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The effectiveness of pain neuroscience education in people with chronic non-specific low back pain: An umbrella review with meta-analysis

José García Cancela [a], Orlando Conde Vázquez [b], Santiago Navarro Ledesma [c,d,*], Leo Pruimboom [c]

[a] Clinical Medicine and Public Health PhD Program, Faculty of Health Sciences, University of Granada, Granada, Querol Street 5, 52004 Melilla, Spain
[b] Department of Functional Biology and Health Sciences, Faculty of Physiotherapy, Campus of Pontevedra, University of Vigo, A Xunqueira No., 36005, Pontevedra, Spain
[c] University Chair in Clinical Psychoneuroimmunology, University of Granada and PNI Europe, Groot Hertoginnelaan 184, 2517 EW Den Haag, Netherlands
[d] Department of Physical Therapy, Faculty of Health Sciences, Campus of Melilla, University of Granada, Granada, Querol Street 5, 52004 Melilla, Spain

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ABSTRACT

Background: Chronic non-specific low back pain (CNLBP) affects millions worldwide and is a major contributor to disability and healthcare costs. Pain neuroscience education (PNE) aims to improve understanding of pain mechanisms, reduce maladaptive beliefs, and promote active coping strategies.
Objective: To evaluate the effectiveness of pain neuroscience education (PNE) on pain intensity, frequency, disability, and quality of life in adults with chronic non-specific low back pain (CNLBP).
Design: Umbrella review (UR) (PROSPERO, CRD42023382825).
Literature search: A comprehensive search was conducted in 8 databases, covering April 2014 to April 2024.
Study selection criteria: Inclusion: adults with CNLBP, PNE interventions provided by healthcare professionals, and systematic reviews (SRs) of randomized controlled trials (RCTs). Exclusion: studies focusing solely on psychological or physical aspects.
Data synthesis: Data on pain intensity, pain frequency, disability, and quality of life measured using validated scales were extracted. The results were shown according to the type of intervention and the period evaluated (short or long-term).
Results: Nineteen SRs with 5200 participants were included. Five studies (1120 participants) showed significant short-term pain reductions with PNE alone but inconsistent long-term effects. Four studies (860 participants) showed enhanced pain reduction with PNE combined with physiotherapy or exercise. Ten studies (3220 participants) indicated that combining PNE with other educational and biopsychosocial interventions led to more sustained pain reductions. Six studies were included in a quantitative review assessing PNE combined with exercise, with MD (mean difference) for pain, -1.11 (95 % CI, -1.57 to -0.66). For disability, SMD (standardized mean difference) was -0.42 (95 % CI, -1.09 to 0.24).
Conclusions: PNE decreases pain intensity in CNLBP, with improved outcomes when combined with physiotherapy, exercise, or additional educational and biopsychosocial strategies. A multidisciplinary approach, including PNE, is recommended. Further research using standardized tools and diverse populations is needed to enhance the efficacy and generalizability of PNE interventions.
Perspective: This umbrella review (UR) demonstrates that PNE can effectively reduce pain intensity and disability in CNLBP, especially when combined with physiotherapy, exercise, or biopsychosocial approaches, and it launches new hypotheses about how PNE may work. Adding PNE to different interventions may enhance participant outcomes and support more sustained pain relief.
Registration: PROSPERO, CRD42023382825.

Abbreviations: AMSTAR-2, measurement tool for systematic reviews; BPS, biopsychosocial; CCA, corrected covered area; CNLBP, chronic non-specific low back pain; COVID-19, Coronavirus disease 2019; GBD, global burden of disease; GRADE, grading of recommendations, assessment, development, and evaluation; GROOVE, graphical representation of overlap for overviews; IC, insular cortex; LBP, low back pain; MD, mean difference; MRI, magnetic resonance imaging; MSKP, chronic musculoskeletal pain; NRS, numerical rating scale; ODI, oswestry disability index; PICO, population, interventions, controls, outcomes, and study designs; PNE, pain neuroscience education; PRISMA, preferred reporting items for overviews of systematic reviews; PSE, pain science education; QBPDS, Quebec back pain disability scale

*Corresponding author.
E-mail address: snl@ugr.es (S.N. Ledesma).

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1. Introduction

Management and care of low back pain (LBP) is a significant challenge for healthcare systems. According to the latest Global Burden of Disease (GBD) update, 619 million people were affected in 2020, a number expected to reach 843 million by 2050 [1]. This figure may be underestimated, as the current GBD data do not reflect the impact of coronavirus disease 2019 (COVID-19). A recent meta-analysis found that the prevalence and intensity of LBP increased during the pandemic [2]. LBP also has a significant economic impact [3], being the leading cause of years lived with disability [1], with treatment costs comparable to cancer, cardiovascular diseases, and mental health disorders in developed countries [4].

Chronic LBP is defined as pain lasting 12 weeks or more [5]. In 85 % of cases, no correlation with radiological findings or biomarkers is observed, and it is classified as chronic non-specific low back pain (CNLBP). Brain-mediated mechanisms such as central sensitization have been implicated in pain persistence [6–8], and factors like perceived threat or beliefs associating pain with damage may contribute to fear, avoidance, and disuse [9–11]. However, some authors highlight the complexity of chronic pain and caution against purely brain-centered approaches [12], calling for further research on immunoception's role in pain chronification [13,14].

Along with advice to remain active, pain neuroscience education (PNE) is considered a first-line treatment for CNLBP [15]. PNE provides people with knowledge about the biology and physiology of pain [16], fostering cognitive changes that may improve pain intensity, kinesiophobia, and disability [17,18]. Over time, PNE has evolved from a primarily didactic, one-way educational intervention to a more interactive and constructivist approach, now often referred to as Pain Science Education (PSE), emphasizing interactive, participant-centered learning [19]. In CNLBP, attributing pain to brain and psychological factors has been shown to reduce its intensity [20].

While some systematic reviews (SRs) suggest greater effectiveness when PNE is added to CNLBP programs [21], others note methodological limitations that preclude firm clinical recommendations [22]. In this context, an umbrella review (UR) helps assess potential biases and synthesize available evidence [23,24]. This study aimed to conduct a UR to critically appraise the effectiveness of PNE in improving pain intensity, pain frequency, disability, and quality of life in people with CNLBP.

2. Material and methods

This UR followed the Preferred Reporting Items for Overviews of Systematic Reviews (PRISMA), incorporating the PRIOR checklist [25]. The protocol was registered in PROSPERO (CRD42023382825) before commencement.

2.1. Inclusion criteria

Criteria were established based on methodological and clinical considerations, including population, interventions, controls, outcomes, and study designs (PICO) [26].

2.1.1. Population

Eligible participants were adults (>18 years) diagnosed with CNLBP.

2.1.2. Intervention and control

Interventions involved PNE alone or combined with other treatments, delivered by healthcare professionals. Studies were excluded if education focused solely on psychological or biomechanical aspects (eg, cognitive behavioral therapy, back school, or pain-coping training). Interventions could be standalone or part of a multimodal approach. Control groups could include various interventions, if the effect of PNE could be isolated, and we included studies even when PNE was not the only differing component between groups.

