Agri 2023;35(3):153–166
doi: 10.14744/agri.2022.33349

ORIGINAL ARTICLE

Physiotherapeutic treatment associated with the pain neuroscience education for patients with chronic non-specific low back pain-single-blind randomized pilot clinical trial

Kronik spesifik olmayan bel ağrısı olan hastalarda ağrı nörobilimi eğitimi ile ilişkili fizyoterapötik tedavi-tek-kör randomize pilot klinik çalışma

Angela Shiratsu YAMADA,[1] Flavia Tasmin TECHERA ANTUNES,[1] Sara Moreno REBELO VAZ,[2] Beatriz VILANOVA SARAIVA,[2] Alessandra Hubner DE SOUZA,[3] Daniel SIMON[1]

Summary

Objectives: Pain Neuroscience Education (PNE) shows improvement in pain and functional capacity in patients with chronic low back pain (CLBP). Therefore, the study aimed to verify if the physiotherapeutic treatment associated with PNE decreases the functional disability of patients with nonspecific CLBP.

Methods: Forty patients were clinically evaluated and answered the following questionnaires: Brief pain inventory, Central Sensitization Inventory (CSI), Roland-Morris disability questionnaire, pain catastrophizing scale, Tampa scale of kinesiophobia, hospital anxiety, and depression scale, SF6D quality of life questionnaire and performed quantitative sensory tests (QSTs). Afterward, they were randomly divided into the intervention group (IG, n=20) and the control group (CG, n=20). Both performed kinesiotherapy exercises twice a week for 6 weeks. The IG received 3 individual PNE sessions and answered the pain neurophysiology questionnaire.

Results: IG showed significant improvement for all variables analyzed (p<0.001). The association decreased the kinesiophobia (estimated difference between CG-IG means: 7.6–95% CI: 2.3–12.9) (p=0.006). In the lumbar paravertebral region (CG and IG), there was a statistical difference in the intensity of CLBP in the QSTs (p<0.05).

Conclusion: The association showed better results compared to only therapeutic exercises to reduce kinesiophobia and change the perception of pain intensity in the lumbar region.

Keywords: Functional disability; kinesiophobia; low back pain; therapeutic exercise.

Özet

Amaç: Ağrı Nörobilimi Eğitimi (ANE), kronik bel ağrısı (KBA) olan hastalarda ağrı ve fonksiyonel kapasitede iyileşme göstermektedir. Bu nedenle, çalışmanın amacı, fizyoterapötik tedavinin ANE ile ilişkili olarak, spesifik olmayan KBA'lı hastaların fonksiyonel engelliliğini azaltıp azaltmadığını doğrulamaktır.

Gereç ve Yöntem: Kırk hasta klinik olarak değerlendirildi ve hastalar aşağıdaki anketleri yanıtladı: Kısa ağrı envanteri, Santral Duyarlılık Envanteri (SDE), Roland-Morris engellilik anketi, ağrı felaketleşme ölçeği, kinofobi tampa ölçeği, hastane anksiyete ve depresyon ölçeği, SF6D yaşam kalitesi anketi ve nicel duyusal testi (NDT). Daha sonra, rastgele olarak müdahale grubu (MG, n=20) ve kontrol grubu (KG, n=20) olarak ayrıldılar. Her iki grup da haftada iki kez altı hafta boyunca kinezyoterapi egzersizleri yaptı. MG, 3 bireysel ANE oturumu aldı ve ağrı nörofizyoloji anketini yanıtladı.

Bulgular: MG, analiz edilen tüm değişkenler için anlamlı bir iyileşme gösterdi (p<0.001). Birleşik tedavi, kinofobiyi azalttı (KG-MG arasındaki tahmini fark: 7.6–%95 GA: 2.3–12.9) (p=0.006). Lomber paravertebral bölgede (KG ve MG), NDT'lerde KBA'nın yoğunluğunda istatistiksel bir fark vardı (p<0.05).

Sonuç: Birleşik tedavi, yalnızca terapötik egzersizlere kıyasla kinofobiyi azaltmak ve lomber bölgedeki ağrı yoğunluğu algısını değiştirmek için daha iyi sonuçlar gösterdi.

Anahtar sözcükler: Fonksiyonel engellilik, kinofobi, bel ağrısı, terapötik egzersiz.

[1]Programa de Pós-Graduação em Biologia Celular e Molecular Aplicada à Saúde, Laboratório de Genética Molecular Humana, Universidade Luterana do Brasil, Canoas - RS, Brasil
[2]Curso de Fisioterapia do Centro Universitário Luterano de Palmas - CEULP/ULBRA, Palmas - TO, Brasil
[3]Doutora em Farmacologia Bioquímica e Molecular pela Universidade Federal de Minas Gerais. Canoas - RS, Brasil

Submitted *(Başvuru)* **02.02.2022** **Revised** *(Revizyon)* **24.03.2022** **Accepted** *(Kabul)* **14.07.2022** **Available online** *(Online yayımlanma)* **14.07.2023**

