Review Article

PTRS Physical Therapy Rehabilitation Science

https://doi.org/10.14474/ptrs.2020.9.4.309
pISSN 2287-7576
eISSN 2287-7584

Phys Ther Rehabil Sci
2020, 9 (4), 309-317
www.jptrs.org

Effects of pain neuroscience education on kinesiophobia in patients with chronic pain: a systematic review and meta-analysis

Hyunjoong Kim[a], **Seungwon Lee**[b]

[a]Sports Rehabilitation Center, The Better Hospital, Gwangju, Republic of Korea
[b]Department of Physical Therapy, College of Health Science and Social Welfare, Sahmyook University, Seoul, Republic of Korea

Objective: One of the treatment strategies for controlling chronic pain and preventing disability is patient education. Pain neuroscience education (PNE) has been proven to be effective in explaining the biological and physiological processes associated with pain experiences to patients. The purpose of this review is to investigate the effectiveness of PNE for kinesiophobia such as avoidance response in patients with chronic pain.
Design: A systematic review and meta-analysis.
Methods: MEDLINE, EMBASE, CINAHL, PEDro, and the Cochrane Central Register of controlled trials databases were searched through November 2020 and included a randomized controlled trials evaluating kinesiophobia in musculoskeletal patients with chronic pain. In 8 randomized controlled trial studies, 'Cochrane's risk of bias (RoB) tool was used for qualitative analysis, and results of post-intervention were analyzed through RevMan 5.4 for quantitative analysis.
Results: For this review, 8 randomized controlled trials of 369 patients with chronic pain were selected for PNE. A systematic review and meta-analysis also included 8 randomized controlled trials. The effect on kinesiophobia was more effective than the control group (−0.86; 95% confidence interval [CI], −1.22 to −0.51; heterogeneity [χ^2=21.18, df=7, I^2=67%]; overall effect [Z=4.80]). In addition, the effect on pain was more effective than the control group (−0.53; 95% CI, −1.05 to −0.01; heterogeneity [χ^2=47.42, df=7, I^2=85%]; overall effect [Z=2.01]).
Conclusions: The results of this review suggest that PNE and combined PNE have a positive effect on the improvement of pain and kinesiophobia in patients with chronic pain.

Key Words: Chronic pain, Education, Musculoskeletal pain, Neurosciences

Introduction

Musculoskeletal pain (MSP) is caused by complex interactions. Factors that can contribute include mechanical, biomechanical, psychological, and social factors. What the various factors mean is that MSP is affected by external factors other than just tissue damage. Management of MSP includes pharmacological and non-pharmacological (physical, psychological, social/environmental) interventions and invasive (surgical) methods [1].

Chronic pain can be defined as pain lasting more than 6 months [2]. However, there are specific pathological mechanisms involved in the chronicization of MSP. It is important to understand the concept of neuroplasticity (a neuron's ability to completely alter its structure, function, or biochemical profile in response to repeated afferent sensory inputs) in order to understand the development of chronic pain due to acute pain. This is because local inflammation of the damaged tissue increases the sensitization of special peripheral sensory neurons (nociceptors), inducing repetitive afferent

Received: 30 November, 2020 **Revised:** 7 December, 2020 **Accepted:** 8 December, 2020

Corresponding author: Seungwon Lee (**ORCID** https://orcid.org/0000-0002-0413-0510)
Department of Physical Therapy, College of Health Science and Social Welfare, Sahmyook University, 815 Hwarang-ro, Nowon-gu, Seoul 01795, Republic of Korea
Tel: 82-2-3399-1630 **Fax:** 82-2-3399-1639 **E-mail:** swlee@syu.ac.kr

input to the central nervous system [3]. Repetitive input of pain signals leads to the development of chronic pain and affects brain regions that are not related to pain, thereby changing the existing activated patterns (default mode network, DMN) [4]. As such, it has been reported that chronic pain induces escape and avoidance behaviors and is closely correlated with kinesiophobia [5,6].

One of the treatment strategies for controlling chronic pain and preventing disability is patient education [7-10]. Existing musculoskeletal educational models have focused on biomedical education focusing on anatomy, biomechanics and pathologic anatomy [7,11-13]. Biomedical education models have shown limited efficacy in relieving pain and disability [7,11,14,15]. Pain neuroscience education (PNE) [16,17] has been used interchangeably with therapeutic neuroscience education [18,19] and has been used to explain pain [20,21]. PNE aims to explain to the patient the biological and physiological processes involved in the experience of pain, and more importantly, not to focus on issues related to the anatomy [16,17,22-24]. PNE consists of educating patients in neurobiology and neurophysiology in pain and pain processing by the nervous system. It is understood that this may be due to sensitive nerves as it alters the 'patient's perception of pain [22,25].

