- **Article title:** Proof of concept of a treatment for fibromyalgia based on physical activity, psychological support, and exposure to nature (NAT-FM)

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- **Abbreviations:** NAT-FM, Nature Activity Therapy for Fibromyalgia; TAU, Treatment-As-Usual; FM, Fibromyalgia; CSA, Classical Structural Assessment; EMA, Ecological Momentary Assessment; RCT, Randomized Clinical Trial; PA, Physical Activity; CBT, Cognitive Behavioral Therapy; CSSU, Central Sensitivity Syndromes Unit; ACR, American College of Rheumatology.

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- **Ethical disclosure:** All procedures performed in this study involving human participants were in accordance with the ethical standards of Ethics Commission in Animal and Human Experimentation of the Autonomous University of Barcelona and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This trial has been submitted for approval by the ethics committee of the Hospital Universitario de Vall d'Hebron (PR(AG)120/2018). This trial has been registered in the National Clinical Trials registry http://ClinicalTrials.gov, identifier NCT04190771.

- **Data sharing statement:** This manuscript reports the original results of a proof of concept of a clinical trial. The data obtained will be shared on demand with any research team after deidentification immediatly following publication. Authors also will share complementary documents: study protocol, statistical analysis plan, and informed consent.

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Proof of concept of a treatment for fibromyalgia based on physical activity and psychological support in nature (NAT-FM)

Abstract

Aim: To provide a preliminary assessment of the efficacy of the NAT-FM protocol as a complimentary treatment in patients with fibromyalgia (FM). **Methods:** A trial was conducted, with two arms: TAU (n = 6) and TAU+NAT-FM (n = 6). **Results:** There was a reduction in physical limitations and anxious/depressive symptoms and an improvement in positive affect in the intervention group. Also, this group showed a decrease in pain, catastrophizing, negative affect, and positively refocusing, and an increase in positive affect. Intrasession assessments showed an increase in positive affect, self-efficacy, and energy, along with a decrease in stress. Intersession assessments revealed an increase in pain, valence, and dominance. **Conclusion:** The results suggest the appropriateness of the NAT-FM protocol.

Trial registration: NCT04190771

First draft submitted; Accepted for publication; Published online

Keywords: Fibromyalgia, treatment, physical activity, cognitive behavioral therapy, nature, randomized controlled trial, proof of concept research.

1. Introduction

Fibromyalgia (FM) is a chronic syndrome, of unknown etiology, characterized by widespread musculoskeletal pain and a constellation of symptoms such as sleep problems, cognitive disorders, fatigue, high levels of distress, anxiety, and depression [1]. Previous research has shown that symptomatology and comorbidity with other diseases directly influence the functional status and quality of life of people with FM [2-4]. Currently, the prevalence of this syndrome is close to 2% worldwide [5] and 2.4% in Spain [6]. The healthcare and societal costs associated with FM represent a high burden for industrialized countries [7].

In recent decades, a wide range of pharmacological and non-pharmacological treatment options for managing FM have been tested [8-10]. The main problem of pharmacological treatments are the side effects (e.g., dizziness, diarrhea,) and the low efficacy_found in RCTs [11]. In general, non-pharmacological treatments combining physical activity (PA) with Cognitive Behavioral Therapy (CBT) have demonstrated good efficacy [12], and RCTs based on PA programs have contributed to the reduction of symptoms and improvements in quality of life [13]. Further, studies focused on CBT have indicated their relevance for the acceptance of FM, development of coping strategies, and reduction of negative affect [14].

Multicomponent treatments that incorporate PA, CBT, and pharmacological treatment have been recognized for their efficacy in increasing functional capacity, reducing pain, and improving the quality of life [12]. There is also evidence that treatments based on activities in nature generate positive effects on mental health in general [15-17] and on the clinical population with chronic pain and depression [18,19]. Recognizing the strengths of these treatments, the NAT-FM (acronym for Nature Activity

Therapy for Fibromialgya) has emerged as a novel intervention that integrates empirical evidence for the benefits of CBT, PA practice, and exposure to natural contexts.

As a proof-of-concept study, the main objective of the present work was to provide a preliminary assessment of the efficacy of the multicomponent NAT-FM treatment as a coadjuvant of treatment as usual (TAU) in patients with fibromyalgia (FM). In this regard, the specific objectives of this work were: (a) to preliminarily evaluate the efficacy of the NAT-FM treatment as coadjuvant of treatment as usual (TAU) for improving a wide range of primary and secondary clinical outcomes in a small sample of patients with FM; (b) to collect information provided by the participants regarding the adequacy of the multicomponent intervention; and (c) to reflect on the improvement plan of the NAT-FM protocol.

2. Patients & Methods

2.1. Study Design

A proof of concept clinical trial of a simplified version of the protocol was carried out, consisting of four 3-hour sessions distributed over 7 consecutive days, with two treatment arms: (a) TAU (control group) and (b) TAU + NAT-FM (intervention group). The clinical trial is registered and available at Clinicaltrials.gov (NCT04190771).

2.2. Participants

Twelve patients with FM were recruited from the Central Sensitivity Syndromes Unit (CSSU) at the Vall d'Hebron University Hospital (Barcelona, Spain). Of these participants, 6 were allocated to the intervention group and 6 to the control group. The participants were recruited from a database with the medical records of patients diagnosed with FM, according to the 2010/2011 diagnostic criteria of the American College of Rheumatology (ACR) [1]. The inclusion criteria were: (a) adults ≥18 years old, (b) to meet the 2010/2011 ACR diagnostic criteria for FM [1], and (c) be able to understand

Spanish and agree to participate in the study. The exclusion criteria were: (a) having participated in concurrent or past RCTs (previous year) and (b) exhibiting comorbidity with severe mental disorders (i.e. psychosis) or neurodegenerative diseases (i.e. Alzheimer's) that limit the ability of the patient to participate in the RCT.