2.1.3. Outcomes

Outcomes included pain intensity, pain frequency, disability, and/or quality of life.

2.1.4. Study design

We included SRs with or without meta-analyses of RCTs. Language restrictions were not imposed, aligning with international criteria [27].

2.2. Search strategy

We conducted our search across multiple databases, including PubMed, Cochrane, Web of Science, Scopus, PEDro, ProQuest, CINAHL, and Dialnet. The search period was 10 years (from April 2014 to April 2024) as most SRs on PNE for CNLBP have been published within this timeframe. We considered this timeframe best to reflect the current state of the evidence base. The search strategy can be checked in supplementary material S1.

Two reviewers (J.G.C. and O.C.V.) independently executed the search following a standardized methodology, with any discrepancies resolved through consensus. Additionally, manual screening of reference sections in original studies was performed, and authors were contacted for supplementary information if necessary.

2.3. Selection criteria and data extraction

Two reviewers independently assessed SRs for relevance based on title, abstract, and keywords. If disagreement or insufficient information arose, a full-text review was conducted. Studies meeting all inclusion criteria underwent full-text evaluation. Discrepancies were resolved by consensus, with a third reviewer involved if needed [28].

From each included SR, reviewers extracted: first author, year of publication, number of participants and study types, number of studies specifically on PNE in CNLBP, objectives, population, detailed interventions, outcome measures, and results (pain intensity, frequency, disability, quality of life).To ensure that we covered the entire literature, we also extracted information from studies that did not focus exclusively on CNLBP, but from which we were able to isolate and extract specific information related to CNLBP. Funding sources for each study included have also been sought.

2.4. Inter-rater agreement

Cohen's kappa coefficient (κ) was used to quantify the inter-rater agreement for full-text selection. We calculated κ to assess reliability before any consensus and estimated the inter-rater reliability using: (1) $\kappa > 0.7$ = high agreement between the reviewers; (2) κ of 0.5 −0.7 = moderate agreement; and (3) $\kappa < 0.5$ = agreement [29].

2.5. Methodology quality and risk of bias assessment

The 2 independent reviewers evaluated the methodological quality of the chosen SRs using the Measurement Tool for Systematic Reviews (AMSTAR-2) [30] and the risk of bias (RoB) using the Risk of Bias in Systematic Reviews tool (ROBIS) [31]. We calculated the interrater agreement for both tools as described in the previous section.

2.6. Overlapping analysis

To quantify overlapping studies in the included SRs we use the Graphical Representation of Overlap for OVErviews (GROOVE) tool [32]. This instrument allows us to quantify the number of primary studies included in each review through an evidence matrix, showing the possible overlapping primary studies in the included SRs. In this way, we avoid repeating data in the meta-analysis of outcomes from different SRs that refer to the same primary study. The GROOVE tool also graphics the overlapping degree between each pair of SRs in

percentages, calculating the overall corrected covered area (CCA), and provides the interpretation of the overall overlap assessment, being slight if the CCA is <5 %, moderate if it is between 6 %−9 %, high if it is ≥10 % and <15 %, and very high if CCA is ≥15 % according to its authors.

2.7. Data synthesis and analysis

The included studies reported data on pain intensity and disability using standardized scales. Pain intensity was measured with the visual analog scale (VAS) and the numerical rating scale (NRS). At the same time, disability was assessed using the Roland-Morris Disability Questionnaire (RMDQ) or the Oswestry Disability Index (ODI). Data on quality of life were insufficient, and pain frequency was not reported; thus, the analysis focused solely on pain and disability outcomes.

2.8. Certainly of evidence

Two authors independently assessed the certainty of evidence following the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [33]. This method considers potential study limitations, including risk of bias, inconsistency (variation in findings), indirectness (applicability of evidence), imprecision (effect estimate variability and confidence intervals), and publication bias (eg, small-study effects, missing negative studies). Certainty ratings were generated using the GRADEpro software [34].

2.9. Deviation of the protocol

This meta-analysis initially sought to assess the efficacy of PNE alone and in combination with other interventions, such as exercise and biopsychosocial approaches, for managing CNLBP. However, due to data limitations, the focus shifted to studies combining PNE with exercise versus single therapies (education, exercise, or motor control and stretching), based on the following scientific justifications: 1) Insufficient homogeneous data for PNE alone: given the limited number of studies on PNE in isolation and the variability in their methodologies, we observe that a robust meta-analysis would not be feasible with fewer than 5 studies [35]. For instance, studies like Moseley [36] and Orhan et al. [37] investigated PNE alone, but inconsistencies in outcome measures and follow-up periods complicated data synthesis. Additionally, critical studies lacked comprehensive reporting on primary outcomes such as pain intensity, disability, and quality of life, further hindering analysis. 2) Heterogeneity in PNE + non-exercise interventions**:** combinations with non-exercise therapies (eg, cognitive functional therapy) varied widely in methodology and outcomes, hindering reliable analysis. 3) Consistency in PNE + exercise studies**:** These studies consistently reported primary outcomes using similar methods, allowing for valid and reliable synthesis.

Meta-analyses were conducted using RevMan 5.4, a software developed for preparing and conducting SRs and meta-analyses, allowing for data entry, analysis, and graphical presentation of results [38].

3. Results

3.1. Study selection and data extraction

The screening process is detailed in the flow chart (Fig. 1). The initial search yielded 419 articles; 19 SRs met inclusion criteria [8,21,39−55], 12 of which included meta-analyses [8,21,39,40,43−45,50−53,55]. Initial screening showed inter-rater agreement of $\kappa = 0.775$; full-text screening yielded $\kappa = 0.481$. This low value led us to repeat the second round, resolving our disagreements. The revised κ for full-text screening was 0.932. The list of excluded studies with reasons is available in the supplementary material (Table S2).

3.2. Characteristics of the included SRs

Main characteristics (design, population, interventions, controls, and outcomes) are provided in supplementary material (Tables S3 and S4). We included reviews where PNE and CNLBP data could be extracted, even if the review addressed broader topics. Eleven of the 19 SRs focused exclusively on CNLBP [21,42,44,46,48−50,52−55], 5 on chronic musculoskeletal pain (MSKP) [8,40,41,47,51], 1 on chronic pain [43], and 2 on non-specific spinal pain [39,45]. Interventions included PNE alone, PNE combined with physiotherapy or physical exercise, or as part of educational/counseling or biopsychosocial (BPS) approaches [42−46,48,54]. Pain intensity was typically measured using VAS or NRS, and disability using the Quebec Back Pain Disability Scale (QBPDS), RMDQ, or ODI. No outcomes were found for pain frequency, and only 2 SRs reported quality of life data [46,54], which is insufficient for solid conclusions.