Correspondence: Dr. Angela Shiratsu Yamada. Programa de Pós-Graduação em Biologia Celular e Molecular Aplicada à Saúde, Laboratório de Genética Molecular Humana, Universidade Luterana do Brasil, Canoas - RS, Brasil.
Phone: +55 63 992 015 484 **e-mail:** angelasyamada@gmail.com

Introduction

Education in pain neuroscience education (PNE) is intended to change people's understanding of what pain is, what its function is, and what biological and physiological processes support it; it is a pragmatic application of the biopsychosocial model of pain.[1] The central objective of PNE is to change the beliefs that patients have about their pain, through a process of (re)conceptualizing pain. Louw et al.[2] considered what is most important is that this approach defocuses attention from issues associated with anatomical structures. The focus is on informing, arguing, and convincing patients that pain does not necessarily result from tissue damage.[3] This conceptual shift has been shown to increase knowledge of pain-related biology, decrease catastrophization, and reduce pain and disability in the short term. Thus, it presents the biological information that justifies a biopsychosocial approach as part of multimodal pain rehabilitation.[1]

Chronic low back pain (CLBP) is known to be multifactorial, influenced by biological, psychological/emotional, and social factors.[4,5] Among these aspects, physical factors such as deconditioning and dysfunctions are associated with deficits in motor control.[6]

Therefore, this study aimed to verify whether physiotherapeutic treatment associated with PNE can contribute to the reduction of functional disability in patients with nonspecific CLBP (NCLBP) through a single-blind randomized clinical trial. The hypothesis is that PNE contributes to the reduction of functional disability when compared to conventional physical therapy treatment. Secondary outcomes are related to decreased pain intensity, improvement in biopsychosocial factors, and quantitative sensory test (QST) parameters by algometry.

Material and Methods

This study is a single-blind randomized clinical trial (RCT) following the recommendations of the CONSORT guidelines,[7] registered in the Brazilian registry of clinical trials as "Education in pain and physical therapy for patients with CLBP," approved by the Human Research Ethics Committee of the University Center Lutheran de Palmas-CEULP/ULBRA (no. 2.292.792). The study was conducted in accordance with the Declaration of Helsinki. All participants were informed about the purpose of the research and signed an informed consent form.

A preliminary study was carried out with 9 participants who had NCLBP. In this study, researchers were trained to perform the assessment, as well as to apply the physiotherapeutic treatment protocol and dialogic exposure of PNE. In addition, this sample was used to calculate the sample size for the present study.

Sample

The sample size was calculated using the method of comparing the proportion between 2 groups in a preliminary longitudinal study (n=9), before and after the intervention, setting the level of significance alpha or type I error at 5% (alpha=0.05, 95% confidence interval), and 80% sample power (or 20% type II error, beta=0.20) according to Hulley et al.[8] As a result of this analysis, the sample size was estimated as 15 participants for each group. Considering that longitudinal studies can have losses as a result of time, we started the sample with 33% more subjects, 20 in each group.

Data Collection

It took place from August 2018 to December 2019. 69 participants registered at the Clinical School of Physiotherapy at CEULP/ULBRA, in Palmas/TO, were invited. Eligibility criteria for constituting the sample were having a medical referral for physical therapy treatment, individuals over 18-years-old, who had CLBP (over 3 months), of both genders. As an inclusion criterion, the participant had to present a minimum score of 35 points in the Central Awareness Inventory (CSI). Exclusion criteria were patients who were in labor lawsuits, pregnant women, athletes, and/or have undergone a surgical procedure in some region of the spine. Patients suspected of having serious illnesses ("red flags") such as cauda equina syndrome, signs of neurological diseases, neoplasia, HIV, infection, trauma, and/or fracture of the spine were also excluded from the study.[9] The evaluation of these participants was carried out by the evaluator researcher, who was blinded throughout the research to the group in which the patient would undergo the treatment, as the same researcher who carried out the pre-treatment evaluation carried out his re-evaluation in the post-physiotherapeutic treatment.

The data collection instruments were: Assessment form for sociodemographic data (gender, age, marital status, declared color, and education). Overweight/obesity was assessed using the body mass index (>25 kg/m^2) considered at risk for LBP.[10] The general health status was evaluated in categories of excellent, good, regular, bad, or very bad.[11] Physical activity was classified as sedentary, insufficiently active, moderate, or vigorous.[12] Validated questionnaires for the multidimensional assessment of pain, functional disability, central sensitization, catastrophic thoughts, kinesiophobia, anxiety and depression, quality of life, and pain neurophysiology were also applied, and clinical algometric tests were performed to assess pressure pain threshold (PPT), temporal summation (TS) and conditioned pain modulation (CPM).

A multidimensional pain assessment was performed using the brief pain inventory.[13] Pain duration was recorded in months and reported pain intensity was assessed on a numerical pain scale (NPS). It was also investigated whether pain interferes with general activity, mood, walking ability, work, relationship with other people, sleep, and the ability to enjoy life on a numerical scale from 0 to 10. The number of painful body regions.