2.3. Procedure

The researchers provided an overview of the study to patients with FM from the hospital. Those interested in participating received a written informed consent form, in which an outline of the sessions was provided. Treatment allocation (TAU or TAU + NAT-FM) was carried out according to the availability of the patients. This research was conducted in accordance with the ethical standards established in the Helsinki Declaration of 1964 and was approved by the university's ethics committee (PR(AG)120/2018).

The proof of concept version of NAT-FM protocol was implemented in a group format. The professional team in charge of delivering the 4 sessions was composed of 3 people (a health psychologist, sports technician, and research assistant). Four central treatment sessions (1, 2, 6, and 11) were selected to ensure the representativeness of the short version of the protocol. The treatment was conducted over a period of 7 days, and each session lasted approximately 3 hours. Of this time, 2 hours and 30 minutes was used to conduct each session and 30 minutes was allocated for receiving feedback from patients regarding the structure and execution of the sessions. Prior to beginning the sessions with the patients, the team carried out an *in situ* preparation trial with the research group.

The activities selected were hiking, yoga, and caving. The sectors were Sant Genís dels Agudells (a forest; coordinates 41° 25.926'N, 2° 8.356'E, for hiking), Escletxes del Papiol (a cave area; coordinates 41° 26.315'N, 2° 1.061'E, for caving and yoga), and the Via Verda del Vallès (a hiking pathway; coordinates 41° 30.562'N, 2° 5.573'E, for the initial functional test). The treatments were applied through a parallel design to reduce

seasonal variability in the study measures. The patients were evaluated before (pre), during (during), and after (post) the treatment. The measurements were made according to the times of administration: (a) Classical Structural Assessment (CSA) of the primary and secondary outcomes: pre and post; and (b) Ecological Momentary Assessment (EMA): intra-sessions (session log) and intersession (daily log between sessions). The flowchart of this proof of concept is presented in Figure 1.

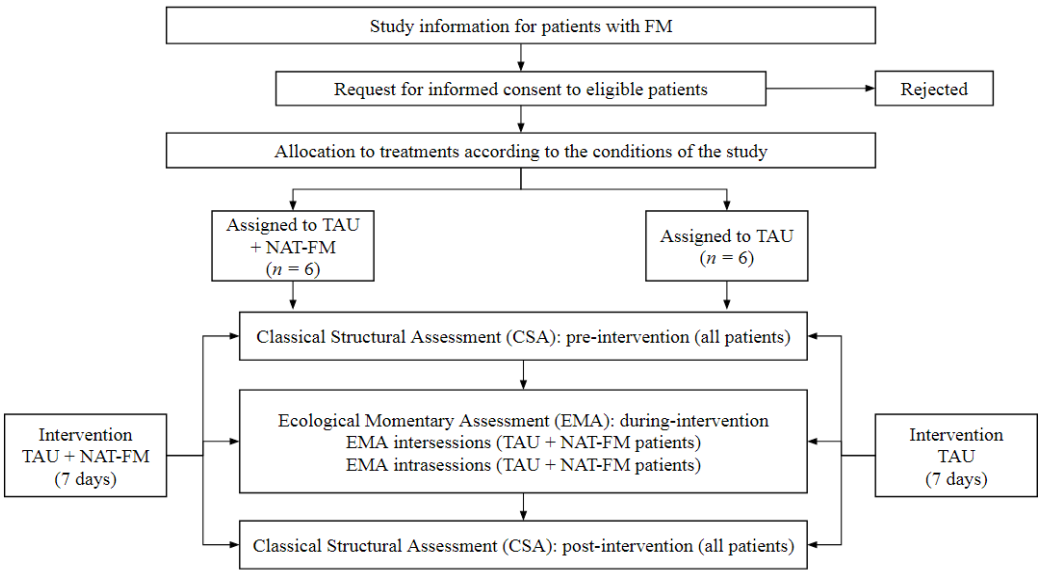

Figure 1. Proof of concept flow chart.

2.4. Treatments

2.4.1. Intervention group (TAU + NAT-FM)

NAT-FM is an adjuvant treatment designed as a primary intervention to help patients reduce the impact of FM on its functionality. The secondary objectives are to increase positive affect, emotional regulation, and self-efficacy, as well as decrease negative affect, pain, fatigue, and pain catastrophizing thoughts. The mechanisms that are not directly targeted, but that could still indirectly be improved during treatment are perceived competence, self-esteem, stress, and sleep quality, and these were therefore also evaluated.

The preparation of the treatment was guided by the procedures established in the protocol. The therapeutic objectives were selected considering the results of a systematic review of the psychological characteristics of people with FM (affective, cognitive, metacognitive, and personality profiles) [20] and the validation of a panel of experts made up of researchers and psychologists (MS, JPS-M, AF-S, JVL, AS, & JM-U). The activities were chosen considering the results of two previous empirical studies specifically aimed at designing the NAT-FM protocol: one concerning the therapeutic potential of 10 activities in nature [21] and another regarding the determinants of therapeutic adherence to a program based on physical activity for FM [22].

The sectors (natural spaces) in which the sessions were held were previously validated by a panel of psychologists (n = 3) and a sports instructor specialized in hiking/mountaineering. The instruments used in the NAT-FM protocol was established according to a consensus regarding the proposed instruments, the assessment times corresponding to each phase of the treatment, and the administration platforms used. The decision to combine different assessment times (CSA + EMA) was part of a strategic approach to obtain more precise information on the dynamics of the variables to be evaluated and, in particular, to record the affective and cognitive impact of each activity, as well as its transfer to everyday life. The frequency of administration of EMA was established based on the analysis of the results of a systematic review of the characteristics of its use in studies with patients with chronic pain [23]. The administration procedures were validated through the results of a usability study involving a panel of experts made up of psychologists and patients with FM.