3.3. Methodological quality (AMSTAR-2)

Results are presented in Table 1. The inter-rater reliability of the methodological quality assessment final score was high ($\kappa = 0.891$). Agreement for individual AMSTAR-2 items is available in supplementary material S5.

3.4. Risk of bias analysis (ROBIS)

Six SRs (6/19, 32 %) had a low risk of bias, and 13 (13/19, 69 %) had a high risk (Tables S6.A and S6.B) and Fig. 2. The inter-rater agreement between reviewers was calculated for each of the 4 items of phase 2 of the ROBIS tool. For the item *Study Eligibility Criteria*, the kappa value was $\kappa = 0.659$, for *Identification and Selection of Studies,* $\kappa = 0.890$, for *Data Collection and Study Appraisal*, the percentage of agreement was 95 % (κ could not be calculated), and for *Synthesis and Findings*, $\kappa = 0.855$. The item of ROBIS phase 3, *Risk of bias in the Review,* showed $\kappa = 0.883$.

3.5. Overlap analysis

The overlap analysis showed a corrected overlap area of 17 %, meaning a very high overlap among SRs. A graphical representation of overlapping and the matrix of evidence can be seen in supplementary materials S7 and S8.

3.6. Grade assessment

The results and the overall certainty of the evidence are summarized in Table 2. No downgrades were applied for inconsistency, indirectness, risk of bias, or publication bias. However, the certainty of evidence was downgraded from high to moderate in the domain of imprecision for both outcomes (pain and disability).

3.7. Qualitative analysis

A subgroup analysis was conducted to homogenize the results. Therefore, a qualitative synthesis was performed for the following sets: (1) PNE alone, (2) PNE with physiotherapy, (3) PNE with physical exercise, and (4) PNE with other educational and biopsychosocial interventions.

3.7.1. Pain intensity

PNE alone

Two SRs report pain reduction in short and long-term chronic MSKP [8,40]. Five SRs provided results on PNE as the only intervention specifically in CNLBP.

Short-term effects

Significant pain improvements were noted in some studies [49,50,55], with SMD, −1.55 (95 % CI, −2.59 to −0.50) in the Shin and

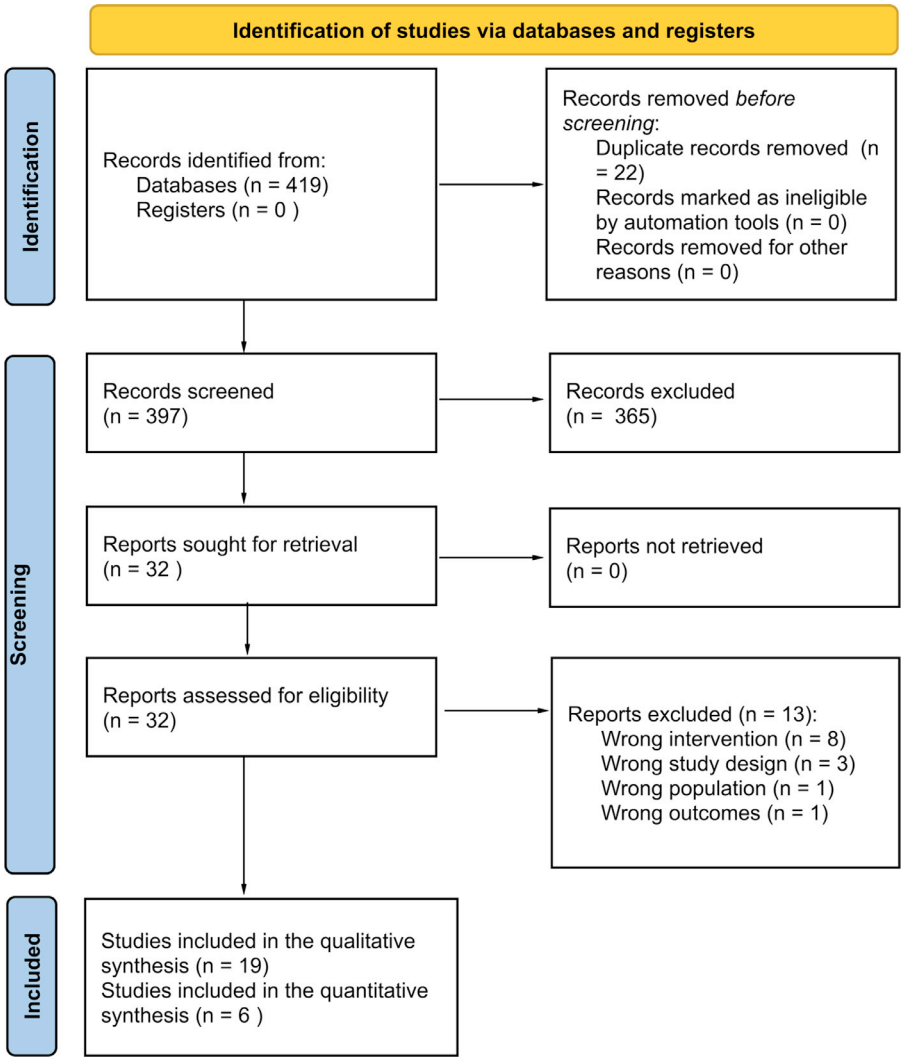

Fig. 1. PRISMA flowchart.

Kim [50] review, but not in others with a weighted mean difference (WMD), 0.73 (95 % CI, −0.14 to 1.61) [55].

Bülow et al. [40] included 15 RCTs in their MSKP study, 10 of which were specific to CNLBP. They reported reductions in pain intensity immediately after intervention: SMD, −0.32; (95 % CI, −0.58 to −0.05) with substantial heterogeneity (I^2 = 85 %). In the study of Watson et al. [8], 5 of the 17 RCTs on MSKP were specific to CNLBP. In the short-term, they found a reduction in pain with a mean difference of 5.91 mm greater on the 100-mm VAS (95 % CI, −13.75 to 1.93) compared to control, despite considerable heterogeneity (I^2 = 85 %).

Long-term effects

Valdés-Orrego et al. [53] showed significant results at 6 months when comparing PNE versus other interventions with an SMD of −0.55 cm (95 % CI, −0.77 to −0.32); $P = 10^{-5}$ and concluded that PNE is effective in reducing pain intensity in CNLBP in the medium-term. Ma et al. [21] and Wood and Hendrick [55] found no significant changes: MD, −0.98, (95 % CI, −3.30 to 1.35); P = 0.41; I^2 = 78 %, and WMD, 0.44, (95 % CI, −1.03 to 1.91); P = 0.560, respectively. Ramós-Martín and Rodríguez-Nogueira [49], in their SR without meta-analysis, reported PNE effectiveness in the short term, but not long term. Bülow et al. [40] reported long-term pain reduction: SMD, −0.40 (95 % CI, −0.78 to −0.03), with substantial heterogeneity (I^2 = 72 %), and stated that increased knowledge of PNE correlates with reduced pain perception. In the medium term, the pooled results of Watson et al. [8], showed a greater mean reduction of 6.27 mm on the 100-mm VAS (95 % CI, −18.97 to 6.44) than control groups. Louw et al. [47] included 6 RCTs about PNE on CNLBP, supporting PNE's effectiveness in improving pain ratings, though results should be considered with caution due study heterogeneity. Cuenda-Gago and Espejo-Antunez [41] also investigated PNE on MSKP (7 out of 10 RCTs were about CNLBP), and they reported that PNE showed positive effects when applied in isolation (except for 1 study).