Chronic pain is controversial about the management of pain as it affects areas of the brain that are not related to pain and alters the DMN. Therefore, it was hypothesized that understanding and learning of their pain could be effective in controlling pain through behavioral changes by changing the DMN for patients with chronic pain. Therefore, in this study, the effect of PNE on kinesiophobia, such as avoidance response in patients with chronic pain, can be identified and used as basic data to suggest the direction of the intervention program in the future.

The purpose of this study was to systematically review the effect of interventional studies on kinesiophobia of PNE in persons with chronic pain and to analyze the effect size by performing a meta-analysis to: 1) Identify the characteristics of motor phobia of persons with chronic pain derived through the search process. 2) Analyzing the effect of PNE on kinesiophobia.

Methods

Study design

This study is a systematic review and meta-analysis study to integrate and analyze PNE studies conducted on persons experiencing MSP and chronic pain abroad.

The method of this study is presented in the protocol, and the protocol is registered in PROSPERO (registration: CRD42020215892).

Search strategy and selection of studies

Inclusion criteria

(1) Participants

Subjects were individuals with MSP, chronic pain excluding spinal disease, and those aged 19 years or older who received PNE.

(2) Intervention

Among the individuals with MSP excluding spinal diseases, the intervention of PNE among those with chronic pain was studied. PNE included neuroplasticity education, therapeutic neuroscience education, and neuroscience pain education interventions.

(3) Comparisons

The control group compared to PNE did not contain PNE. Completely different interventions were performed or compared with other educational programs. Also, in the case of a single group, it was compared with the pre-test value.

(4) Outcomes

The selection criterion was the quantitative value or the result description of the variable measured after education intervention was performed on persons with chronic pain who received PNE.

(5) Types of studies

We included randomized clinical trials (RCTs) involving PNE in individuals with chronic, MSP, excluding spinal disease.

Exclusion criteria

Studies that did not target persons with MSP, studies involving spinal disorders, and studies with biomedical education as an intervention were excluded.

Literature-search strategy

The content and method of this study were approved for exemption from the deliberation of the Institutional Review Board at Sahmyook University (IRB No. 2-1040781-A-N-012020121HR).

Data was searched and collected in November 2020. The data was searched independently by two researchers (HK and SL) with experience in meta-analysis research. The search formula is constructed by merging terms representing chronic pain patients (P) and PNE (I).

The following electronic database was searched from record to October 2020: Pre-identified keywords (pain AND (Physiology OR Neuroscience OR Neurophysiology OR Biology) AND Education AND Chronic pain AND Randomized Controlled Trial) and the index terms were searched across all included databases (MEDLINE, EMBASE, CINAHL, PEDro and the Cochrane Central Register of controlled Trials).

Study selection and data extraction

First, documents searched through the database were removed from duplicate data in referencing software (EndNote X9, Thomson Reuters, NY, USA). Related theses were first checked through the theses titles and abstracts and then the original text of the selected theses were reviewed according to the selection criteria. In this process, the researchers explained the reasons for the excluded literature. General characteristics, intervention characteristics, and research results were extracted from the final selected study. The entire process of selecting and extracting the data was independently performed by two researchers. If the data did not match, the original text was reviewed together to make a final decision.

Quality assessment

For RCT studies, the 7-item Cochrane's risk of bias (RoB) tool developed by The Cochrane Bias Method Group was used. To evaluate the quality of the study, two researchers with experience in meta-analysis studies evaluated the RoB as low (+), uncertain (?), and high (-), and then re-evaluated the unmatched items after reviewing the original text. Questions with different evaluations between researchers were agreed through discussions between researchers.

Strategy for data synthesis

The review was analyzed using RevMan 5.4 (The Cochrane Collaboration, Oxford, England). Meta-analysis was performed when there were the same outcome variables that could be analyzed or when there were quantitative values pre-test and post-test the outcome variables. Meta-analysis was performed when there were 3 or more studies by outcome variable. For the effect size, a standardized mean