2.4.2. Control group (TAU)

The usual treatment (TAU) provided to the control group was based primarily on the prescription of drugs adjusted to the symptomatic profile of each patient, with complementary advice on aerobic exercise adapted to the physical abilities of the patients. None of the patients had practiced any of the activities of the NAT-FM treatment before entering the study.

2.5. Study Measures

The assessment were organized considering the time points (CSA + EMA) that were established based on the results of the usability study. Table 1 shows the collection times and assessment measures.

2.5.1. Classical Structural Assessment (CSA)

2.5.1.1. General measures

The *Clinical and sociodemographic information questionnaire* was used to obtain the general and clinical data of patients (including age, educational level, employment status, and medical history).

2.5.1.2. Measurements of primary outcomes.

The *Revised Fibromyalgia Impact Questionnaire (FIQR)* was used to measure the impact generated by FM during the last week. It consisted of 21 items that are answered on a numerical rating scale of 11 points. Higher scores reflect greater impairment. The Spanish version has adequate internal consistency (α = .93) and test-retest reliability (r = .84) [24,25].

2.5.1.3. Measures of secondary outcomes.

The *Hospital Anxiety and Depression Scale (HADS)* was used to quantify the severity of anxiety and depression symptoms. It consisted of 14 items that are answered on a 4-point Likert scale. Higher scores indicate greater severity of the specific

symptomatology. The Spanish version presents an adequate internal consistency for anxiety (α = .83) and depression (α = .87) [26,27].

The *Positive and Negative Affect Schedule (PANAS)* was used to assess positive and negative affect. It consisted of two dimensions (positive affect and negative affect) of 10 items each that are answered on a 5-point Likert scale. Higher scores indicate a greater presence of specific affectivity. The Spanish version presents adequate internal consistency for positive affect (α = .92) and for negative affect (α = .88) [28,29].

The *Cognitive Emotion Regulation Questionnaire (CERQ)* was used to assess individual differences in the cognitive regulation of emotions. In this study, the short 18-item version was used, which has a 5-point Likert response format. Higher scores indicate higher frequency of the use of each cognitive strategy. The Spanish version has adequate internal consistency (α = .77 to .93) and test-retest reliability (r = .60 to .85) for the subscales [30,31].

The *Personal Perceived Competence Scale (PPCS)* was used to measure perceived competition. It consisted of 8 items that are answered on a 6-point Likert scale. Higher scores indicate greater perceived competition. The Spanish version has an adequate internal consistency (α = .83) [32,33].

The *Rosenberg Self-Esteem Scale (RSES)* was used to measure self-esteem. It consisted of 10 items that are answered on a 4-point Likert scale. Higher scores indicate greater self-esteem. The Spanish version has adequate internal consistency (α = .87) and test-retest reliability (r = .72 to .74) [34,35].

The *Pain Catastrophizing Scale (PCS)* was used to evaluate pain catastrophizing thoughts. It consisted of 13 items that are answered on a 5-point Likert scale. Higher scores indicate a higher number of catastrophic thoughts. The Spanish version has adequate internal consistency (α = .79) and test-retest reliability (r = .84) [36,37].

The *Perceived Stress Scale (PSS-4)* was used to assess the stress perceived by people during the last month. In this study, the short 4-item version was used, which is answered on a 5-point Likert scale. Higher scores indicate greater perceived stress. The Spanish version has an acceptable internal consistency (α = .77) [38,39].

2.5.2. Ecological Momentary Assessment (EMA)

EMA was addressed to assess: (a) the specific short-term impact of each activity and (b) the extent to which the effects of treatment transfer to daily life. Measurements during the sessions (intra-session assessment) were made before and after each activity in nature using an online form. Measurements of the daily records between sessions (inter-session assessment) were carried out through an app, in which patients had to respond 6 times a day (twice in the morning, twice in the afternoon, and twice at night). The instruments of the intersession and intrasession assessment were applied exclusively to the intervention group.

2.5.2.1. Measures of secondary outcomes

The *Self-Assessment Manikin (SAM)* [40] was used to assess the emotional state of people. It consisted of 3 blocks of diagrammed pictograms in a continuous line, representing the following three dimensions of the affective response: valence, arousal, and dominance. Each scale has a 9-point Likert response format. The total scores on each scale range from 1 to 9. Higher scores on valence indicate greater positive mood; higher scores on arousal indicate greater activation and alert; whilst for dominance a higher score indicates greater perception of control and personal confidence. These three dimensions of the affective response were evaluated both in intra-session assessment and in inter-session assessment.

Unique item questionnaires. For the assessment of the variables fatigue, pain, and sleep quality, the three items of the Visual Analog Scale (VAS) of the FIQR were

selected. For stress and self-efficacy, *ad hoc* questions were designed with a single item, rated on a scale from 0 to 10, in a VAS format. For comprehension purposes, fatigue was inversely operationalized as "energy". Higher scores indicate greater perceived fatigue, pain, sleep quality, stress, and self-efficacy. The variables fatigue, pain, and sleep quality were evaluated by inter-session assessment, whereas the variables energy, pain, stress, and self-efficacy were evaluated by intra-session assessment.

2.5.3. Assessment of the NAT-FM

The *Adequacy Questionnaire* was used to record information regarding the patients' opinions on the NAT-FM program. It consisted of 8 items that are answered on a 5-point Likert scale (*strongly disagree* to *strongly agree*), 11 items on a scale of 11 points (range 0 to 10), and 1 item with an open question. The closed-ended items explored information of interest for protocol improvement, such as, for example, the appropriateness of treatment structure and instrument delivery formats; and the open-ended item examined the general perception of NAT-FM treatment.