PNE combined with physiotherapy

Two SRs provided results on PNE combined with physiotherapy specifically in CNLBP.

Short-term effects

Three SRs reported significant post-treatment pain reductions [21,41,52], with MD, −1.15 (95 % CI, −1.67 to −0.64) and SMD, −1.03 (95 % CI, −1.52 to −0.55). One SR reported a 3-month follow-up [52], SMD, −1.09 (95 % CI, −2.17 to 0.00), based on 3 studies. Only 2 provided long-term data (up to 1 year), insufficient for meta-analysis. Most RCTs combined PNE with physiotherapy. Cuenda-Gago and Espejo-Antúnez [41] also found significant NPRS reductions over time.

PNE combined with physical exercise

Two SRs provided results on PNE combined with physical exercise, specifically in CNLBP.

Short-term effects

Significant reductions were seen for Ma et al. [21], MD, −1.14 (95 % CI, −1.55 to −0.72) and for Ramós-Martín et al. [49], which reported

Table 1
Results of the methodological quality assessment (AMSTAR-2).

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Score
Geneen et al. [40]	Yes	Yes	No	Partial Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	L
Otoo et al. [45]	Yes	Partial Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	N/A	N/A	Yes	Yes	N/A	Yes	CL
Louw et al. [44]	Yes	No	Yes	Partial Yes	Yes	No	No	Yes	Partial Yes	No	N/A	N/A	Yes	Yes	N/A	Yes	CL
Cuenda-Gago & Espejo-Antunez [38]	Yes	Partial Yes	Yes	Partial Yes	Yes	Yes	No	Yes	No	No	N/A	N/A	Yes	No	N/A	No	CL
Tegner et al. [49]	Yes	No	Yes	Partial Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	CL
Valdes-Orrego et al. [50]	Yes	Partial Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	Yes	CL
van Erp et al. [51]	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	N/A	N/A	Yes	Yes	N/A	Yes	CL
Watson et al. [8]	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	L
Wood & Hendrick [52]	Yes	Partial Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	CL
Bülow et al. [37]	Yes	Yes	Yes	Partial Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	CL
Jones et al. [42]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	H
Ramós-Martín & Rodríguez-Nogueira [46]	Yes	Partial Yes	No	No	Yes	Yes	No	Yes	Yes	No	N/A	N/A	Yes	No	N/A	Yes	CL
Bonatesta et al. [36]	Yes	No	No	Partial Yes	Yes	Yes	No	Yes	No	Yes	No	No	Yes	Yes	No	Yes	CL
Ferlito et al. [39]	Yes	Partial Yes	Yes	Partial Yes	Yes	No	No	Yes	Yes	No	N/A	N/A	Yes	Yes	N/A	Yes	CL
Kovacs et al. [53]	Yes	Yes	No	Yes	Yes	Yes	Partial Yes	Yes	Yes	No	N/A	N/A	Yes	Yes	N/A	Yes	L
Siddall et al. [48]	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	L
Hochheim et al. [41]	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	L
Ma et al. [21]	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	L
Shin & Kim [47]	Yes	Yes	No	No	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	CL

CL, critically low; H, high; L, low; 1: Did the research questions and inclusion criteria for the review include the components of PICO? 2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? 3: Did the review authors explain their selection of the study designs for inclusion in the review? 4: Did the review authors use a comprehensive literature search strategy? 5: Did the review authors perform study selection in duplicate? 6: Did the review authors perform data extraction in duplicate? 7: Did the review authors provide a list of excluded studies and justify the exclusions? 8: Did the review authors describe the included studies in adequate detail? 9: Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review? 10: Did the review authors report on the sources of funding for the studies included in the review? 11: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? 12: If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis? 13: Did the review authors account for risk of bias in individual studies when interpreting/ discussing the results of the review? 14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? 15: If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review.

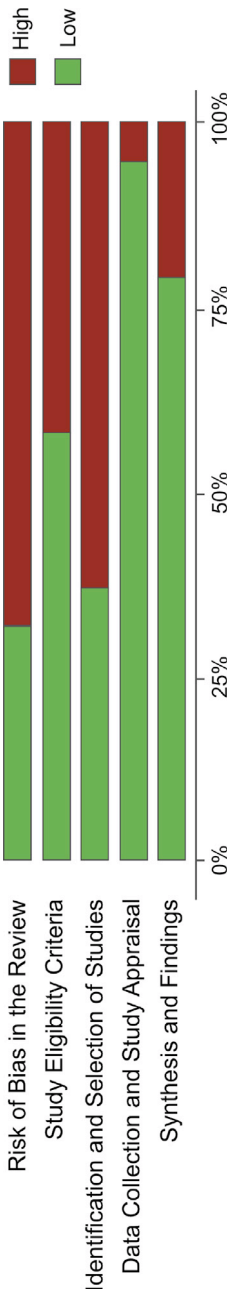

Fig. 2. ROBIS assessment summary plot.

that the combination of PNE plus exercise provides sustained improvements in pain intensity compared to PNE alone, even in the long-term.

Most studies included by Bonatesta et al. [39] on chronic spinal pain referred to CNLBP. Four RCTs evaluating PNE plus exercise showed short-term pain reduction versus exercise alone, SMD, −0.53 (95 % CI, −0.86, −0.20), with a moderate effect size. Siddall et al. [51] reviewed PNE plus exercise, including 5 RCTs on MSKP (4 on CNLBP), reporting a WMD, −2.09 (95 % CI, −3.38 to −0.80), though evidence quality was low due to high heterogeneity (I^2 = 86 %).

Long-term effects

Bonatesta et al. [39] showed improvement at the intermediate term, with SMD, −0.57 (95 % CI, −1.01 to −0.14).

PNE combined with other educational and biopsychosocial interventions

Short-term effects

Several studies reported significant short-term pain intensity reduction [44,45,54], except Otoo et al. [48] and Geneen et al. [43]. Among

Table 2
GRADE assessment: summary of findings.

		Certainly assessment					No patients		Effect	Certainly
No. of studies	Study design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations	PNE + exercise	Single therapy	Absolut (95 % CI)	
Pain intensity										
6	Randomized trials	Not serious[a]	Not serious[b]	Not serious	Serious[c]	None[d]	198	205	MD **−1.11***** (CI: −1.57, −0.66)	⊕⊕⊕◯ Moderate
Disability										
6	Randomized trials	Not serious[a]	Not serious[b]	Not serious	Serious[c]	None [d]	203	200	SMD −0.42 (CI −1.09, 0.24)	⊕⊕⊕◯ Moderate

Abbreviations: CI, confidence interval; MD, mean difference; SMD, standardized mean difference.