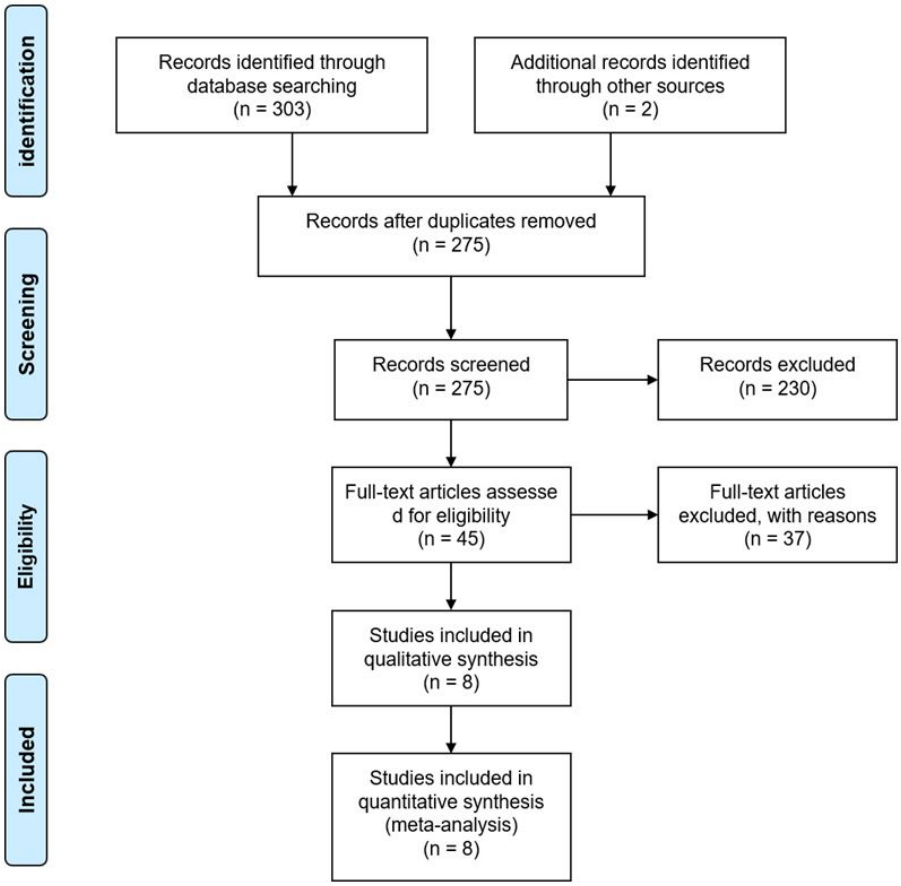

Figure 1. PRISMA flow diagram of search and the study selection process.

difference for the same outcome variable was selected as an analysis method, and a random effect model calculated that resets the weights in consideration of the variation between subjects of individual studies and the heterogeneity between each study [26]. The homogeneity of the selected studies was confirmed through Cochrane's chi-square test and I^2 test, and the I^2 value of 0% indicated that there was no heterogeneity, 30%-60% meant moderate heterogeneity, and