The CSI proposed by Mayer et al.[14] and validated in Brazil by Caumo et al.[15] was applied. The CSI consists of 25 questions with answer options ranging from never, rarely, sometimes, often, and always. The score is added, ranging from 0 to 100 points, with central sensitization being considered above 35 points in the Brazilian version.[15]

the Roland Morris disability questionnaire (RMDQ)[16] has 24 items related to activities of daily living, ranging from 0 to 24, with a score >14 points indicating significant functional physical disability.[17,18]

The pain catastrophizing scale[19] has 9 questions for the items of rumination and hopelessness. Higher scores indicate a greater presence of catastrophic thoughts.

The Tampa scale of Kinesiophobia[20] consists of a questionnaire composed of 17 questions, which classify kinesiophobia with increasing scores. There is also a categorical classification in mild kinesiophobia from 17 to 34 points, moderate from 35 to 50 points, and severe from 50 to 68 points.[21]

The hospital anxiety and depression scale[22] has 14 items, with a subscale to assess depression and anxiety, ≥9 points for each.[23]

The SF-6D questionnaire adapted and validated for the Portuguese language by Campolina et al.[24] was used to assess the quality of life was used to assess the quality of life. This questionnaire assesses six dimensions: functional capacity, global limitation due to physical and emotional aspects, social aspects, pain, mental health, and vitality. The SF-6D score ranges from 0 to 1, with zero being the worst health status and 1 meaning the best health status.[25]

Related to QSTs, PPT was evaluated to quantify the minimum pressure threshold that induces pain[26] using a digital pressure algometer commercially available in Brazil with a 1 cm^2 tip (EMG System do Brasil, São José dos Campos, Brazil). The evaluation protocol for the test site (lumbar paravertebral) and control site (back of the hand) was applied according to Starkweather et al.[27] Pressure is manually applied increasing by 1 Kgf/cm^2 every second until the participant reports when the pressure sensation becomes a painful stimulus, pressing the indicator button on the algometer and recording the pain intensity in NPS. Three measurements were collected at these locations and the mean was calculated for analysis.

TS is used as an indicator of central sensitization. From the average PPT value, the algometer was applied in the same places (test and control) with the pressure of the average PPT. The painful stimulus was performed 10 times, with one application every second, with the patient being asked about the NPS.[28]

CPM is expressed by the reduction of pain perception through the application of a new painful conditioning stimulus being represented by a subjective numerical pain score.[29] It is an indication of the functioning of the endogenous opioid analgesic system, of the descending tracts that control and modulate pain perception.[27] The CPM was performed through

ischemic compression in the non-dominant arm using an inflated sphygmomanometer up to 270 mmHg, recording the PPT during the application of the conditioning stimulus and the NPS. Ischemic compression was removed and after 5 min, PPT and NPS data were collected again.[28]

Allocation and Study Design

Participants were randomly allocated in equal numbers to the control group (CG) or intervention group (IG). Randomization by electronic drawing was previously performed by an administrative employee, with the allocation sequence using a block randomization model. Allocation concealment was ensured using manila envelopes, sealed and sequentially numbered from 1 to 40. After the evaluation, if the participant was included in the study, the evaluation researcher communicated with the employee to refer him to treatment. At that moment, this employee opened the sealed manila envelope that indicated which group to refer the patient to for physical therapy treatment, or the CG or IG. The information of the participants in each group was kept confidential by this employee in files on the computer with a password.

The clinical trial compared the physical therapy treatment performed for two groups: IG: in which PNE and physical therapy treatment protocol for CLBP was performed, and CG: in which only the physical therapy treatment protocol for CLBP was performed.

For the physical therapy treatment, a protocol through kinesiotherapy was elaborated, as proposed in systematic reviews by Louw et al.[2] and Malfliet et al.,[30] and a study by Magalhães et al.[31] The protocol was applied by the treatment researcher, who was blinded as to which group the participant belonged to, and the same protocol was applied to both the IG and CG. The treatment was carried out during 12 physiotherapy sessions, the sessions being twice a week for 6 weeks. Each session lasted 50 min, containing kinesiotherapy exercises: bridge; board; spinal mobility exercise; walking on the treadmill for 4 min, within the patient's submaximal heart rate (from 50 to 70% of the maximum heart rate); sensory-motor training; motor coordination; trunk extension; hip abduction (starting at 0.5 kg and progressing to 2 kg); pelvic tilt and posterior chain muscle stretch.

The PNE intervention was performed by the education researcher, addressing the neurophysiology of pain based on neuroscience as the initial phase of physical therapy treatment for the IG, with 3 first individual sessions of dialogued exposure, with 50 min being proposed of duration each.[32] Thus, the IG held 3 educational sessions before the 12 kinesiotherapy sessions, totaling 15 sessions.

The neurophysiology of pain questionnaire (NDQ) was designed to assess how an individual conceptualizes the biological mechanisms that support their pain,[33] considered a useful tool to assess the effects of cognitive interventions in clinical practice and research, with psychometric properties for use in patients with CLBP, with cross-cultural adaptation to Portuguese.[34] In this study, it was applied only to the IG, at the beginning of the first educational session and at the end of the third, to assess the effectiveness of the PNE.