*** P < 0.001.

[a] Risk ok bias: not downgraded, because potential limitations are unlikely to lower confidence in the estimate of effect.

[b] Inconsistency: not downgraded, as all studies show effects in the same direction (favoring PNE + exercise) with clinically meaningful reductions in pain and disability. Variations in effect sizes are within an expected range for this type of intervention.

[c] Imprecision: downgraded once, because of low number of studies containing small sample sizes.

[d] Publication bias: not downgraded as funnel plots are unreliable with fewer than 10 studies, and no other indicators of publication bias were identified.

them, Hochheim et al. [44] found that primary care BPS interventions reduce pain immediately post-treatment SMD, −1.09 (95 % CI, −1.84 to −0.34) using low-dosed (≤15 treatment hours) sessions. Van Erp et al. [54] found moderate-quality evidence on the effectiveness of education/advice in the short-term SMD, −0.39 (95 % CI, −1.71 to −0.38). Jones et al. [45] provided low-quality evidence on reducing pain MD, −8.2 (95 % CI, −12.5, to 3.9), with substantial heterogeneity (I^2 >50 %). Kovacs et al. [46] examined educational programs including PNE and found that active management education, which encompasses PNE, was more effective than postural hygiene (the set of rules and habits for maintaining proper body posture during daily activities, to prevent back pain and relapses) or sham education (SMD values not provided).

However, Otoo et al. [48] compared the effectiveness of advice/education, including PNE, versus active physiotherapy and found that exercise therapy was more effective in reducing pain in the short term, with significant improvements in the exercise groups compared to advice/education ($P < 0.5$). Specific SMD values were not consistently reported. The SR carried out by Geneen et al. [43] found that educational interventions, including PNE, had no significant improvement in pain intensity compared to usual care immediately post-intervention, SMD, −0.01 (95 % CI, −0.19 to 0.17).

Long-term effects

Significant results of PNE plus BPS interventions were obtained for Hochheim et al. [44], SMD, −0.79 (95 % CI, −1.42 to −0.17). Van Erp et al. [54] informed that all included studies in their systematic review without meta-analysis reported that participants improved over time. Ferlito et al. [42] reviewed RCTs that included PNE as part of various interventions such as cognitive behavioral therapy and multidisciplinary rehabilitation (including psychological support). The intervention was effective in reducing pain in participants with chronic low back pain. Despite methodological heterogeneity, the review supports the integration of PNE into treatment protocols for its potential medium-term benefits.

3.7.2. Disability

PNE alone

Five SRs provided results on PNE as the only intervention specifically in CNLBP [21,48,49,53,55].

Short-term effects

Mixed results were found, with some researchers finding significant improvements, as Ramós-Martín et al. [49], who concluded that PNE alone seems to be more effective in the short-term, and Wood & Hendrick [55], who showed an overall WMD of 2.28 (95 % CI, 0.20, 4.25), $P = 0.020$ regarding the RMDQ, indicating both clinically and statistically significant improvement. On the other hand, Ma et al. [21] indicated no significant effects between the experimental and control groups: SMD, −0.19 (95 % CI, −0.79 to 0.40), $P = 0.52$, and $I^2 = 76$ %, as Otoo et al. [48], whose SR only included 1 RCT evaluating isolated PNE and found no positive effects on disability levels.

Regarding those studies focusing on MSKP, the SR of Watson et al. [8] showed a mean disability reduction of PNE to be 4.09 out of 100 greater than control ($P = 0.028$). The evidence was of moderate quality with considerable heterogeneity ($I^2 = 86$ %). Bülow et al. [40] observed a post-intervention SMD, −0.17 (95 % CI, −0.34 to −0.01), indicating a small but significant result favoring PNE.

Medium-term effects

Valdés-Orrego et al. [53] obtained an SMD for the RMDQ of −2.02 points (95 % CI, −3.43, −0.61), $P = 0.005$), indicating that PNE appears beneficial in improving disability at six-month follow-up. Bülow et al. [40] reported a mean disability reduction of 8.14/100 greater than control ($P = 0.032$) with moderate quality and high heterogeneity ($I^2 = 96$ %).

Long-term effects

No positive effects reported by 2 SRs [49,55], with WMD, 2.18 (95 % CI, −0.67 to 5.02), $P = 0.13$. Bülow et al. [40] reported no effects, with an SMD −0.27 (95 % CI, −0.59 to 0.06).

The qualitative results of Louw et al. [47] supported evidence for PNE reducing disability, both at short-term and long-term follow-up.

PNE combined with physiotherapy

Two SRs provided results on PNE combined with physiotherapy for disability specifically in CNLBP [21,52].

Short-term effects

The review of Ma et al. [21] shows a significant improvement in disability, SMD, −0.85 (95 % CI, −1.29 to −0.40) with low heterogeneity ($I^2 = 16$ %). Tegner et al. [52] found a post-intervention reduction SMD, −0.47 (95 % CI, −0.80 to −0.13) and at 3-months follow-up SMD, −0.38; 95 % CI, −0.74 to −0.02).

Focusing on MSKP, Cuenda-Gago and Espejo-Antunez [41] reported notable improvements in disability measures (7/10, 70 %) RCTs on CNLBP, with significant reductions in RMDQ scores both in the short and medium/long term.

PNE combined with physical exercise

Short-term effects

Two CNLBP-specific SRs showed a significant reduction in disability. Ma et al. [21] SMD, −0.80 (95 % CI, −1.13 to −0.47) with notable heterogeneity ($I^2 = 72$ %), and Ramós-Martín and Rodríguez-Nogueira [49] (no meta-analysis performed).

Siddall et al. [51] reported a SMD of −0.68 (95 % CI, −1.17 to −0.20) in MSKP, mainly focused on CNLBP, despite low-quality evidence due to high heterogeneity ($I^2 = 86$ %).

Medium-term effects

Bonatesta et al. [39] showed a significant improvement in disability SMD, −0.93 (95 % CI

−1.08 to −0.03) for chronic spinal pain, but not in the short-term SMD, −0.24;([95 % CI, −0.53 to 0.05).

Long-term effects

Ramós-Martín and Rodríguez-Nogueira [49] reported sustained improvements in disability over the long term with combined PNE and exercise compared to PNE alone.

PNE combined with other educational and biopsychosocial interventions

Short-term effects

Geneen et al. [43] found that PNE showed no significant difference compared to usual care (SMD 0.02, 95 % CI −0.31 to 0.34), but a significant improvement was found when compared to other educational interventions (SMD 0.52, 95 % CI 0.09 to 0.95). Hochheim et al. [44] found positive results for disability immediately post-treatment SMD, −1.33 (95 % CI, −2.17 to −0.49), as van Erp et al. [54] who offered moderate-quality evidence that BPS interventions (including PNE) were more effective than education/advice SMD, −0.31 (95 % CI, −1.50 to 0.88). Jones et al. [45] showed a small effect of advice/education, including PNE,P on disability MD, −4.5 (95 % CI, −7.9 to −1.0), with high heterogeneity ($I^2 > 50$ %).