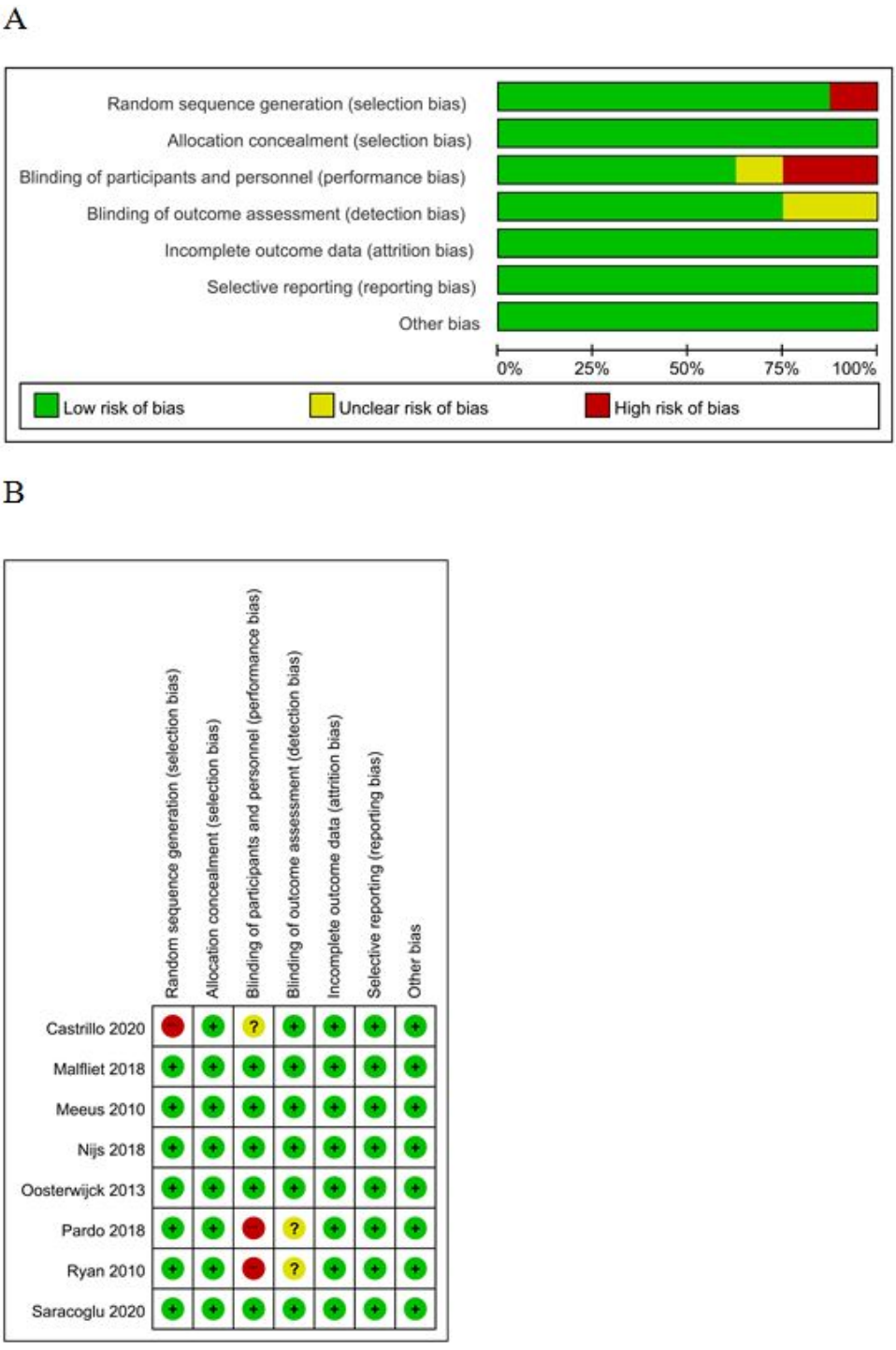

Figure 2. Risk of bias of the systematic review. (A) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies, (B) risk of bias summary: review authors' judgements about each risk of bias item for each included study.

more than 75%, indicated that the heterogeneity is large [26]. When data was input, the standard deviation was calculated by the pooled standard deviation formula. Publication bias of the searched research papers was tested using a funnel plot [27].

Results

Literature search and characteristics of the included randomized clinical trials

Since there is no research conducted in Korea, a total of 303 articles were searched through international databases. Duplicate materials were excluded through the EndNote X9, resulting in 275 international publications. After that, according to the data selection and exclusion criteria, two researchers reviewed mainly the title and abstract, and since 230 articles were excluded because they did not meet the selection criteria, 43 studies were selected first. Two additional studies were selected through manual search, and 45 studies were reviewed in the original text.

Among them, 37 studies were not RCTs, pain and kinesiophobia were not included in the outcome variables, and chronic pain was not included. Therefore, 8 studies were finally selected. A total of 8 studies were analyzed by systematic review and meta-analysis (Figure 1).

Methodological quality evaluation of pain neuroscience education applied to chronic pain

For the quality evaluation, a pilot test was conducted and evaluated for three studies. The questionnaire 'blind folded by the result evaluator' required consensus among researchers, and the concordance rate of the subsequent evaluation was 100%. The methodological quality evaluation for 8 RCTs were as follows: random sequence generation (low: 7, high: 1), blinding of participants and personnel (low: 5, uncertain: 1, high: 2), blinding of outcome assessment (low: 5, uncertain: 2), and other biases (low: 8) (Figure 2).

Pain neuroscience education on kinesiophobia and pain for chronic pain patients

In this review, 8 RCTs were selected that included 369 patients with chronic pain. Each selected study included an additional type of intervention. The Tampa scale of kinesiophobia was used in selected studies to investigate the effect of PNE on kinesiophobia. In addition, Visual Analog Scale, Numeric Pain Rating Scale, Pressure Pain Threshold, Pain Disability Index, Pain Catastrophizing Scale were used in selected studies to investigate the effect on pain. All studies selected had a positive effect of PNE compared to the control except for only one study (Table 1) [28-35].

Methodological quality evaluation of pain neuroscience education applied to chronic pain

For quality evaluation, a pilot test was conducted and evaluated for three studies. The questionnaire 'blind folded by the result evaluator' required consensus among the researchers, and the concordance rate of the subsequent evaluation was 100%. The methodological quality evaluation for 8 RCTs were as follows: random sequence generation (+: 7, −: 1), blinding of participants and personnel (+: 5, ?: 1, −: 2), blinding of outcome assessment (+: 5, ?: 2), and other biases (+: 8).

Effectiveness of pain neuroscience education on kinesiophobia

In 369 patients with chronic pain, 8 RCTs evaluated kinesiophobia. Compared to the control group, the kinesiophobia was significantly improved. The results analyzed through the random-effect model showed significant heterogeneity (−0.86; 95% confidence interval [CI], −1.22 to −0.51; heterogeneity [χ^2=21.18, df=7, I^2=67%]) and significant overall effect (Z=4.80) (Figure 3).

Effectiveness of PNE on pain

In 369 patients with chronic pain, 8 RCTs evaluated pain. Compared to the control group, the pain was significantly improved. The results analyzed through the random-effect model showed significant heterogeneity (−0.53; 95% CI, −1.05 to −0.01; heterogeneity [χ^2=47.42, df=7, I^2=85%]) and significant overall effect (Z=2.01) (Figure 4).