Data Analysis

It was performed by intention-to-treat, of the 40 participants, with post-treatment (immediate) data being reproduced through pre-intervention data. No follow-up was performed. Initially, an exploratory data analysis was carried out considering measures of central position and dispersion. Qualitative variables were summarized considering absolute and relative frequencies. A univariate analysis was performed to verify which explanatory variables differ between groups at baseline. This analysis was performed using the Chi-square test for qualitative variables and quantitative variables, the nonparametric Wilcoxon-Mann–Whitney test for independent samples. The comparison between the pre-and post-treatment times in each group (CG or IG) and between the groups (CG and IG) at each time (pre-and post-treatment) was performed considering the orthogonal contrasts in the linear regression model of mixed effect. An analysis of the model's residuals was performed using Q-Q plot, histogram, and scatter plots to confirm whether the model was adequate. All these analyzes were implemented in the SAS version 9.4 program (SAS Institute Inc., Cary, USA). Values of $p<0.05$ were considered statistically significant.

Results

Of the 69 eligible patients (Fig. 1), 40 participants were randomized to start treatment, with 20 being divided for the CG and 20 for the IG, as shown in Figure 1. Even, so, there were discontinuity criteria (absences greater than 25% of the total period of treatment sessions and performing surgeries during treatment). The sociodemographic and clinical data of the CG and IG (Table 1) demonstrate that there was no difference between the groups' characteristics, indicating that randomization was adequate.

The NDQ was applied to assess the effectiveness of the 3 educational lecture sessions on pain neuroscience. The maximum score is 12 points, with the results before the lecture being 4.2±1.5 and the score after being 8.6±2.0, this difference was statistically significant ($p<0.001$) with satisfactory improvement in the neurophysiological knowledge of pain.

The results presented in Table 2 demonstrate that both the CG and the IG showed a clinically relevant decrease in functional disability, with the most accentuated improvement in the IG. However, there was no statistical significance for this difference between the IG and the CG (Table 3), refuting our hypothesis that PNE would significantly contribute to the reduction of functional disability when compared to conventional physical therapy treatment.

When comparing the effect of physical therapy treatment between the CG and GI groups, it was observed that there was an improvement in the secondary outcome of kinesiophobia (Table 3), with an estimated difference between the means between the CG and GI of 7.6 points in the score ($p=0.006$, 95% CI: 2.27–12.93). The IG had a statistically significant lower kinesiophobia compared to the CG ($p<0.001$). Comparing the pre-and post-treatment data, kinesiophobia in the GI changed from moderate (44.9 points in the pre-treatment) to mild (32.4 points in the post-treatment).

The mean values and standard deviations of the QST data for PPT, TS, and CPM for the pre- and post-treatment times and comparing the CG and IG groups are shown in Table 4. Both in the CG and the IG, the algometry values decreased in the post-treatment of all tests in the control site and the GI for the lumbar region.

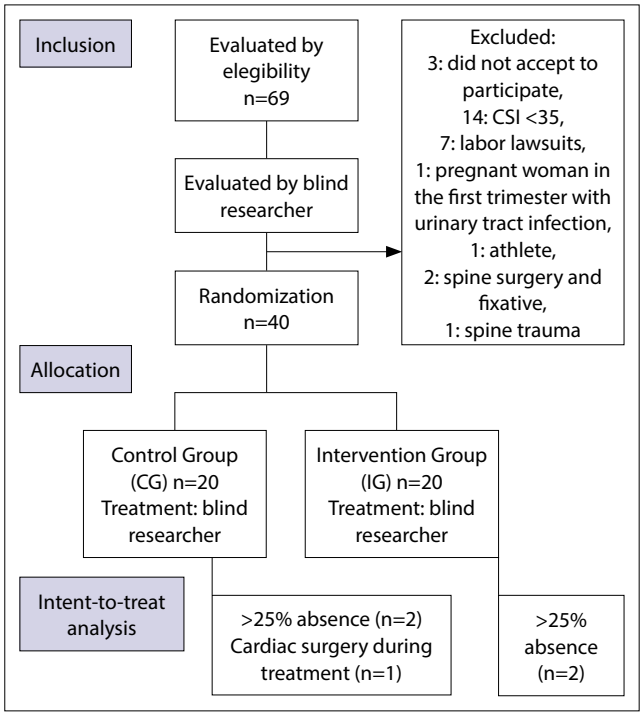

Figure 1. Flowchart of clinical trial recruitment, allocation and analysis.

Clinical characteristics of multidimensional assessment of pain, functional disability, central sensitization, kinesiophobia, catastrophizing, anxiety, depression, and quality of life in the pre-treatment period are presented in Appendix Table 1. The results of the variables analyzed intra-groups in the pre-and post-treatment times are described in Appendix Table 2 for the CG and in Appendix Table 3 for the IG.

Data on the difference between measures 10 and 1 of TS are presented in Appendix Table 4. The intervention effect was effective to change the perception of pain intensity, mainly in the lumbar region (Appendix Table 5 to control site -hand-, and Appendix Table 6 – paravertebral muscles), but also with the application of nociceptive stimuli such as in the TS and CPM. It is because the post-treatment data (comparing CG and IG) at the control site indicated that there was a statistically significant difference for NPS both for TS and 5 min after CPM. In the lumbar paravertebral, there was a statistical difference in the intensity of LBP both in PPT, TS, and CPM.