Medium-term effects

Ferlito et al. [42] reported a notable reduction, and Kovacs et al. [46] noted that active management education, incorporating PNE, shows significant improvements in disability scores compared to control and other educational methods (they included one RCT on CNLBP, with 3-month follow-up).

Long-term effects

Both Hochheim et al. [44] SMD, −1.17 (95 % CI, −2.06 to −0.28) and van Erp et al. [54] SMD, −9.70 (95 % CI, −12.70 to −6.70) reported positive results for disability.

3.8. Results of the meta-analysis

PNE + exercise

The meta-analysis included 6 studies: Bodes Pardo et al. [56], Gorji et al. [57], Rabiei et al. [58], Ryan et al. [59], Pires et al. [60], and O'Keeffe et al. [61]. Detailed reasons for the inclusion/exclusion of primary studies can be seen in Supplementary Material S9. It is essential to highlight that 2 of these studies compared PNE + Exercise versus PNE

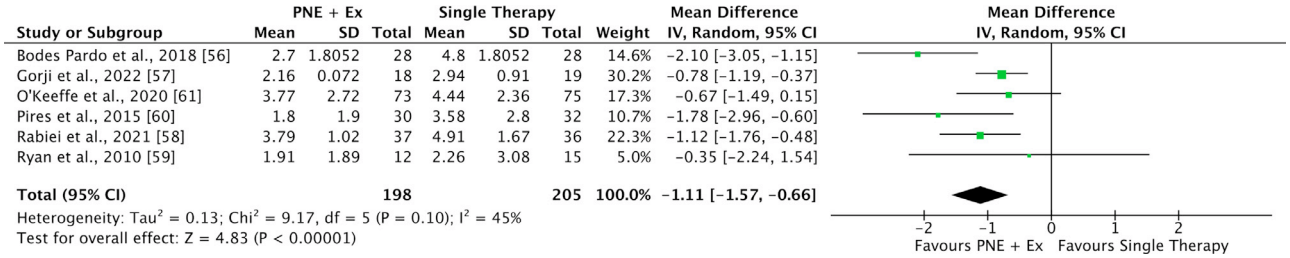

Fig. 3. Forest plot for pain.

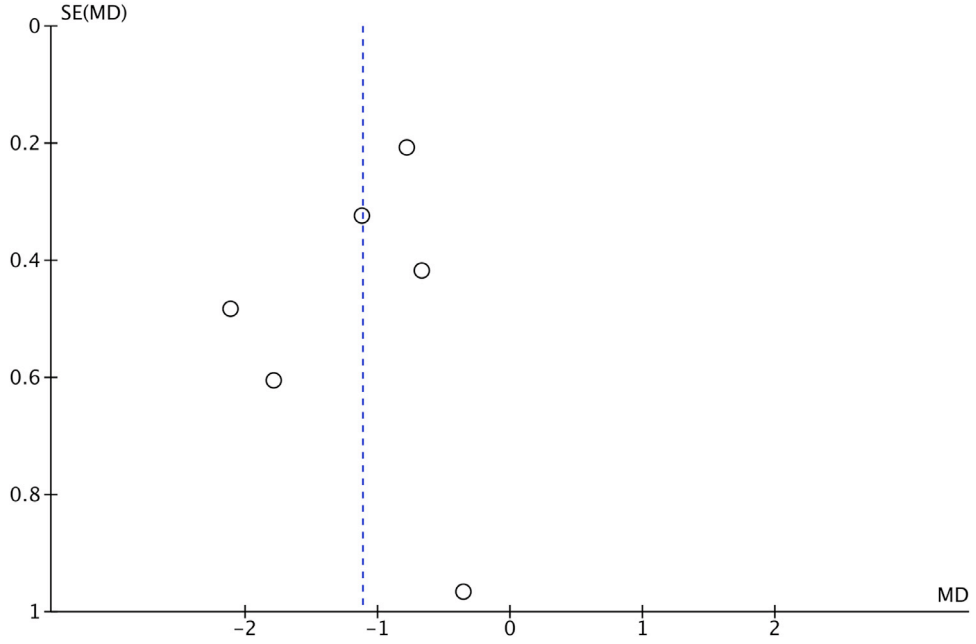

Fig. 4. Funnel plot for pain.

alone [59,61]. This could pose a problem in the meta-analysis, as it would assess the exercise aspect itself rather than the impact of PNE. To address this, a sensitivity analysis was performed, extracting data from these 2 articles from the meta-analysis. The results are therefore published with $k = 6$ and $k = 4$ articles. Furthermore, a comparative table between meta-analyses can be seen in Supplementary Material S10.

Pain intensity

A total of $k = 6$ studies were included in the analysis. The studies used a 10-point or 100-point VAS or NRS scale, thus allowing for obtaining MDs after rescaling them appropriately. Pooled SD at follow-up was calculated for the variable. However, the follow-up data varied from 2 months [57,58] to 3 months [56,59,60] or 6 months [61]; thus, we assumed they were comparable data. The estimated average MD based on the random-effects model was −1.11 (95 % CI, −1.57 to −0.66). Therefore, the average outcome differed significantly from zero ($Z = 4.83$, $P < 10^{-5}$). According to the Q-test, there was a moderate amount of heterogeneity in the actual outcome ($Q_{(5)} = 9.17$, $P = 0.10$, $Tau^2 = 0.13$, $I^2 = 45$ %) (Figs. 3 and 4).

Removing data from Ryan et al. [59] and O'Keeffe et al. [61] resulted in a slightly increased effect size, up to −1.30 (95 % CI, −1.89 to −0.71), with heterogeneity remaining stable ($I^2 = 45$ %).

Disability

A total of $k = 6$ studies were included in the analysis. The studies used the RMDQ [56–59], the ODI scale [61], or the QBPDS [60]. Pooled SDs at follow-up were calculated for the outcome, assuming comparable follow-up data moments. The estimated average SMD based on the random-effects model was −0.42 (95 % CI, −1.09 to 0.24). Therefore, the average outcome did not differ significantly from zero ($Z = 1.25$; $P = 0.21$). According to the Q-test, there was a highly significant amount of heterogeneity in the actual outcome ($Q_{(5)} = 48.79$; $P < 0.10^{-5}$; $Tau^2 = 0.61$; $I^2 = 90$ %). To better interpret the clinical significance of the calculated SMD, we explored a data transformation using an internal deviation reference [62], specifically the RMDQ scale. The internal $SD_{(RMDQ)}$ obtained was 3.04. So, the SMD and 95 % CI expressed in RMDQ units were −1.27 (95 % CI, −3.31 to 0.73) (Figs. 5 and 6).