Publication bias

As a result of visually checking the degree of symmetry through a funnel plot for the bias test, the study was evenly distributed even in areas that were not statistically significant, indicating that there was relatively no publication bias (Figure 5). As for the statistical significance of the degree of asymmetry, Egger's regression test was not conducted because there were fewer than 10 studies included in the meta-analysis.

Table 1. Characteristics of included studies

Study	Sample size	Participants	Interventions	Therapeutic intensity	Control	Outcome measures	Authors conclusions	Conuntry, setting
Valiente-Castrillo, *et al*. (2020) [28]	41	Chronic myofascial neck pain	PNE＋TrPDN	Total intervention period: 2 weeks EG: 6 sessions of DN (3 day/week), 3 sessions of PNE (30 minutes) CG: 6 sessions of DN	TrPDN	Kinesiophobia : TSK Pain: VAS	The inclusion of PNE combined with DN resulted in greater improvements in kinesiophobia, pain anxiety, and pain-related beliefs	Spain, Hospital Universitario Infanta Sofia
Malfliet, *et al*. (2018) [29]	94	Chronic spinal pain	PNE＋TCE Cognition-targeted, Biopsychosocial approach	Total intervention period: 12 weeks EG: 3 sessions of PNE, 15 exercise sessions CG: 3 sessions of BNE, 15 exercise sessions	BNE＋PCE Biomedical approach	Kinesiophobia : TSK Pain: NPRS	PNE combined with CTMCTappears to be more effective than current best-evidence physiotherapy for improving pain, symptoms of central sensitization, disability, mental and physical functioning, and pain cognitions in individuals with chronic spinal pain	Belgium, Vrije Universiteit Brussel
Meeus, *et al*. (2010) [30]	46	Chronic fatigue syndrome	PPE	Total intervention period: immediately EG: 1 session (30 minutes) CG: 1 session (30 minutes)	PSE	Kinesiophobia : TSK Pain: PPT	A 30-minute educational session on pain physiology imparts a better understanding of pain and brings about less rumination in the short term	Belgium, University-based chronic fatigue clinic
Malfliet, *et al*. (2018) [31]	111	Chronic spinal pain	Blended-learning PNE	Total intervention period: 2 weeks EG: 3 sessions of PNE (30 minutes to 1 hour) CG: 3 sessions of BNE (30 minutes to 1 hour)	BNE	Kinesiophobia : TSK Pain: PDI	Blended-learning PNE was able to improve kinesiophobia and illness perceptions in participants with chronic spinal pain	Belgium, University hospitals in Ghent and Brussels
Oosterwijck, *et al*. (2013) [32]	30	Fibromyalgia	PPE	Total intervention period: 2 weeks EG: 2 sessions (30 minutes) CG: 2 sessions (30 minutes)	AME	Kinesiophobia : TSK Pain: PCS	Pain physiology education seems to be a useful component in the treatment of FM patients as it improves health status and endogenous pain inhibition in the long term	Belgium, Vrije Universiteit Brussel
Pardo, *et al*. (2018) [33]	56	Chronic low back pain	PNPE＋TE	Total intervention period: 3 months EG: 2 sessions of PNPE (30 to 50 minutes), TE (daily) CG: TE (daily)	TE	Kinesiophobia : TSK Pain: NPRS	Combining PNE with TE resulted in significantly better results for participants with CLBP, with a large effect size, compared with TE alone	Spain, Alcala' University
Ryan, *et al*. (2010) [34]	34	Chronic low back pain	PBE＋EX	Total intervention period: immediately EG: 1 sessions of PBE (2 hours 30 minutes), EX (1 day/week, 30-55 minutes) CG: 1 sessions of PBE (2 hours 30 minutes)	PBE	Kinesiophobia : TSK Pain: NPRS	In the short term, pain biology education alone was more effective for pain and pain self-efficacy than a combination of pain biology education and group exercise classes	UK, Glasgow Caledonian University

Table 1. Continued

Study	Sample size	Participants	Interventions	Therapeutic intensity	Control	Outcome measures	Authors conclusions	Conuntry, setting
Saracoglu *et al.* (2020) [35]	57	Chronic low back pain	PNE+MT+HEP	Total intervention period: 4 weeks EG: MT (2 day/week, 30 minutes), PNE (each week, 40-45 minutes), HEP (3 day/week, 10 repetitions) CG: MT (2 day/week, 30 minutes), HEP (3 day/week, 10 repetitions)	MT+HEP	Kinesiophobia: TSK Pain: NPRS	Multimodal treatment program combining PNE, MT, and HEP is an effective method for improving back performance and reducing pain, disability, and kinesiophobia in the short (4 weeks) and midterm (12 weeks)	Turkey, Kutahya Health Sciences University Hospital

AME: activity management education, BNE: back and neck education, CG: control group, CLBP: chronic low back pain, CTMCT: cognition-targeted motor control training, DN: dry needling, EG: experimental group, EX: exercise, FM: fibromyalgia, HEP: home exercise therapy, NPRS: numeric pain rating scale, MT: manual therapy, PBE: pain biology education, PCE: pain-contingent exercise, PCS: pain catastrophizing scale, PDI: pain disability index, PNE: pain neuroscience education, PNPE: pain neurophysiology education, PPE: pain physiology education, PPT: pressure pain threshold, PSE: pacing and self-management education, RE: relaxation education, TCE: time-contingent exercise, TE: therapeutic exercise, TrPDN: trigger point dry needling, TSK: tempa scale, VAS: visual analog scale.