Table 1. Sociodemographic and clinical characteristics of patients with chronic low back pain comparing Control group (CG) and Intervention group (IG) at the inclusion of the study (physiotherapeutic pretreatment)

Variable	Groups				p
	Control group		Intervention group		
	n	%	n	%	
Gender					0.311
Female	15	75	12	60	
Male	5	25	8	40	
Age, (Mean±SD)	50.1±14.1		44.5±17.5		0.267
Scholarity					0.077
Up to high school	8	40	3	15	
High school and more	12	60	17	85	
Heath state					0.999
Good, very good, or excellent	6	30	6	30	
Regular, bad, or very bad	14	70	14	70	
Comorbities					0.633
No	2	10	3	15	
Yes	18	90	17	85	
BMI, (Mean±SD)	27.1±4.7		26.2±4.2		0.663
LBP family history					0.677
No	4	20	3	15	
Yes	16	80	17	85	
Physical activity					0.356
Inactive/sedentary	12	60	16	80	
Insufficiently active	2	10	2	10	
Mild active	5	25	1	5	
Vigorous	1	5	1	5	
Ocupational situation					0.507
Active/working	12	60	14	70	
No working	8	40	6	30	
Time in pain					0.919
From 3 to 12 months	7	35	6	30	
From 13 to 60 months	5	25	6	30	
More than 60 months	8	40	8	40	
Days in pain during the last month, (Mean±SD)	22.2±9.4		21.9±8.9		0.772

SD: Standard deviation; BMI: Body mass index.

Discussion

Regarding the improvement of patients' knowledge about pain, this study showed satisfactory improvement with statistically significant results between knowledge of pain neurophysiology before and after PNE ($p<0.001$). It is in line with Louw et al.,[2] who showed the acquisition of neurophysiological knowledge of pain after the PNE to validate the intervention.[35]

The primary outcome of this study was the improvement in functional disability, which was not statistically significant when comparing the CG and IG, indicating that the physical therapy treatment associated with PNE was not superior to the conventional one. Despite this, there was a clinical improvement in IG. Thus, although the hypothesis was not confirmed, it suggests at least in part, that PNE is an aspect of clinical relevance for the improvement of functional disability, as a change of 8 to

Table 2. Clinical characteristics and impacts of psychosocial factors in patients with chronic low back pain comparing control (CG) and intervention (IG) groups before and after physical therapy treatment

	Control group		Intervention group	
	Pre	**Post**	**Pre**	**Post**
NPS (0 a 10)	7.45±2.37	4.30±2.60	7.90±1.77	3.20±2.69
Activity	5.70±3.66	3.90±2.85	7.25±3.18	2.80±3.46
Humor	5.85±3.50	3.70±3.54	7.80±2.42	3.60±3.47
Walking	5±3.66	2.65±2.78	6.55±2.84	1.90±2.38
Working	5.5±4.01	4±3.51	6.85±3.5	3.10±3.13
Relationship	3±3.58	2±2.94	4.50±3.63	1.65±2.80
Sleep	5.30±3.79	3.6±3.78	6.30±3.56	2±2.92
Enjoying life	3.84±3.66	2.25±2.95	5.35±3.34	2±2.96
Body regions (n)	8.95±5.03	4.75±3.18	8.95±5.40	4.90±5.70
Functional disability	15.1±5.05	11.6±6.46	15.9±4.79	9.10±7.28
Central sensitization	54.2±9.37	37.65±17.8	56.7±11.23	40.3±14.16
Kinesiophobia	44.85±8.68	40±7.33	44.9±8.4	32.4±8.83
Catastrophization	1.93±1.18	1.29±1.12	2.11±1.27	0.89±1.07
Anxiety	10.05±2.48	8.5±4.01	10.7±3.31	6.45±3.47
Depression	7.15±2.68	6.7±3.54	7.25±3.86	5.10±4.08
Quality of life	0.70±0.04	0.75±0.08	0.69±0.04	0.75±0.09

Table 3. Comparison of the variables analyzed in the time after physical therapy treatment between the CG and IG groups

Variables	**Estimation of the difference between the means (CG-IG)**	**IL**	**SL**	**p**
Pain intensity	1.1	-0.42	2.626	0.153
Activity	1.1	-1.012	3.212	0.298
Humor	0.1	-1.991	2.191	0.923
Walking	0.75	-1.138	2.638	0.426
Working	0.892	-1.411	3.194	0.438
Relationship	0.35	-1.737	2.437	0.736
Sleep	1.6	-0.658	3.858	0.159
Enjoying life	0.25	-1.822	2.322	0.808
Body regions (n)	-0.15	-3.305	3.005	0.924
Central sensitization	-2.65	-11.307	6.007	0.539
Functional disability	2.5	-1.330	6.330	0.194
Kinesiophobia	7.6	2.267	12.933	**0.006**
Catastrophization	0.399	-0.344	1.143	0.283
Anxiety	2.05	-0.102	4.202	0.061
Depression	1.6	-0.692	3.892	0.166
Quality of life	-0.003	-0.044	0.039	0.885

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.

