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*Published in:*  
The Clinical Journal of Pain

*DOI:*  
[10.1097/AJP.0000000000000594](https://doi.org/10.1097/AJP.0000000000000594)

*Publication date:*  
2018

*Document version*  
Final published version

*Document license*  
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*Citation for pulished version (APA):*  
Tegner, H., Frederiksen, P., Esbensen, B. A., & Juhl, C. (2018). Neurophysiological Pain Education for Patients With Chronic Low Back Pain: A Systematic Review and Meta-Analysis. *The Clinical Journal of Pain*, 34(8), 778–786. <https://doi.org/10.1097/AJP.0000000000000594>

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# Neurophysiological Pain Education for Patients With Chronic Low Back Pain

## A Systematic Review and Meta-Analysis

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**Objective:** To evaluate the effect of neurophysiological pain education (NPE) for patients with chronic low back pain (CLBP).

**Methods:** A systematic search was performed in 6 electronic databases. Eligible randomized-controlled trials were those with at least 50 % of patients with CLBP and in which NPE was compared with no intervention or usual care. Methodological quality was assessed independently by 2 of the authors using the Cochrane Collaboration Risk of Bias Tool. The effect of NPE was summarized in a random effect meta-analysis for pain, disability, and behavioral attitudes. Effect was estimated as weighted mean difference (WMD) if outcomes were on the same scale or as standardized mean difference (SMD). The overall quality of evidence was evaluated according to GRADE guidelines.

**Results:** Seven randomized-controlled trial studies (6 low and 1 high quality) were included. Statistically significant differences in pain, in favor of NPE, were found after treatment, WMD = -1.03 (95% confidence interval [CI], -0.55 to -1.52), and after 3 months, WMD = -1.09 (95% CI, -2.17 to 0.00). Furthermore statistically significant lower disability was found in the NPE group after treatment, SMD = -0.47 (95% CI, -0.80 to -0.13) and after 3 months SMD = -0.38 (95% CI, -0.74 to -0.02). The difference in favor of NPE in reduction in Tampa Scale of Kinesiophobia was not statistically significant, WMD = -5.73 (95% CI, -13.60 to 2.14) and after 3 months WMD = -0.94 (95% CI, -6.28 to 4.40).

**Discussion:** There was moderate evidence supporting the hypothesis that NPE has a small to moderate effect on pain and low evidence

of a small to moderate effect on disability immediately after the intervention. NPE has a small to moderate effect on pain and disability at 3 months follow-up in patients with CLBP.

**Key Words:** education, neurophysiology, low back pain, systematic review

(*Clin J Pain* 2018;34:778–786)

Chronic low back pain (CLBP), defined as low back pain (LBP) lasting for >3 months, is a major cause of medical expenses, absenteeism, and disability.<sup>1,2</sup>

The treatment offered to patients with CLBP is largely dependent on the individual health care provider.<sup>3</sup> Over the past 15 years there has been an exponential increase in availability of different treatments such as spinal injections, physical therapies, surgical interventions, and pharmacological treatments. Only 8% to 15% of patients with CLBP have an identified pathoanatomic diagnosis, leaving most patients as having “nonspecific” CLBP.<sup>4,5</sup> Therefore health care providers are challenged in providing adequate treatment and information to patients with LBP.<sup>4,6</sup> Furthermore, pathoanatomic findings such as annular tears, fissures, facet joint arthrosis, degenerative disc disease, and disc bulges are not strong predictors of future LBP,<sup>7</sup> which emphasizes the limitation in explaining LBP on the basis of radiologic imaging. Factors such as depression, lifestyle factors, cognitive and physical behaviors, and stress are more predictive of future LBP episodes than are radiographic findings.<sup>7,8</sup>

Recent advances in neuroimaging can identify the extent of changes within the central nervous system due to chronic pain, and show how emotional and cognitive influences such as hypervigilance, catastrophizing, anxiety, and depression can all influence pain perception in individuals with chronic pain via a descending pain modulatory system.<sup>9</sup> This emphasizes that pain is a subjective experience also influenced by memories and emotional, pathologic, genetic, and cognitive factors.

Neurophysiological pain education (NPE) is a cognitive-behavioral intervention that provides education in pain neurophysiology to change maladaptive illness beliefs, to alter maladaptive pain cognition and to re-conceptualize beliefs about pain.<sup>10,11</sup> NPE has different formats ranging from intensive one-on-one, small group tutorial type sessions to large group seminars lasting up to three hours.<sup>12</sup> It has been performed as a single intervention or in combination with other treatment modalities.<sup>11</sup>

Three systematic reviews examined the effect of NPE.<sup>13–15</sup> One, published in 2011, examined NPE for patients with CLBP, it included only 2 studies, and they were of moderate quality; due to the sparseness of the data

Received for publication September 28, 2017; revised January 15, 2018; accepted January 30, 2018.

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Supported by Department of Occupational Therapy and Physiotherapy, Rigshospitalet Glostrup, Denmark and the former Nursing and Health Sciences Research Unit, Glostrup Hospital, Glostrup, Denmark. The authors declare no conflict of interest.