Table 1

Study periods at which measures and data were collected

	Pre	During	Post
Classical Structural Assessment (CSA)			
General measures			
Sociodemographic information (age, education level, etc.)	X		
Clinical information (medical history, FM history, etc.)	X		
Primary outcome measure			
FIQR (functional impairment)	X		X
Secondary outcome measures			
HADS (anxiety and depression)	X		X
PANAS (negative and positive affect)	X		X
CERQ (cognitive emotion regulation)	X		X
PPCS (perceived competence)	X		X
RSES (self-esteem)	X		X

PCS (pain catastrophizing)	X		X
PSS-4 (stress)	X		X
Ecological Momentary Assessment (EMA)			
Secondary outcome measures			
SAM (emotional state: valence, arousal and dominance)		X	
VAS (energy, pain, sleep quality)		X	
VAS (self-efficacy and stress)		X	
Assessment of the NAT-FM			
Adequacy measures			
Appropriateness of treatment structure			X
Appropriateness of instrument delivery formats			X
General perception of NAT-FM treatment			X

HADS: Hospital Anxiety and Depression Scale; FIQR: Revised Fibromyalgia Impact Questionnaire; PANAS: Positive and Negative Affect Schedule; CERQ: Cognitive Emotion Regulation Questionnaire; PPCS: Personal Perceived Competence Scale; RSES: Rosenberg Self-Esteem Scale; PCS: Pain Catastrophizing Scale; PSS-4: Perceived Stress Scale; SAM: Self-Assessment Manikin; VAS: Visual Analog Scale.

2.6. Statistical Analysis

The analysis was conducted using the SPSS statistical program (v25). Initially, descriptive analyses were conducted for all study outcomes. Before proceeding to the inferential analyses of CSA and EMA assessments, a compliance review was conducted regarding the required normality of all variables using the Shapiro-Wilk test (< 30 participants), and the homogeneity of variance was checked using Levene's test. The results obtained allowed us to accept the assumption of normality of the distribution of the variables in the study groups, as well as the assumption of equal variance. In this regard, it was not necessary to use non-parametric models. In this study there were no missing data for any of the variables assessed.

The comparison of baseline (pre) CSA measurements between the two intervention arms was conducted using Chi-square tests (X^2) for categorical variables, and Student *t* tests for independent samples (*t*), when dealing with the continuous variables. To assess the overall effect of the treatment, a 2 x 2 mixed model ANOVA was conducted, with the two-stage *phase* as a within-subject factor (pre vs. post), and with the two-level

group as the between-subject factor (TAU vs. TAU + FM). The effect size was estimated using the ηp^2 (partial eta-square) for each model factor. The data from EMA intra-sessions were subjected to a Student t-test for dependent samples, whilst the EMA intersessions were analyzed both on a time-domain (single regression linear model for each dependent variable), in order to assess the transfer of the treatment effects to daily life. For this linear model, in total, 48 administrations (6 administrations x 8 days) were used for the secondary clinical outcomes of emotional state (valence, arousal, and dominance), energy, and pain, and 8 administrations (1 administration x 8 days) for sleep quality.

Given the sample size, Hedge g (g) was used as an indicator of the effect size for this analysis, which was classified according to the following proposal: strong ($g > 0.8$), moderate ($0.5 < g < 0.80$), weak ($0.2 < g < 0.5$) and null ($g < 0.2$) [41].

3. Results

3.1. Baseline characteristics

As shown in Table 2, statistically significant differences were found for the pain catastrophizing scores ($p = .01$), severity of the symptoms ($p = .03$), and cognitive emotion regulation strategy of positive refocusing ($p = .01$). The mean age of all patients was 53.42 years ($SD = 7.51$; range 41 to 65), BMI of 26.44 ($SD = 5.9$; range 19.5 to 36.7), and the mean number of years diagnosed with FM was 37.5 ($SD = 9.72$; range 20 to 50). Of the sample, 25% were actively employed, 41.7% reported a level of primary education, 75% had a certified disability, and 58.3% had a comorbid mental disorder. In addition, 66.7% consumed medications for depression, 58.3% for anxiety, 91.7% for pain, and 75% for sleep problems.

Table 2

Baseline characteristics of TAU + NAT-FM patients vs. TAU

	TAU + FM (*n* = 6)	TAU (*n* = 6)	*t / x2*	*p*
General measures				
Age (*M, SD*)	52.7 (5.71)	54.17 (9.5)	-0.33	.75
BMI (*M, SD*)	26.12 (3.99)	26.77 (7.78)	-0.18	.86
Years with FM (*M, SD*)	41.17 (7.41)	33.83 (10.98)	1.36	.20
Persons in charge (*M, SD)*	1.83 (1.17)	1.33 (1.03)	0.78	.45
Employees (*f, %*)	2 (33.3)	1 (16.7)	0.44	.50
With primary studies (*f, %*)	2 (33.3)	3 (50)	0.34	.56
Certified disability (*f, %*)	4 (66.7)	5 (83.3)	0.44	.50
Comorbid mental disorders (*f, %*)	4 (66.7)	3 (50)	0.34	.56
Medication (f, %)				
For depression	3 (50)	5 (83.3)	1.50	.22
For anxiety	2 (33.3)	5 (83.3)	3.09	.08
For pain	5 (83.3)	4 (66.7)	1.09	.29
For sleep problems	5 (83.3)	4 (66.7)	0.44	.50
Measures of primary outcomes (M, SD)				
FIQR_Physical function (0-30)	18.17 (2.62)	18.72 (4.36)	-0.27	.79
FIQR_General impact (0-20)	9.5 (2.81)	13.50 (4.09)	-1.97	.08
FIQR_Severity symptoms (0-50)	27.67 (4.1)	33.42 (4.02)	-2.45	.03*
FIQR_Total (0-100)	55.33 (6.82)	65.64 (9.61)	-2.14	.06
Measures of secondary outcomes (M, SD)				
HADS_Anxiety(0-21)	11.33 (1.63)	11.67 (2.73)	-0.26	.80
HADS_Depression(0-21)	10.33 (2.94)	10.67 (4.5)	-0.15	.88
HADS_Total (0-42)	21.67 (4.08)	22.33 (6.89)	-0.20	.84
PANAS_Positive (10-50)	22 (8)	19 (6.75)	0.70	.50
PANAS_Negative (10-50)	19.33 (8.29)	25.5 (8.78)	-1.25	.24
CERQ_Self-blame (2-10)	3.5 (1.76)	5.33 (3.08)	-1.27	.23
CERQ_Other-blame (2-10)	2.17 (0.41)	4.33 (3.14)	-1.68	.15
CERQ_Acceptance (2-10)	5 (2.37)	7.67 (2.1)	-2.08	.06
CERQ_Refocus on planning (2-10)	6.5 (1.52)	4.83 (1.83)	1.71	.12
CERQ_Positive refocusing (2-10)	6.33 (2.34)	3.5 (0.84)	2.79	.02*
CERQ_Rumination (2-10)	3.67 (1.75)	4.83 (1.94)	-1.09	.30
CERQ_Positive reappraisal ((2-10)	5.83 (1.72)	5.83 (2.48)	0.00	1
CERQ_Putting into perspective (2-10)	6.5 (2.07)	6.83 (1.72)	-0.30	.77
CERQ_Catastrophizing (2-10)	3.5 (1.97)	5.33 (2.07)	0.94	.15