12% or 2 points in the RMDQ was considered clinically relevant.[36] This may indicate that there is clinical relevance for both proposed treatments, the IG being better.

The presence of psychological factors such as depression, anxiety, catastrophizing, anxiety, kinesiophobia, and low self-efficacy is associated with

Table 4. Mean value and standard deviation of Pressure Pain Threshold (PPT), Temporal Summation (TS) and Conditioned Pain Modulation (CPM), in pre-and post-physiotherapeutic treatment times for groups CG and IG in lumbar paravertebral and control site

	Control group		Intervention group	
	Pre	Post	Pre	Post
Local control: Hand				
PPT	2.13±0.74	2.09±0.8	2.1±0.65	2.02±0.72
PPT pain intensity	3.8±1.75	3.35±1.75	3.38±1.77	2.88±1.7
TS	4.94±2.86	3.64±2.31	4.86±2.12	3.61±2.48
CPM PPT during compression	2.23±0.68	2.05±0.67	2.35±0.82	2.12±0.79
CPM intensity pain during compression	4.17±2.04	3.63±2.22	4.05±1.71	3.2±1.8
CPM PPT after 5 min	2.1±0.6	1.93±0.61	2.17±0.71	1.87±0.64
CPM intensity pain after 5 min	3.43±1.62	3.23±1.86	3.55±1.64	2.32±1.58
Local test: Low back				
PPT	2.73±0.82	2.70±0.89	3.04±1.17	2.69±1.14
PPT pain intensity	4.13±1 87	3.92±2.05	3.57±1.68	3.27±1.96
TS	4.92±2.47	4.30±2.29	5±2.04	3.28±2.36
CPM PPT during compression	2.95±0.93	2.97±1.21	3.13±1.37	2.82±1.16
PPT pain intensity during compression	4.53±2.46	4.10±2.14	4.52±1.99	2.85±1.94
CPM PPT after 5 min	2.74±1.22	2.75±1.16	2.95±1.57	2.74±1.31
CPM pain intensity after 5 min	4.40±2.4	3.55±1.91	4.17±1.84	2.53±1.79

an increased risk of developing a disability.[4,37] A systematic review of chronic musculoskeletal pain found strong evidence of an association between a greater degree of kinesiophobia with pain intensity and disability.[38] It is confirmed by our study, where kinesiophobia was a factor that showed a statistically significant difference when comparing the data between the CG and IG (p=0.006) in this study.

Regarding the QST, patients with NCLBP tend to have lower pain thresholds and increased central sensitization compared to healthy individuals.[39,40] The PPT values in this study were low both in the lumbar region, similar to those by Moura et al.[41] and also in distant regions, as in the study by Imamura et al.[40] Low PPT in the lumbar spine indicates primary hyperalgesia, and in the distant region, it indicates secondary hyperalgesia, which may suggest central sensitization.[42]

The increase in the pain intensity can be observed in the pre-treatment time for both CG and IG in this study. And in the post-treatment time of the IG, the increase was <20%, indicating a decrease in nociceptive facilitation and central sensitization for this group effectively. After the therapeutic intervention, lumbar PPT increased in the study by Bodes Pardo et al.[43] and was also observed in a systematic review and meta-analysis by Belavy et al.,[44] diverging from the results of the present study in which the lumbar PPT decreased in the IG with a significant difference between the pre- and post-treatment times. Results in the post-treatment group in the comparison of the CG and IG were statistically significant for the perception of pain intensity in the PPT, in the TS, in the intensity of low back pain during CPM and 5 min after CPM (Appendix Table 6), indicating that in all parameters evaluated, pain perception was lower in IG, although the PPT was significantly decreased.

In general, the QST can help to quantify and make a variable as complex and subjective as pain in a given objective, being considered a positive point of this pilot study. The limitations of this study may be related to the small sample size, as some outcomes were clinically relevant, but not statistically significant. This pilot study generates data that allows the calculation of the sample size necessary to observe significant differences in the proposed interventions. We also do not carry out the follow-

up to assess the effects in the medium and long term. However, the results seem to be promising as they already have clinical relevance for the outcomes of pain and functional disability, statistical significance for kinesiophobia, and QST, with the IG showing better results when compared to the CG. Thus, it is necessary to continue studies with larger samples, with follow-up analysis so that the results can present greater external validity and a better understanding of pain sensitivity mechanisms, responses to treatment with therapeutic exercises in populations with chronic pain.

PNE associated with therapeutic exercises did not show superior results compared to the group that performed only therapeutic exercises for the primary outcome of functional disability. For secondary outcomes, the IG showed significant improvement ($p<0.001$) for all variables analyzed between the pre- and post-treatment intragroup times, presenting better results than the CG, but not statistically significant between groups. Thus, the IG was not superior to the CG for pain intensity and the interference of pain in daily activities, central sensitization, catastrophizing, anxiety, depression, and quality of life. The proposed intervention was superior to the control for kinesiophobia, with a statistically significant decrease from moderate to mild kinesiophobia. As for the QST, the effect of the intervention was effective in changing the perception of pain intensity, especially in the lumbar region, although it did not increase the pain threshold quantitatively. For TS, the IG showed an increase lower than that established, being effective in decreasing central sensitization.