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Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.clinicalpain.com.

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DOI: 10.1097/AJP.0000000000000594

and the quality of the included studies the authors concluded very low evidence for an effect of NPE.<sup>13</sup>

Two other reviews published in 2011 and 2016, both by Louw et al,<sup>14,15</sup> examined NPE for patients with musculoskeletal pain. Both studies concluded that there was compelling evidence that an educational strategy addressing neurophysiology and neurobiology of pain can have a positive effect on pain, disability, catastrophizing, and physical performance in patients with musculoskeletal pain.

As most patients with CLBP do not receive a confirmed pathoanatomic diagnosis, and different cognitive approaches have shown effects, re-conceptualizing beliefs about pain is relevant for CLBP. Therefore a new systematic review was performed to analyze NPE for patients with CLBP including an analysis of subgroups of CLBP patients (addressing age, duration of LBP, education, and body mass index [BMI]). Furthermore in order to improve the effect of NPE in subgroups of patients with CLBP we investigated the effect of different types of NPE and the impact of intensity and duration.

## AIM

The aim of this systematic review was to evaluate the effect of neurophysiological pain education (NPE) for patients with CLBP, measured through pain, disability and behavioral attitudes. A second aim was to investigate the effect of different types of NPE in order to identify the effective type for different subgroups of CLBP patients.

The following comparisons were investigated: (1) NPE versus placebo, no treatment, waiting list, or other control interventions, (2) individual NPE versus NPE in groups and (3) NPE versus other kinds of nonpharmacological and pharmacological treatment.

## METHODS

### Types of Studies

Randomized-controlled trials (RCTs) were included.

### Types of Participants

Participants were included if they were older than 18 and had CLBP defined as back pain for  $\geq 3$  months. RCTs including patients with CLBP caused by red flag disorders (infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, spondylarthritits, fractures, cauda equine syndrome or paresis caused by intervertebral disc prolapse) were excluded. Studies were included if  $> 50\%$  of the participants had CLBP.

### Types of Interventions

Verbal education interventions with the core objective of explaining to patients with CLBP the key biological concepts that underpin pain were addressed. Studies were included if they evaluated group or individual education, and investigated NPE either as the only intervention or as part of an intervention program.

### Types of Outcome Measures

Eligible studies measured at least 1 of the following outcomes: pain, disability, ability to return to work, and outcomes reflecting behavioral attitudes (fear-avoidance beliefs, kinesiophobia, anxiety, catastrophizing, and depression).

## Search Strategy for Identification of Studies

Eligible RCTs were identified by the following ways: (1) a computer-aided systematic search of the Cochrane Database of Controlled Trials (Central), Web of Science, Medline, Embase, PsycINFO, and Cinahl databases (see Appendix A, Supplemental Digital Content 1, <http://links.lww.com/CJP/A476> for Supplementary Material showing the search strategy); (2) references of relevant RCTs were checked to identify additional studies; and (3) searching for ongoing trials in ClinicalTrial.gov. No restrictions were set for the searches with respect to publication year, but studies in only English, Swedish, Norwegian, or Danish were included.

## Study Selection

Two reviewers (H.T. and P.F.) independently scrutinized titles and abstracts. Full text was obtained for articles judged eligible by at least 1 reviewer. The same reviewers independently judged eligibility of these full-text articles and consensus was reached by discussion.

## Risk of Bias Assessment

The risk of bias was independently assessed by the 2 review authors (H.T. and P.F.), using the Cochrane Collaboration Risk of Bias Tool evaluating the following domains: (1) sequence generation, (2) allocation concealment, (3) blinding of participants, personnel, and outcome assessors, (4) incomplete outcome data, (5) selective outcome reporting, and (6) other potential threats to validity not already identified.<sup>16</sup> Consensus on risk of bias assessment was reached by discussion between the 2 review authors or by including a third reviewer (C.J.).

## Data Extraction

Customized data-extraction forms were used to collect data on the study populations and the types of intervention, as well as quantitative data from the outcome measures. The following information was mandatory: authors, year of publication, and number of participants allocated to the NPE group and the control groups. Patient characteristics included age, sex, BMI, education, baseline pain, and duration of symptoms. Two reviewers (H.T. and P.F.) independently extracted final scores and SDs for the following domains: (1) pain intensity, (2) functional status, (3) overall improvement, (4) ability to return to work, and (5) behavioral/cognitive outcomes.