Excluding Ryan et al. [59] and O'Keeffe et al. [61] increased the effect size, reaching a statistically significant −0.86 (−1.37 to −0.34; $P = 0.001$). However, heterogeneity decreased from $I^2 = 90$ % to 71 %, indicating a somewhat more homogeneous subset of studies.

4. Discussion

This UR synthesized evidence on the effectiveness of PNE for CNLBP over the past decade and included studies on PNE alone and in combination with other interventions. Despite mixed results, it appears that PNE, whether used alone, combined with physiotherapy, exercise, or as part of a broader educational or biopsychosocial approach, can significantly reduce pain intensity and disability in people with CNLBP.

PNE alone showed mixed short-term benefits and limited long-term effects, although heterogeneity among studies influenced the consistency of results. For instance, Shin and Kim's [50] meta-analysis demonstrated substantial short-term pain reduction, while Watson et al. [8] reported less significant changes. Long-term effects varied, with studies like Valdés-Orrego et al. [53] showing sustained reductions in pain

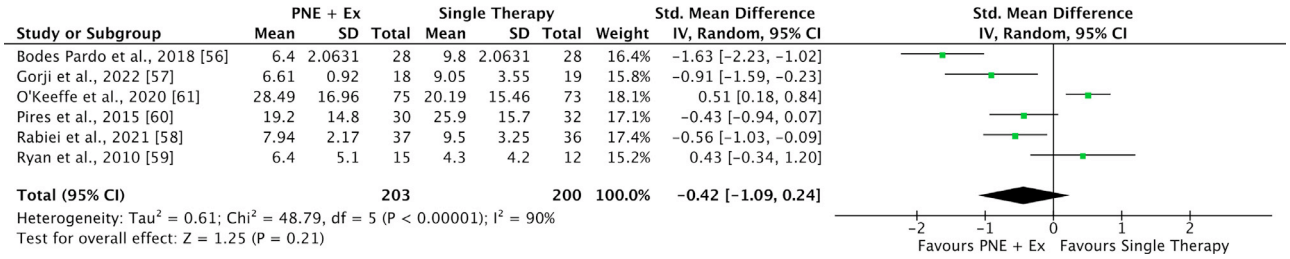

Fig. 5. Forest plot for disability.

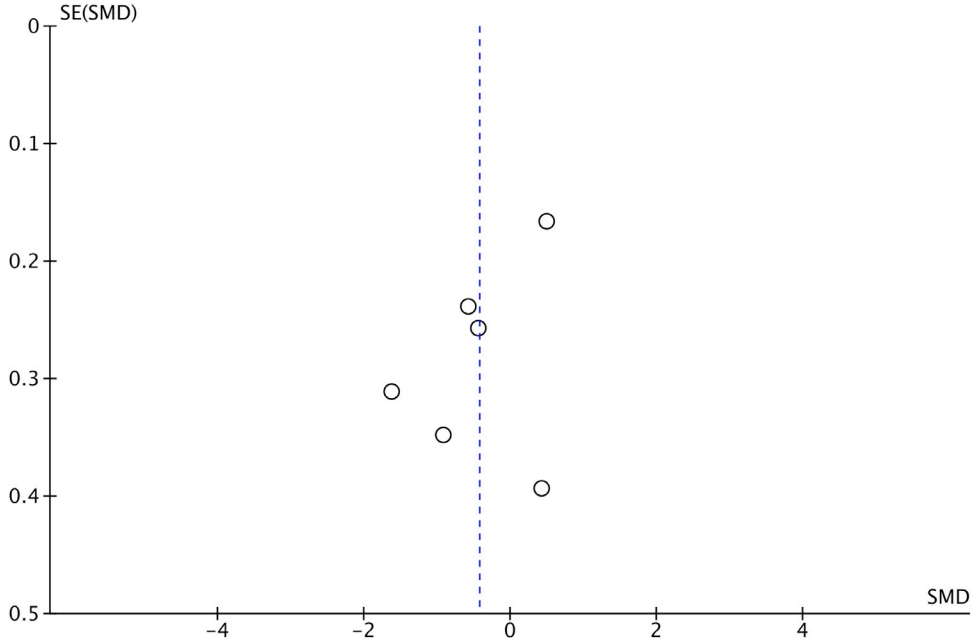

Fig. 6. Funnel plot for disability.

intensity while others, such as Ma et al. [21], found no significant changes over time. However, combining PNE with physiotherapy, exercise, or educational approaches produces better short and long-term outcomes, supporting its use in combination with other CNLPB interventions to enhance its benefits. Recent publications highlight the concept of "PNE plus" as the most evidenced way of coping with persistent pain [63]. Combining PNE with biopsychosocial interventions produced mixed results, with some studies demonstrating significant short-term pain reduction, while others found exercise therapy to be more effective.

For disability reduction, results were mixed depending on the intervention combination. PNE alone showed inconsistent effects, with some studies reporting significant improvements, while others, such as Ma et al. [21] found no notable changes. However, when PNE was combined with physiotherapy or physical exercise, more consistent reductions in disability were observed. Notably, Tegner et al. [52] reported significant short-term improvements with PNE plus physiotherapy, while Bonatesta et al. [39] found sustained improvements in the medium term when PNE was combined with exercise. The combination of PNE with BPS interventions also showed effectiveness in reducing disability, particularly in the long-term, as seen in studies by Hochheim et al. [44] and van Erp et al. [54].

According to the Cochrane Risk of Bias tool [64], all the studies presented a performance bias related to the lack of blinding of participants, therapists, and assessors. The rest of the biases were assessed as low. The results of the meta-analysis show that the combination of PNE and exercise has a significant effect on reducing pain intensity in people with CNLBP. Although consistent and clinically relevant, this effect was accompanied by moderate heterogeneity, possibly attributed to variability in follow-up times and characteristics of the included studies. In contrast, effects on disability did not reach statistical significance and had considerable heterogeneity. However, when the 2 studies analyzing PNE plus exercise vs PNE alone were excluded from the analysis, a significant effect was observed, with reduced heterogeneity. Transformation of the data to RMDQ units allowed a more precise clinical interpretation, although limited by high inter-study variability. The asymmetry observed in the Funnel Plots underlines the need to interpret the results cautiously. These findings suggest that the combination of PNE and exercise may effectively reduce pain intensity, considering the clinical context and the possible reduced generalizability. Furthermore, the impact of PNE and exercise on disability may be positive, but the strength of the evidence is poor due to the small population studied.

PNE is a clinical intervention that aims to teach people about the neurophysiology of pain [65], reducing maladaptive beliefs and encouraging active coping strategies [66,67]. Our findings indicate that PNE combined with other strategies produces better results than PNE alone, and PNE reinforces the results of active treatments compared to those applied without PNE. So, PNE may enhance the effectiveness of active treatments by facilitating decision-making and long-term behavioral change.

Although PNE is increasingly recommended for CNLBP [15], its effectiveness depends on factors like curriculum complexity, ethnocultural context, individual pain experience, and language, all requiring further study [49,68,69]. More high-quality research is needed with standardized methods, consistent session content, intervention durations, evaluation tools, and long-term follow-up, as noted by Sidiq et al.