Peer-rewiew: Externally peer-reviewed.

Ethics Committee Approval: The Human Research Ethics Committee of the University Center Lutheran de Palmas-CEULP/ULBRA granted approval for this study (date: 22.09.2017, number: 2.292.792).

Conflict-of-interest issues regarding the authorship or article: None declared.

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Appendices

Appendix 1. Comparison of the variables analyzed in the time before physical therapy treatment between the control (CG) and intervention (IG) groups

Variables	Estimation of the difference between the means (CG-IG)	IL	SL	p
NPS (0–10)	-0.45	-1.9765	1.0765	0.554
Activity	-1.55	-3.6617	0.5617	0.145
Humor	-1.95	-4.0409	0.1409	0.067
Walking	-1.55	-3.4384	0.3384	0.105
Working	-1.35	-3.6257	0.9257	0.237
Relationship	-1.5	-3.5868	0.5868	0.154
Sleep	-1	-3.2576	1.2576	0.375
Enjoying life	-1.498	-3.5952	0.5992	0.156
Body regions (n)	0.00	-3.1546	3.1546	>0.999
Central sensitization	-2.5	-11.157	6.157	0.562
Functional disability	-0.8	-4.6299	3.0299	0.675
Kinesiophobia	-0.05	-5.3834	5.2834	0.985
Catastrophization	-0.1725	-0.916	0.571	0.641
Anxiety	-0.65	-2.8023	1.5023	0.545
Depression	-0.1	-2.3921	2.1921	0.930
Quality of life	0.015	-0.02659	0.05659	0.470

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.

Appendix 2. Comparison of the variables analyzed in the post and pre-physiotherapeutic treatment times in the CG

Variables	Estimation of the difference between the means (CG-IG)	IL	SL	p
NPS (0 a 10)	-3.15	-4.5524	-1.7476	<**0.0001**
Activity	-1.8	-3.681	0.081	0.060
Humor	-2.15	-3.7883	-0.5117	**0.011**
Walking	-2.35	-4.0327	-0.6673	**0.007**
Working	-1.5083	-3.423	0.4064	0.119
Relationship	-1	-2.3788	0.3788	0.150
Sleep	-1.7	-3.463	0.06299	0.058
Enjoying life	-1.602	-3.4244	0.2203	0.083
Body regions (n)	-4.2	-5.839	-2.561	<**0.0001**
Central sensitization	-16.55	-23.5426	-9.5574	<**0.0001**
Functional disability	-3.5	-6.2887	-0.7113	**0.015**
Kinesiophobia	-4.85	-9.1063	-0.5937	**0.027**
Catastrophization	-0.6455	-1.205	-0.086	**0.025**
Anxiety	-1.55	-2.865	-0.235	**0.022**
Depression	-0.45	-1.8654	0.9654	0.524
Quality of life	0.047	0.01247	0.08153	**0.009**

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.

Appendix 3. Comparison of the variables analyzed in the post and pre-physiotherapeutic treatment times in the GI

Variables	Estimation of the difference between the means (CG-IG)	IL	SL	p
NPS (0 a 10)	-4.7	-6.1024	-3.2976	<**0.0001**
Activity	-4.45	-6.331	-2.569	<**0.0001**
Humor	-4.2	-5.8383	-2.5617	<**0.0001**
Walking	-4.65	-6.3327	-2.9673	<**0.0001**
Working	-3.75	-5.6324	-1.8676	**0.0003**
Relationship	-2.85	-4.2288	-1.4712	**0.0002**
Sleep	-4.3	-6.063	-2.537	<**0.0001**
Enjoying life	-3.35	-5.1431	-1.5569	**0.0005**
Body regions (n)	-4.05	-5.689	-2.411	<**0.0001**
Central sensitization	-16.4	-23.3926	-9.4074	<**0.0001**
Functional disability	-6.8	-9.5887	-4.0113	<**0.0001**
Kinesiophobia	-12.5	-16.7563	-8.2437	<**0.0001**
Catastrophization	-1.2175	-1.777	-0.658	<**0.0001**
Anxiety	-4.25	-5.565	-2.935	<**0.0001**
Depression	-2.15	-3.5654	-0.7346	**0.004**
Quality of life	0.065	0.03047	0.09953	**0.0005**

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.

Appendix 4. Mean difference between measures 10 and 1 of the Temporal summation (TS) pressure stimuli performed in the control site (hand) and in the lumbar region in the pre- and post-treatment times of the CG and IG groups

Temporal summation	Control group		Intervention group	
	Pre	Post	Pre	Post
Hand	2.40±2.04	1.85±2.01	3.50±2.11	1.70±1.87
Low back	2.50±2.24	2.15±1.53	3.15±1.78	1.70±2.32

CG: Control group; IG: Intervention group.