Discussion

This review was performed to confirm the effects of PNE on kinesiophobia and pain in persons with chronic pain. It

was found that PNE alone was more effective when combined with trigger point dry needling and manual therapy [28,36]. In addition, regardless of therapeutic intensity, a single session alone showed significant improvement [30,35], and indirect online education rather than direct education also showed significant improvement [29,34].

In patients with chronic pain, the function is affected by kinesiophobia and fear of pain in a persistant pain sequence even after treatment. Also, it can be said that the influence of the biopsychosocial focus was revealed rather than the biomedical focus, which was explained as part of educational treatment until recently. Expletively, it is a new approach to manage chronic pain in rehabilitation and clinical, and could be included in telerehabilitation tailored to COVID-19. In relation to telerehabilitation, studies that observe the effects through distance education, such as PNE through Youtube, is gradually in progress [31].

This review was conducted to determine the effects of PNE on kinesiophobia and pain compared to general interventions in chronic pain. The review did not take into account the type, intensity, or duration of the PNE protocol. In addition, only the results measured post intervention were used. In further studies, sub-analysis including similarity to combined interventions and classification according to follow-up period is considered necessary.

The implications of this study can be explained by dividing into qualitative and quantitative factors. Through the review of qualitative components, PNE should consider the method of delivery and the importance of the communicator because it is important to intervene with professional knowledge. Also, the implications through the quantitative evaluation were that PNE was effective in chronic pain by comparing it with other interventions so it could be combined with qualitative components to provide a more useful method.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

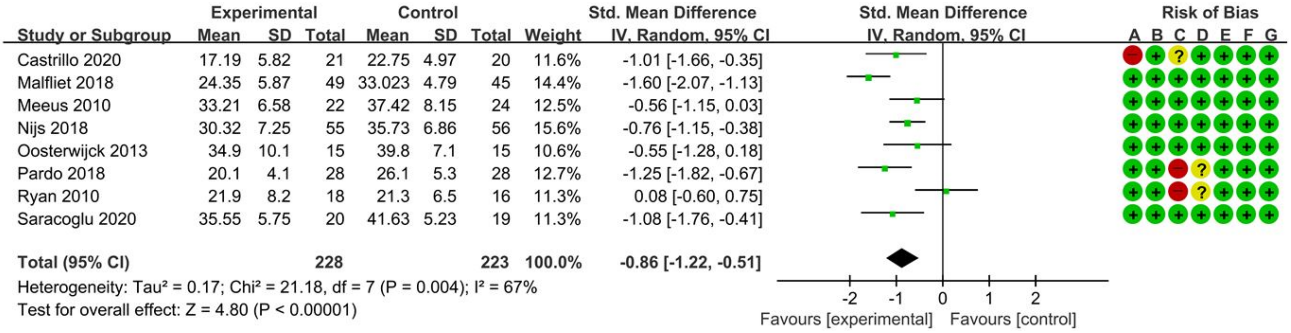

Figure 3. Forest plot of pain neuroscience education versus control in the post-intervention; primary outcome kinesiophobia. Std: standardized, CI: confidence interval, IV: weighted mean difference, A: random sequence generation, B: allocation concealment, C: blinding of participants and personnel, D: blinding of outcome assessment, E: incomplete outcome data, F: selective reporting.

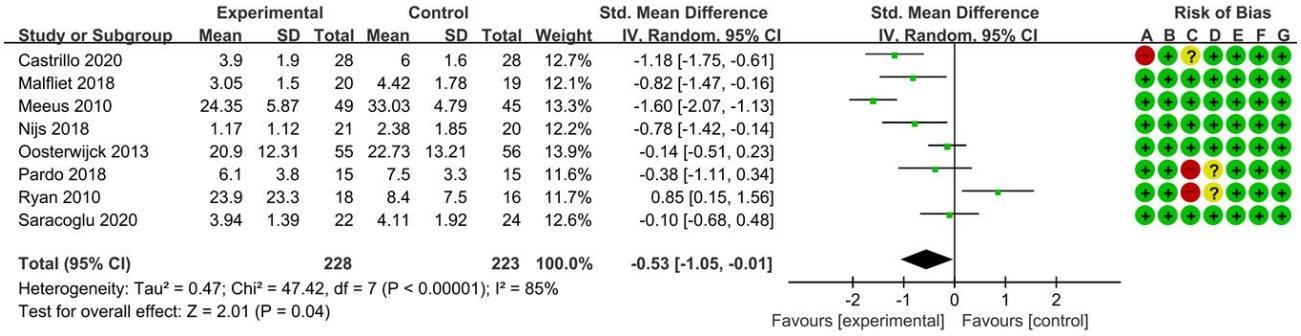

Figure 4. Forest plot of pain neuroscience education versus control in the post-intervention; secondary outcome pain. Std: standardized, CI: confidence interval, IV: weighted mean difference, A: random sequence generation, B: allocation concealment, C: blinding of participants and personnel, D: blinding of outcome assessment, E: incomplete outcome data, F: selective reporting.

