity. Zarit Caregiver Burden Interview ranges from 22 to 110, with higher scores indicating higher level of caregiver burden by their relatives' health problem. Values represent mean with 95% CI. B, Percentage of change from baseline to month 3 and month 5, in each domain of the continuous secondary outcomes in both study groups. C, Patient Global Impression of improvement at month 5 of both study groups.

in Supplement 2). Even though the employment change status was not a primary outcome, 20% of patients within the multidisciplinary treatment group returned to work/studies at the end of the trial. Finally, a randomized clinical trial[14] evaluated the impact of CBT and CBT plus adjunctive physical activity against standard medical care. An improvement in motor function and mental health aspects was reported in both active groups compared with the nontreated group. Interestingly, no differences between active groups were observed in symptom severity at the end of the treatment. A nonsignificant additional decrease in anxiety and depression was observed in the combined-intervention group, suggesting a potential benefit of combined approaches in some aspects such as nonmotor symptoms. This type of physical intervention (structured low-/moderate-intensity walking) differs from our education-based physiotherapy, making it difficult to compare both combined treatments.

Strengths and Limitations

Our study had several strengths. In comparison with previous noncontrolled studies, one of the strengths of our study was the baseline similarities of both groups, the similar diagnosis approach, and the randomized process to either the multidisciplinary treatment or the control intervention. Interestingly, at month 5, both groups improved in self-rated (EQ VAS) and mental health aspects of quality of life (MCS). The negligent approach of current health systems for patients with an FMD and the lack of systematic assessment of these patients might explain why they improved in aspects such as mental health or general health perception;

highlighting the importance of a proper diagnosis and explanation.[29]

In terms of safety, apart from a worsening of the depressive symptoms in a patient with a previously diagnosed depression disorder from the control group, no adverse events were observed in the study groups (eTable 6 in Supplement 2). Additionally, there was a nonsignificant lower number of emergency department attendance (related to the FMD) in the multidisciplinary treatment group (eTable 7 in Supplement 2). This result is in line with previous studies that showed a reduction in the use of medical care and a potential cost-effectiveness of the active treatments for FMD.[13,22]

This study also had a few limitations. Our relatively small sample size may have limited our statistical power to find between-group differences during analysis. A sample size calculation was predefined based on previous studies (eMethods in Supplement 2). The moderate-severe burden of main comorbidities in our groups (pain and/or fatigue) may have interfered with the potential impact of the therapy in some aspects, such as physical functioning. Second, our study was a single-center study; therefore, further multicenter studies would be necessary to assess the potential implementation of the proposed approach in different health systems and their potential benefits. Interestingly, longitudinal prospective cohorts showing a multidisciplinary approach for FMD in diverse countries and health systems support our results.[12,13,15,24] This might suggest that the proposed therapy might be well-accepted and valid in a cross-cultural way. Third, our interventions were asymmetric with an increased time invested in the multidisciplinary program compared with the control intervention. Finally, our combined multidisciplinary approach may complicate distinguishing between the physiotherapy and CBT effect. However, the similarities between our results in physical aspects of quality of life and those previously reported with the same physiotherapy approach suggest that the addition of CBT might have improved nonmotor aspects, such as pain. Although these limitations were inherent to the multidisciplinary nature of our studied intervention, it should make our results cautiously interpreted.

Conclusions

Results of this randomized clinical trial showed that multidisciplinary treatment (combining specialized physiotherapy and CBT) effectively improved physical components of the quality of life of patients with an FMD and the severity of their motor symptoms. This effect on the physical aspects of quality of life is superior to a comprehensive diagnosis followed by psychoeducation and psychological support, and it seems to be driven by improvements in mobility and pain. Multidisciplinary treatment may also improve social functioning and may be cost-effective regarding return to work; however, further studies with larger cohorts and longer follow-up periods must clarify these aspects. Health systems might consider exploring this approach to solve the significant socioeconomic impact of FMDs.

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