PPCS_ Perceived competence (8-48)	27 (4.52)	24.67 (6.25)	0.74	.48
RSES_Self-esteem (10-40)	29.17 (4.26)	24.33 (5.24)	1.75	.11
PCS_Pain catastrophizing (0-52)	12 (4.73)	24.5 (8.22)	-3.23	.01*
PSS-4_Stress (0-16)	8.33 (2.34)	10.33 (3.44)	-1.17	.27

Note. The values represent means (*M*) and standard deviation (*SD*) or frequency (*f*) and percentages (*%*), in their respective order of presentation. The ranges of measurements corresponding to each instrument are presented in parentheses. BMI = Body Mass Index. * <.05, ** < .01, *** < .001

3.2. Impact of NAT-FM treatment on primary and secondary outcomes

For the *interaction phase* (pre-post) *x group* (TAU + FM vs. TAU) *analysis*, Table 3 shows that for the intervention group there was a significant increase in positive affect ($F(1,10) = 19.73$; $p < .001$; $np^2 = 0.66$), as well as a decrease in physical function limitations ($F(1,10) = 5.38$; $p = .04$; $np^2 = 0.35$), in anxiety ($F(1,10) = 14.35$; $p = .004$; $np^2 = 0.59$), and in anxious/depressive symptoms ($F(1,10) = 9.61$; $p = .01$; $np^2 = 0.49$). The *within-subjects analysis* (pre-post), revealed that for both groups there was a significant increase in positive affect ($F(1,10) = 22.70$; $p < .001$; $np^2 = 0.69$) and in the emotion regulation strategy of other-blame ($F(1,10) = 5.00$; $p = .04$; $np^2 = 0.33$). The *between-group analysis* (TAU + FM vs. TAU), revealed that in the intervention group there was a decrease in pain catastrophizing thoughts ($F(1,10) = 11.85$; $p = .01$; $np^2 = 0.54$), negative affect ($F(1,10) = 6.17$; $p = .03$; $np^2 = 0.38$), and the emotional regulation strategy of positively refocusing ($F(1,10) = 6.90$; $p = .02$; $np^2 = 0.41$), as well as an increase in positive affect ($F(1,10) = 7.27$; $p = .02$; $np^2 = 0.42$). The effect sizes reported in these differences were moderate to strong, ranging between 0.33 and 0.69.