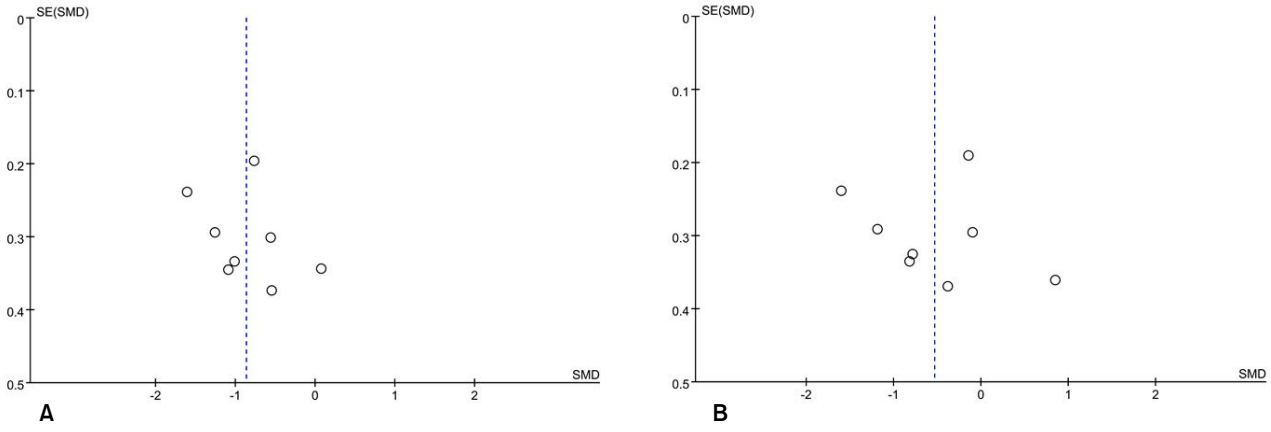

Figure 5. Funnel plots of standard error by standardized mean difference. (A) Kinesiophobia, (B) pain. SE: standard error, SMD: standardized mean difference.

References

1. Ploumis A, Gkiatas I. Musculoskeletal pain management. In: Paschos N, Bentley G, editors. General orthopaedics and basic science. Cham: Springer; 2019. p. 105-10.
2. Main CJ, Spanswick CC. Pain management: an interdisciplinary approach. Edinburgh: Churchill Livingstone; 2000.
3. Ekman EF, Koman LA. Acute pain following musculoskeletal injuries and orthopaedic surgery: mechanisms and management. Instr Course Lect 2005;54:21-33.
4. Baliki MN, Geha PY, Apkarian AV, Chialvo DR. Beyond feeling: chronic pain hurts the brain, disrupting the default-mode net-