[70] (though without assessing long-term outcomes). Additionally, the risk of bias should be minimized using appropriate criteria. ROBIS scores were lower mainly due to restrictive eligibility criteria, while AMSTAR-2 rated most studies low for insufficient description of study design. For study selection and data extraction, only 1 review showed selection bias, but many had search strategy bias per ROBIS. AMSTAR-2 showed high reliability in assessing literature search bias. No significant differences emerged between tools regarding synthesis, findings, study quality, or heterogeneity.

The appropriate dosage for PNE in chronic pain has also been investigated in recent literature [17,71,72]. Another factor to consider in PNE sessions and research could be the physician's empathy, which has been associated with better pain outcomes than other usual treatments [73]. The importance of therapist-participant interaction is supported by the fact that trust and bonding are related to the release of oxytocin [74], a hormone with reported analgesic properties [75,76].

Since CNLBP is not associated with tissue damage, recent advances in neuroscience suggest that CNS intervention, the so-called pain neuromatrix [77], may provide a remedy for people with CNLBP. However, agreeing with other researchers [12], we consider chronic pain a complex phenomenon that should not be attributed solely to neural mechanisms. Despite the absence of image damage, we cannot discard the intervention of the peripheral nervous system in the process, as CNLBP has been related to low-grade inflammation [78] and gut dysbiosis [79], neither of which is identifiable in a magnetic resonance imaging (MRI). Furthermore, central neuroinflammation has also been evidenced [80].

Chronic pain and the work pathway of PNE may be explained through neuroimmune connections. The concept of "immunoception" describes bidirectional communication between the brain and immune system, forming a neural representation of the body's immune state, called an immunogram. This immunogram includes memory cells in the brain and peripheral tissues, allowing the brain to recall and reactivate immune responses based on past experiences. Experimental studies have shown that stimulating specific neurons in the insular cortex (IC), which were active during previous inflammation, can trigger immune responses, potentially preparing the body for threats or causing unnecessary reactions without the original trigger [13,14].

The IC has emerged as a key player in various processes, such as sensory processing, body homeostasis, emotions, motivation, and decision making, as well as maladaptive conditions such as anxiety, depression, drug addiction, eating disorders, and chronic pain. Due to their high number of connections and their capacity to generate immunological memory, one question is whether these memory neurons could generate some activity when stimulated. Furthermore, these recent findings on immunoception raise the question: For people with CNLBP, is the first episode of pain a peripheral inflammation that enhances neuro-immunological memory? The next question is whether PNE could modulate the activity of these memory neurons and therefore decrease pain? Considering that the IC is rich in opioid receptors, and that cognitive factors can modulate physical and emotional states through the site-specific activation of mu-opioid receptor signaling in the human brain, including the IC.

Another way in which PNE could work is through the induction of a positive mindset, since relevant and useful information offered to people can be considered a positive stimulus and therefore activate dopaminergic neurons of the reward system, mainly those belonging to the ventral tegmentum (VT). Experimental studies have recently shown that stimulation of the reward system produces powerful and unexpected effects. In an unpublished study by Hedva Hawkin, they stimulated the VT in mice that had recently suffered a heart attack and found that the hearts of mice that had undergone VT stimulation were significantly healthier than those that had not. They observed that activation of the VT caused changes in the immune system associated with a dramatic reduction in scar tissue. The team of Ben-Shaanan demonstrated anti-tumor activity of the brain reward system, finding that its stimulation in mice significantly decreased tumor size. Stimulation of the reward system can also reduce pain through the release of dopamine, whose metabolism is reduced in people with chronic back pain. Furthermore, it has been established that dopamine is an essential precursor for the synthesis of endogenous morphine in animals and plants, a substance known for its potent analgesic properties. Taking these data into account, we suggest that providing deep learning to the participants (which perhaps they have been searching for a long time), via PNE, can be a powerful stimulus for their reward system that translates into an analgesic effect in CNLBP through the dopamine-morphine axis. Going a little further, we also suggest that any medical or paramedical intervention should always be accompanied by a transfer of knowledge to the participants. Finally, it is essential to recognize that the proposed mechanisms underlying PNE are still preliminary and require further research to be fully confirmed.

4.1 Strengths and limitations

This review strictly followed PRISMA guidelines, offering a comprehensive overview and highlighting the versatility of PNE across treatment paradigms. While a previous overview [22] included 8 SRs, our UR expanded the analysis to 19 SRs by incorporating additional studies with extractable data relevant to CNLBP. We assessed study quality using AMSTAR-2 and added ROBIS and GRADE for a consistent, reliable evaluation of evidence. Data extraction and management with the GROOVE tool streamlined the process and minimized handling errors.

As limitations, we detected significant heterogeneity. These include considerable inconsistency between session content, intervention duration, control groups, assessment tools, and quality of methodology. It is also important to recognize that the pain education interventions span a developmental continuum. Earlier forms of PNE were predominantly didactic, whereas more recent approaches, referred to as PSE, incorporate constructivist principles and emphasize interactive, learner-centered strategies [19]. This natural evolution of the intervention may account for some of the heterogeneity in the way PNE has been delivered and its observed effects. Many studies focused on short-term outcomes, with relatively few assessing the long-term impact of PNE.

Methodological quality and RoB often showed low quality, and there was substantial overlap among studies analyzed. A further limitation of this UR is its focus on a limited set of outcomes (pain intensity and disability). Even though these domains represent the core of research in CNLBP, other frequently evaluated outcomes, such as pain catastrophizing, kinesiophobia, and emotional distress, were not assessed. Future reviews should consider including a broader range of outcome measures to capture the multidimensional effects of PNE better.

5. Conclusion

This UR and MA support the effectiveness of PNE, particularly when delivered in combination with exercise, for reducing pain intensity in adults with CNLBP. The pooled data from six RCTs showed a statistically significant and clinically meaningful reduction in pain intensity, with moderate heterogeneity. Disability outcomes showed a limited yet statistically significant improvement when PNE plus exercise was compared to treatments not involving PNE, supporting the value of this combined intervention, and were accompanied by considerable heterogeneity across studies. These findings suggest that while PNE alone may provide some benefit, its integration into multimodal treatment programs—particularly when combined with physical exercise or physiotherapy—enhances its therapeutic impact.

Study details

Registration: PROSPERO, CRD42023382825.

CRediT authorship contribution statement

J.G.C. and O.C.V. conceptualized, designed, and performed the literature searches, data extraction and assessment of quality and risk of bias. J.G.C., O.C.V. and S.N.L. did the initial write-up and revision. O.C.V., S.N.L. and L.B.P. reviewed the manuscript and supplementary material, and provided a critical review. All authors read the manuscript and approved its definitive version.

Data sharing

All data relevant to the study is included in the article or is available as supplemental files.

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Conflict of interests

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.rehab.2025.102020.

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