Table 3

CSA of primary and secondary outcomes before and after treatment

	TAU + FM (*n* = 6)		TAU (*n* = 6)		Phase (pre-post)			Group (TAU + NAT-FM vs. TAU)			Interaction Phase x Group		
	Pre	Post	Pre	Post	*f*	*p*	*np2*	*f*	*p*	*np2*	*f*	*p*	*np2*
Measures of primary outcomes (M, SD)													
FIQR_Physical function (0-30)	18.17 (2.62)	13.83 (3.06)	18.72 (4.36)	19.50 (4.84)	2.6	.14	0.21	2.63	.14	0.21	5.38	.04*	0.35
FIQR_General impact (0-20)	9.5 (2.81)	7.5 (3.62)	13.50 (4.09)	13.17 (4.26)	1.75	.21	0.15	6.02	.03	0.38	.89	.37	0.08
FIQR_Severity symptoms (0-50)	27.67 (4.1)	29 (4.46)	33.42 (4.02)	29.33 (3.64)	0.80	.39	0.07	2.92	.12	0.23	3.12	.11	0.24
FIQR_Total (0-100)	55.34 (6.82)	50.33 (10.22)	65.64 (9.61)	62 (9.94)	2.17	.17	0.18	6.06	.03	0.38	0.05	.82	0.01
Measures of secondary outcomes (M, SD)													
HADS_Anxiety(0-21)	11.33 (1.63)	8 (2.83)	11.67 (2.73)	13.17 (3.31)	2.06	.18	0.17	3.74	.08	0.27	14.35	.004**	0.59
HADS_Depression(0-21)	10.33 (2.94)	9.5 (3.89)	10.67 (4.5)	10.83 (4.35)	0.75	.40	0.07	0.14	.72	0.01	1.70	.22	0.14
HADS_Total (0-42)	21.67 (4.08)	17.5 (6.09)	22.33 (6.89)	24 (6.39)	1.77	.21	0.15	1.17	.30	0.10	9.61	.01*	0.49
PANAS_Positive (10-50)	22 (8)	36.33 (4.76)	19 (6.75)	19.5 (7.69)	22.70	.001***	0.69	7.27	.02*	0.42	19.73	.001***	0.66
PANAS_Negative (10-50)	19.33 (8.29)	15.33 (3.33)	25.5 (8.78)	29 (9.32)	0.01	.91	0.01	6.17	.03*	0.38	3.22	.10	0.24
CERQ_Self-blame (2-10)	3.5 (1.76)	3.17 (1.17)	5.33 (3.08)	4.17 (2.79)	4.17	.07	0.29	1.19	.29	0.10	1.29	.28	0.11
CERQ_Other-blame (2-10)	2.17 (0.41)	2 (0)	4.33 (3.14)	3.67 (3.20)	5.00	.04**	0.33	2.22	.17	0.18	1.80	.21	0.15
CERQ_Acceptance (2-10)	5 (2.37)	5 (2.37)	7.67 (2.1)	5 (2.19)	2.44	.15	0.20	1.85	.20	0.16	2.44	.15	0.20
CERQ_Refocus on planning (2-10)	6.5 (1.52)	6.83 (3.19)	4.83 (1.83)	5.67 (1.75)	0.92	.36	0.08	1.66	.23	0.14	0.17	.69	0.02
CERQ_Positive refocusing (2-10)	6.33 (2.34)	6.67 (2.42)	3.5 (0.84)	4 (1.67)	1.24	.29	0.11	6.90	.02*	0.41	0.05	.83	0.01
CERQ_Rumination (2-10)	3.67 (1.75)	3.67 (1.03)	4.83 (1.94)	6 (2.61)	1.79	.21	0.15	2.96	.12	0.22	1.79	.21	0.15
CERQ_Positive reappraisal ((2-10)	5.83 (1.72)	6.83 (1.33)	5.83 (2.48)	5.33 (1.97)	0.25	.62	0.02	0.57	.47	0.05	2.28	.16	0.19
CERQ_Putting into perspective (2-10)	6.5 (2.07)	6.83 (1.83)	6.83 (1.72)	7 (2.19)	0.23	.64	0.02	0.06	.81	0.01	0.03	.87	0.01
CERQ_Catastrophizing (2-10)	3.5 (1.97)	3.17 (1.33)	5.33 (2.07)	5.33 (2.80)	0.16	.70	0.01	3,06	.11	0.23	0.16	.70	0.01
PPCS_ Perceived competence (8-48)	27 (4.52)	29.17 (3.25)	24.67 (6.25)	31.83 (5.45)	4.20	.07	0.30	0.01	.93	0.01	1.21	.30	0.11
RSES_Self-esteem (10-40)	29.17 (4.26)	30.33 (4.08)	24.33 (5.24)	23.17 (6.79)	0.01	1	0.01	4.44	.06	0.31	1.46	.25	0.13
PCS_Pain catastrophizing (0-52)	12 (4.73)	12.5 (6.77)	24.5 (8.22)	25.5 (9.14)	0.12	.73	0.01	11.85	.01*	0.54	0.01	.91	0.01
PSS-4_Stress (0-16)	8.33 (2.34)	6.83 (1.83)	10.33 (3.44)	10.5 (3.15)	2.02	.18	0.17	3.44	.09	0.26	3.16	.11	0.24

Nota. *np2* = eta2 parcial como tamaño de efecto. * < .05, ** < .01, *** < .001

3.3. Register of secondary outcomes in intra-session measures (group TAU + NAT-FM)

Table 4 indicated that no statistically significant differences were found between pre-post scores on affective response (valence, arousal, and dominance), energy, pain, stress, and self-efficacy in any of the activities carried out during the sessions. However, in the hiking activity of Session 2 there were reports of moderate/strong effect increases in self-efficacy (g = 0.63) and energy (g = 0.76), as well as a decrease in stress (g = 0.95). In the caving activity of Session 3, improvements in the affective response of valence (g = 0.88) and arousal (g = 1.24) were identified, as well as in self-efficacy (g = 0.98), with high effect sizes.

In the caving activity of Session 4, increases in the affective response of valence (g = 0.93), energy (g = 1.05), and self-efficacy (g = 1.31), as well as stress reduction (g = 2.68) were identified, with strong effect sizes. In the yoga activity of Session 4 there was, with a strong effect size, a decrease in the affective response of dominance (g = 0.99). Overall, the weighted average of the effect sizes (ranging from 0.25 to 1.01) for the three activities that made up the prototyped sessions (hiking, caving, and yoga) of the trial indicated an increase in self-efficacy (g = 0.8) and energy (g = 0.68), and a decrease in stress (g = 1.01).

Table 4

EMA measures of secondary outcomes intra-sessions *(group TAU + NAT-FM)*

	TAU + FM (n = 6)				
Measures of secondary outcomes (M, SD)	Pre	Post	*t*	*g*	*p*
Session 2: hiking (n = 5)					
SAM_Valence (1-9)	7.2 (1.48)	7.2 (2.05)	0	0	1
SAM_Arousal (1-9)	6.4 (1.34)	7 (2.0)	-.49	0.32	.65
SAM_Dominance (1-9)	6.8 (0.84)	7.2 (0.84)	-.78	0.43	.48
VAS_Energy (0-10)	6.4 (1.67)	7.8 (1.64)	-.97	0.76	.38
VAS_Pain (0-10)	6.6 (1.52)	5.6 (3.5)	.66	0.33	.55
VAS_Stress (0-10)	5.2 (1.64)	3 (2.45)	1.54	0.95	.19