work dynamics. J Neurosci 2008;28:1398-403.
5. Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull 1999;125:356-66.
6. Lundberg M, Larsson M, Ostlund H, Styf J. Kinesiophobia among patients with musculoskeletal pain in primary healthcare. J Rehabil Med 2006;38:37-43.
7. Brox JI, Storheim K, Grotle M, Tveito TH, Indahl A, Eriksen HR. Systematic review of back schools, brief education, and fear-avoidance training for chronic low back pain. Spine J 2008; 8:948-58.
8. Engers A, Jellema P, Wensing M, van der Windt DA, Grol R, van Tulder MW. Individual patient education for low back pain. Cochrane Database Syst Rev 2008;2008:CD004057.
9. Heymans MW, van Tulder MW, Esmail R, Bombardier C, Koes BW. Back schools for nonspecific low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine 2005;30:2153-63.
10. Liddle SD, Baxter GD, Gracey JH. Chronic low back pain: patients' experiences, opinions and expectations for clinical management. Disabil Rehabil 2007;29:1899-909.
11. Maier-Riehle B, Härter M. The effects of back schools--a meta-analysis. Int J Rehabil Res 2001;24:199-206.
12. Moseley GL. A pain neuromatrix approach to patients with chronic pain. Man Ther 2003;8:130-40.
13. Moseley GL. Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. Eur J Pain 2004;8:39-45.
14. Koes BW, van Tulder MW, van der Windt WM, Bouter LM. The efficacy of back schools: a review of randomized clinical trials. J Clin Epidemiol 1994;47:851-62.
15. Waddell G. The back pain revolution. 2nd ed. Edinburgh: Churchill Livingstone; 2004.
16. Nijs J, Roussel N, Paul van Wilgen C, Köke A, Smeets R. Thinking beyond muscles and joints: therapists' and patients' attitudes and beliefs regarding chronic musculoskeletal pain are key to applying effective treatment. Man Ther 2013;18:96-102.
17. Nijs J, Paul van Wilgen C, Van Oosterwijck J, van Ittersum M, Meeus M. How to explain central sensitization to patients with 'unexplained' chronic musculoskeletal pain: practice guidelines. Man Ther 2011;16:413-8.
18. Louw A, Puentedura EJ, Diener I, Peoples RR. Preoperative therapeutic neuroscience education for lumbar radiculopathy: a single-case fMRI report. Physiother Theory Pract 2015;31:496-508.
19. Zimney K, Louw A, Puentedura EJ. Use of Therapeutic Neuroscience Education to address psychosocial factors associated with acute low back pain: a case report. Physiother Theory Pract 2014;30:202-9.
20. Butler DS, Moseley GL. Explain pain. Adelaide: Noigroup Publications; 2003.
21. Moseley GL, Butler DS. Fifteen years of explaining pain: the past, present, and future. J Pain 2015;16:807-13.
22. Louw A, Diener I, Butler DS, Puentedura EJ. The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain. Arch Phys Med Rehabil 2011;92:2041-56.
23. Moseley GL. Reconceptualising pain according to modern pain science. Phys Ther Rev 2007;12:169-78.
24. Moseley GL, Nicholas MK, Hodges PW. A randomized controlled trial of intensive neurophysiology education in chronic low back pain. Clin J Pain 2004;20:324-30.
25. Nijs J, Lluch Girbés E, Lundberg M, Malfliet A, Sterling M. Exercise therapy for chronic musculoskeletal pain: innovation by altering pain memories. Man Ther 2015;20:216-20.
26. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane handbook for systematic reviews of interventions. 2nd ed. Hoboken (NJ): Wiley-Blackwell; 2019.
27. Oh PJ, Kim YL. Effectiveness of non-pharmacologic interventions in chemotherapy induced peripheral neuropathy: a systematic review and meta-analysis. J Korean Acad Nurs 2018;48: 123-42.
28. Saracoglu I, Arik MI, Afsar E, Gokpinar HH. The effectiveness of pain neuroscience education combined with manual therapy and home exercise for chronic low back pain: A single-blind randomized controlled trial. Physiother Theory Pract 2020. doi: 10.1080/09593985.2020.1809046. [Epub ahead of print]
29. Malfliet A, Kregel J, Meeus M, Roussel N, Danneels L, Cagnie B, et al. Blended-learning pain neuroscience education for people with chronic spinal pain: randomized controlled multicenter trial. Phys Ther 2018;98:357-68.
30. Ryan CG, Gray HG, Newton M, Granat MH. Pain biology education and exercise classes compared to pain biology education alone for individuals with chronic low back pain: a pilot randomised controlled trial. Man Ther 2010;15:382-7.
31. Heathcote LC, Pate JW, Park AL, Leake HB, Moseley GL, Kronman CA, et al. Pain neuroscience education on YouTube. PeerJ 2019;7:e6603.
32. Van Oosterwijck J, Meeus M, Paul L, De Schryver M, Pascal A, Lambrecht L, et al. Pain physiology education improves health status and endogenous pain inhibition in fibromyalgia: a double-blind randomized controlled trial. Clin J Pain 2013;29:873-82.
33. Bodes Pardo G, Lluch Girbés E, Roussel NA, Gallego Izquierdo T, Jiménez Penick V, Pecos Martín D. Pain neurophysiology education and therapeutic exercise for patients with chronic low back pain: a single-blind randomized controlled trial. Arch Phys Med Rehabil 2018;99:338-47.
34. Malfliet A, Kregel J, Coppieters I, De Pauw R, Meeus M, Roussel N, et al. Effect of pain neuroscience education combined with cognition-targeted motor control training on chronic spinal pain: a randomized clinical trial. JAMA Neurol 2018;75:808-17.
35. Meeus M, Nijs J, Van Oosterwijck J, Van Alsenoy V, Truijen S. Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: a double-blind randomized controlled trial. Arch Phys Med Rehabil 2010;91:1153-9.
36. Valiente-Castrillo P, Martín-Pintado-Zugasti A, Calvo-Lobo C, Beltran-Alacreu H, Fernández-Carnero J. Effects of pain neuroscience education and dry needling for the management of patients with chronic myofascial neck pain: a randomized clinical trial. Acupunct Med 2020. doi: 10.1177/0964528420920300. [Epub ahead of print]