Appendix 5. Estimate of the difference between the means for the Pressure Pain Threshold (PPT), Temporal Summation (TS) and Conditioned Pain Modulation (CPM) values during ischemic compression and after 5 min, in the pre and post physiotherapeutic treatment times of the groups CG and IG at the control site (hand)

Variables	Estimative of the difference between the means	IL	SL	p
Pre (CG-IG)				
PPT control	0.034	-0.1946	0.2626	0.770
PPT pain intensity control	0.4167	-0.1566	0.9899	0.153
TS control VAS (visual analogue scale)	0.085	0.6914	-0.3352	0.505
CPM PPT control	-0.1227	-0.3569	0.1115	0.303
CPM pain intensity control	0.1167	-0.5255	0.7589	0.721
5 min CPM PPT control	-0.068	-0.2518	0.1158	0.467
5 min CPM pain intensity control	-0.1167	-0.6742	0.4409	0.680
CG (post-pre)				
PPT control	-0.04383	-0.2724	0.1847	0.706
PPT pain intensity control	-0.45	-1.0232	0.1232	0.123
TS intensity pain control	-1.2975	<0.0001	-1.7177	-0.877
CPM PPT control	-0.1798	-0.414	0.05437	0.132
CPM pain intensity control	-0.5333	-1.1755	0.1089	0.103
5 min CPM PPT control	-0.1703	-0.3541	0.01345	0.069
5 min CPM pain intensity control	-0.2	-0.7575	0.3575	0.480
IG (post-pre)				
PPT control	-0.071	-0.2996	0.1576	0.541
PPT pain intensity control	-0.5	-1.0732	0.07322	0.087
TS pain intensity control	-1.25	<0.0001	-1.6702	-0.830
CPM PPT control	-0.2287	-0.4629	0.005532	0.056
CPM pain intensity control	-0.85	-1.4922	-0.2078	**0.0097**
5 min CPM PPT control	-0.3025	-0.4863	-0.1187	**0.0014**
5 min CPM pain intensity control	-1.2334	-1.7934	-0.6734	<**0.0001**
Post (CG-IG)				
PPT control	0.06117	-0.1674	0.2897	0.598
PPT pain intensity control	0.4667	-0.1066	1.0399	0.110
TS pain intensity control	0.0375	0.861	-0.3827	**0.032**
CPM PPT control	-0.07383	-0.308	0.1604	0.535
CPM pain intensity control	0.4333	-0.2089	1.0755	0.185
5 min CPM PPT control	0.06417	-0.1196	0.2479	0.492
5 min CPM pain intensity control	0.9167	0.3567	1.4768	**0.0014**

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.

Appendix 6. Estimate of the difference between the means for the Pressure Pain Threshold (PPT), Temporal Summation (TS) and Conditioned Pain Modulation (CPM) values during ischemic compression and after 5 min, in the pre and post physiotherapeutic treatment times of the groups CG and IG in the symptomatic lumbar paravertebral muscles

Variables	Estimative of the difference between the means	IL	SL	p
Pre (CG-IG)				
PPT low back	0.5667	-0.02875	1.1621	0.062
PPT pain intensity in low back	-0.1227	-0.3569	0.1115	0.303
TS pain intensity in low back	-0.08	0.7021	-0.4904	0.33
CPM PPT low back	-0.1795	-0.5279	0.1689	0.311
CPM pain intensity in low back	0.01667	-0.6729	0.7063	0.962
5 min CPM PPT low back	-0.208	-0.5951	0.1791	0.291
5 min CPM pain intensity in low back	0.2333	-0.4339	0.9006	0.491
CG (post-pre)				
PPT low back	-0.02333	-0.3052	0.2585	0.87
PPT pain intensity in low back	-0.2167	-0.8121	0.3787	0.474
Ts pain intensity in low back	-0.62	0.0031	-1.0304	-0.21
CPM PPT low back	0.01383	-0.3345	0.3622	0.938
CPM pain intensity in low back	-0.4333	-1.1229	0.2563	0.217
5min CPM PPT low back	0.0095	-0.3776	0.3966	0.961
5min COM pain intensity in low back	-0.85	-1.5172	-0.1828	**0.013**
IG (post-pre)				
PPT low back	-0.3467	-0.6285	-0.0648	**0.016**
PPT pain intensity in low back	-0.3	-0.8954	0.2954	0.322
TS pain intensity in low back	-1.725	<0.0001	-2.1354	-1.315
CPM PPT low back	-0.3143	-0.6627	0.03405	0.077
CPM pain intensity in low back	-1.6667	-2.3563	-0.9771	<**0.0001**
5 min CPM PPT in low back	-0.2068	-0.5939	0.1802	0.293
5 min CPM pain intensity in low back	-1.6333	-2.3006	-0.9661	<**0.0001**
Post (CG-IG)				
PPT low back	0.009667	-0.2722	0.2915	0.946
PPT pain intensity in low back	0.65	0.05459	1.2454	0.032
TS pain intensity in low back	1.025	<0.0001	0.6146	**0.032**
CPM PPT low back	0.1487	-0.1997	0.497	0.401
CPM pain intensity in low back	1.25	0.5604	1.9396	**0.0004**
5 min CPM PPT in low back	0.008333	-0.3787	0.3954	0.966
5 min CPM pain intensity in low back	1.0167	0.3494	1.6839	**0.003**

CG: Control group; IG: Intervention group; IL: Inferior limit; SL: Superior limit (IC 95%); CI: Confidence interval.