VAS_Self-efficacy (0-10)	6.4 (1.51)	7.4 (1.34)	1.32	0.63	.29
Session 3: caving (n = 3)					
SAM_Valence (1-9)	7.33 (0.57)	8.33 (1.15)	-1.73	0.88	.22
SAM_Arousal (1-9)	6.33 (1.15)	8 (1.0)	-5	1.24	.04
SAM_Dominance (1-9)	7 (1.0)	7.67 (1.15)	-.76	0.49	.53
VAS_Energy (0-10)	6.67 (2.08)	7.67 (1.53)	-.87	0.44	.48
VAS_Pain (0-10)	4.67 (3.21)	4 (3.6)	.20	0.16	.86
VAS_Stress (0-10)	2.67 (2.52)	2.67 (3.05)	0	0	1
VAS_Self-efficacy (0-10)	6.67 (1.53)	8.33 (1.15)	-1.39	0.98	.3
Session 4: caving (n = 3)					
SAM_Valence (1-9)	7.33 (1.53)	8.67 (0.58)	-2	0.93	.18
SAM_Arousal (1-9)	8 (1)	8.67 (0.58)	-2	0.65	.18
SAM_Dominance (1-9)	7.33 (2.08)	8.67 (0.58)	-1.51	0.71	.27
VAS_Energy (0-10)	7.33 (2.08)	9.33 (0.58)	-2	1.048	.18
VAS_Pain (0-10)	6.33 (0.58)	5.33 (3.05)	.58	0.36	.62
VAS_Stress (0-10)	6 (1)	1.67 (1.53)	2.98	2.68	.09
VAS_Self-efficacy (0-10)	8 (1)	9.33 (0.58)	-4	1.31	.06
Session 4: yoga (n = 3)					
SAM_Valence (1-9)	8.33 (1.15)	7.67 (1.52)	.55	0.39	.63
SAM_Arousal (1-9)	8 (1.73)	7.33 (1.15)	.46	0.36	.69
SAM_Dominance (1-9)	8.33 (1.15)	7 (1)	1.1	0.99	.38
VAS_Energy (0-10)	8.33 (1.15)	7 (3.46)	.55	0.41	.63
VAS_Pain (0-10)	6.67 (1.53)	6.33 (4.04)	.23	0.09	.84
VAS_Stress (0-10)	2 (2.65)	1 (0)	.65	0.43	.58
VAS_Self-efficacy (0-10)	8.67 (1.53)	7.67 (2.31)	.58	0.41	.62

Note. *g* = *g* of Hedges as effect size. * < .05, ** < .01, *** < .001

3.4. Register of secondary outcomes in EMA between-sessions measures (group TAU + NAT-FM)

As shown in Table 5, during the intervention week a statistically significant increase was found in pain (B = 0.03*;* t = 2.53*;* p = .01), and in the affective response of valence (B = 0.02*;* t = 2.15*;* p = .04) and dominance (B = 0.02*;* t = 2.53*;* p = .002). No significant differences were found in the secondary outcomes of energy, quality of sleep, and the affective response of arousal. In general, the average scores recorded daily during the trial sessions indicated regular fluctuations in these scores.

Table 5

EMA of secondary outcomes inter-sessions (TAU + NAT-FM)

Dependent variables	*Constan*	*Ajusted R2*	*t*	*B*	*p*
SAM_Valence (1-9)	5.40	.07	2.15	0.02	.04*
SAM_Arousal (1-9)	4.90	.02	1.34	0.01	.19
SAM_Dominance (1-9)	5.57	.18	3.34	0.02	.002**
VAS_Energy (0-10)	4.44	-.01	0.74	0.01	.46
VAS_Pain (0-10)	5.15	.10	2.53	0.03	.01*
VAS_Sleep quality (0-10)	2.93	-.07	0.72	0.04	.50

Note. * < .05, ** < .01, *** < .001

3.5. Assessment of the NAT-FM

In the close-ended question, 80% of the patients indicated that the duration of the sessions was adequate, 100% reported that the explanations of the therapists were understandable, 100% stated that the presence of a team made up of a psychologist and a sports technician provided them with a feeling of security, and 40% clearly identified the difference between the roles of the two people in charge of the sessions. They also stated that they would be willing to engage in a psychological intervention based on physical activities in nature.

The patients obtained a mean score of 8.6 (*SD* = 1.05) on a 0-10 scale for the understanding of the CSA and EMA instructions, with a score of 9.3 (*SD* = 0.67) for their respective presentation formats; and 8.8 (*SD* = 1.25) for their extension. They also reported that a between-sessions EMA frequency of 4 times a day is optimal (*SD* = 1.67) for the duration of the clinical trial. The total adherence of responses (twice in the morning, twice in the afternoon, and twice at night) to the between-sessions EMA was 86.7% and adherence to the morning, afternoon, and night-time periods was 85.9%.

In addition, in the open-ended question, they highlighted that their participation in the trial had been a great opportunity to demonstrate to themselves that they were

capable of carrying out this type of activity, as well as to discover that their physical abilities could be similar to those of the general population:

> *It's been a great experience. I proved to myself that I am capable of doing things I didn't imagine. This intervention has helped me to know myself better (...) I feel better, motivated to see that I can be like healthy people (female, 59 years old).*

4. Discussion

The main objective of the study was to provide a preliminary assessment of the efficacy of the multicomponent NAT-FM treatment as coadjuvant of treatment as usual (TAU) in patients with fibromyalgia (FM). In this regard, the specific objectives of this work were: (a) to evaluate the efficacy of the NAT-FM treatment as coadjuvant of treatment as usual (TAU) in improving a wide range of primary and secondary outcomes in a small sample of patients with FM; (b) to collect information provided by the participants regarding the adequacy of the multicomponent intervention; and (c) to reflect on the improvement plan of the NAT-FM protocol.

In accordance with previous research, we found that implementing therapeutic interventions based on PA in nature had a positive effect in terms of improving emotional, cognitive, and behavioral functioning [15-19]. The results of the CSA provided evidence of the effect of TAU + NAT-FM treatment on improving positive affect, as well as reducing limitations in physical functioning and anxious/depressive symptoms [13]. In comparison with TAU, the NAT-FM treatment as coadjuvant indicated a decrease in pain catastrophizing thoughts, negative affect, and a shift in emotional regulation strategy to positively refocusing, as well as an increase in positive affect. The data from intra-session EMA indicated an increase in affective responses, self-efficacy and energy, along with a decrease in stress, whilst those of the inter-session EMA indicated an increase in pain and

in the affective responses of valence and dominance [12,14]. The increase in short-term pain, as reported in other studies, could indicate an improvement in this variable over the medium to long term [42]. In this regard, the patients considered that, despite the increased pain experienced due to the activities, it was a useful intervention for improving their functionality and well-being.

The lack of randomization, small sample size, and reduced number of prototyped sessions suggest that we should interpret these findings as a preliminary demonstration of the effects of the NAT-FM protocol. The statistical analyses, however, revealed baseline differences between treatment arms in some variables, which could compromise their interpretation. Nonetheless, the main purpose of this proof of concept study was to prepare the procedural protocol, to test for the first time the components of the NAT-FM treatment, and to evaluate the adequacy of its structure by testing across four representative sessions. Following this order of ideas, the information provided by the participants shows an understanding of the instructions of the CSA and EMA, the adequacy of the presentation formats of the questionnaires, and the acceptance of their extension.

The total adherence of responses to the intersession questionnaires was approximately 85%, which provides evidence to suggest the importance of maintaining the 6-session administration regime tested in this study (twice in the morning, twice in the afternoon, and twice at night). Regarding the structure of the treatment, the participants indicated the adequacy of the duration of the sessions, the understanding of the therapists' explanations, and the feeling of security due to having a team composed of a psychologist and a sports technician. The participants also assured us that they would be willing to participate in an intervention based on physical activities in nature.

This proof of concept study reinforced the need to include a passive control condition (TAU) in the definitive two-arm RCT, with the purpose of establishing a comparison with respect to NAT-FM treatment. The definitive treatment will also include 6 and 9-month follow-up assessments of the study variables. The sample size in each of the arms and the treatment follow-up period will be estimated so that it is sufficiently representative to obtain significant results. The sizes of the effects obtained in this study will serve as the basis for this protocol. Another aspect that will be taken into account after carrying out this study is that the treatment will be based on Pain Neuroscience Education (PNE) [43]. Unlike this study, the EMA intersession will also be applied to the control group to obtain more precise information about the dynamics of the variables under assessment.

The NAT-FM protocol will also include measures of clinical features and screening, along with additional outcomes such as psychological inflexibility, muscular stiffness, functionality, adverse effects, and pain-specific impression of change, with the purpose of identifying their effects on the treatment. In the RTC, in addition to assessing the clinical effects of NAT-FM treatment in the medium and long term, we will seek to recognize the variables related to personal factors (e.g., age, years of evolution, severity, initial cognitive status, psychological inflexibility, and functionality) that could act as moderators of efficacy. The researchers of this study are aware that implementation of the NAT-FM protocol could require certain adjustments to both the activities and the validated geographical sectors. In this regard, the RCT will be adapted according to the specific needs of the center in which it will be carried out, preserving the structure of the treatment and the therapeutic potential identified in each activity in nature. All the information and reflections collected in this proof of concept study will be useful for consolidating the NAT-FM protocol [44].

5. Conclusion & Future perspectives

The development of complementary treatments based on new approaches could improve the functionality of patients. This would be of considerable benefit, both on a social level (due to the current high consumption of healthcare resources and frequent sick leave), and individually (due to the functional improvements brought about by the proposed treatments). The NAT-FM treatment is presented as the first intervention to integrate CBT, PA practice, and exposure to the natural environment. The integrative commitment of this treatment is based on the recognition of the scientific evidence identified in different studies on the three central components of the treatment (NAT: Nature-Activity-Therapy). The results obtained here constitute preliminary empirical evidence for the effectiveness of this new generation of therapeutic treatments for FM intervention. An understanding of the specific therapeutic effects of NAT-FM could be very useful when considering the relevance of this complementary model of health intervention.

6. Summary points

- This is a proof of concept of a new multicomponent treatment for fibromyalgia, named NAT-FM (Nature Activity Therapy for Fibromylagia) that combines behavioural cognitive therapy, physical activity and nature exposure.
- This study compared the effectiveness of NAT-FM treatment plus Treatment as Usual (NAT-FM + TAU) *versus* TAU alone.

- In this study, a simplified version of the full therapy consisting on four intervention sessions, distributed over a two-week period, was tested. The patients carried out the guided practice of three physical activities in various natural contexts that had been previously validated: hiking, yoga and caving. After the practice of each of the activities, a psychological intervention was carried out in situ to reinforce their therapeutic effects.
- The main outcome was the patients' functional status, assessed with FIQ-R. Secondary outcomes were anxiety, depression, self-efficacy, perceived competence, self-esteem, catastrophism, emotional regulation, stress and sleep quality.
- Three evaluation moments were established: (1) A classical structural pre-post intervention assessment to quantity the overall effectiveness of the NAT-FM intervention in comparison with TAU, (2) an inter-session evaluation to be able to evaluate the process of transference of therapy benefits to daily life, and (3) an intra- session evaluation to quantify the short-term effect of each of the activities carried out.
- The results indicated clinically significant effects on most of the variables evaluated in the three evaluation periods. The results were generally in the sense of an improvement in the clinical status of patients who received NAT + FM treatment compared to those who only received TAU: The most relevant were: pre-post reduction of the functional impact of the disease, of anxiety and increase of positive affectivity; increase of positive affectivity and dominance, as well as reduction of intersession pain. Globally, the results show a moderate to strong effect size on primary and secondary outcomes.

- Although the results should be taken with caution, considering (1) the differences in baseline values between groups probably due to lack of randomization and (2) that we have tested a simplified version of the NAT-FM protocol, we conclude (a) considering the results obtained and (b) the opinion of the patients about the adequacy of the protocol, that the NAT-FM protocol is ready for conducting a randomized controlled clinical trial to test the efficacy of this treatment in its current design as a complementary intervention to TAU for the treatment of fibromyalgia.

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