## Summary Measures

A meta-analysis using a random effects model was applied to trials with clinically homogeneous study populations, types of treatment, outcomes, and measurement instruments (pain, disability, and behavioral attitude). The effect in the individual studies was calculated as weighted mean difference (WMD) if all outcomes within a domain were estimated on the same scale or as the standardized mean difference (SMD), allowing pooling and comparison of the various outcomes assessed in individual trials. The SMD was estimated as the difference between the postintervention mean scores in the intervention and control groups divided by the pooled SD. The SD was estimated from the SE, the 95% confidence interval (95% CI), *P*-value, or other method recommended by the Cochrane Collaboration.<sup>16</sup> This estimate of the effect size has a slight bias, overestimating the effect size, and a correction factor was applied to convert the effect size to the Hedges *g*. The SMD was clinically interpreted as originally proposed by Cohen.<sup>17</sup> An SMD of 0.2 was considered small, 1 of 0.5 was considered moderate (and will be recognized as clinically important), and 1 of 0.8 will be considered

large.<sup>17</sup> The effect size measured as SMD on pain and physical function were transformed into a numerical rating scale (NRS) from 0 to 10 using the approach proposed by Bliddal and Christensen.<sup>18</sup>

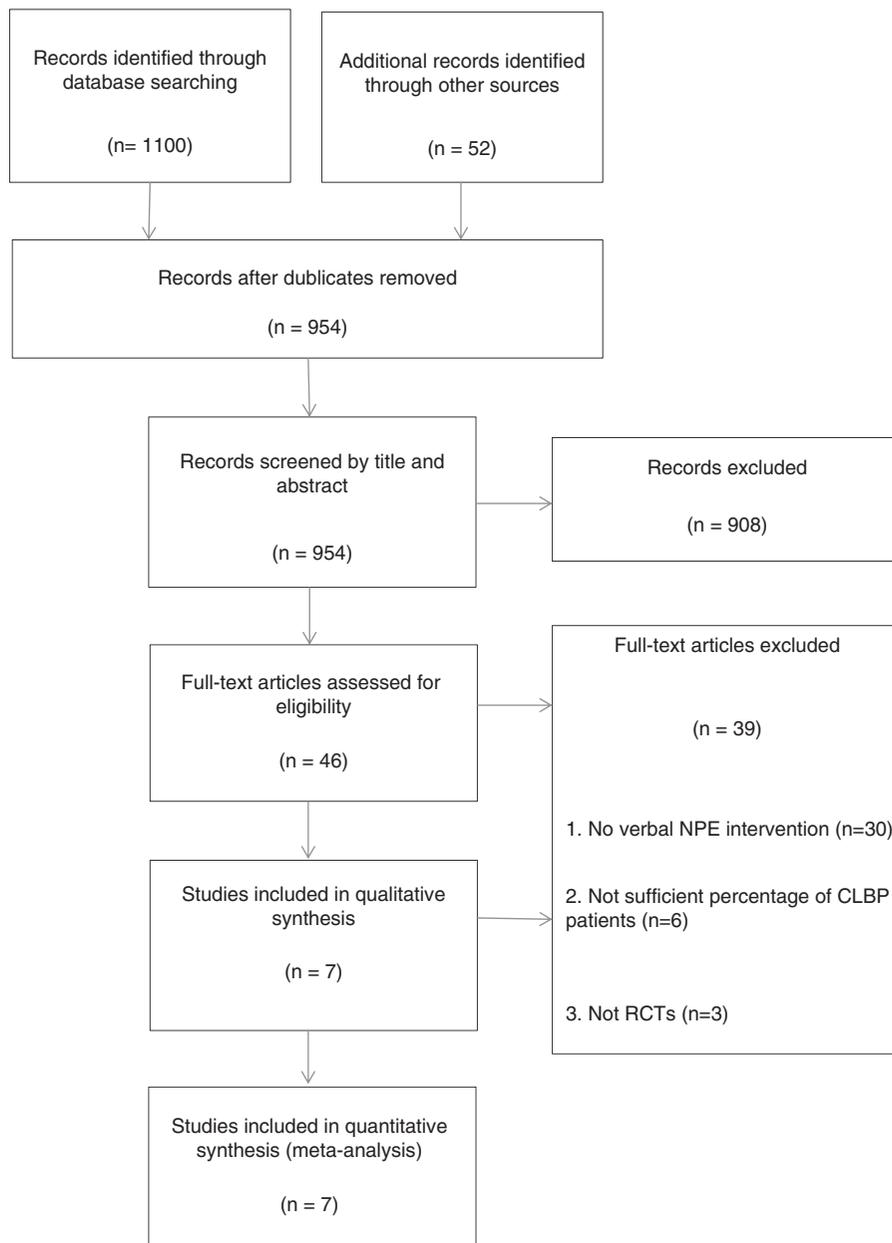
### Summary of Findings Table

The overall quality of evidence was evaluated according to the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) guidelines, judging the evidence based on the risk of bias, inconsistency, imprecision, indirectness, and publication bias.<sup>19</sup> The results were presented in a summary of findings (Table 2).

## RESULTS

### Literature Search and Study Selection

The literature search resulted in 1100 hits (Medline 74, Embase 529, Cinahl 38, Web of Science 175, PsycINFO 41, and Cochrane 243). Screening earlier reviews and references in articles resulted in identification of 52 additional references. After review of title and abstract, and removal of duplicates, 46 studies were identified as being potentially eligible of which 39 were excluded. Among the 39 excluded articles 30 did not use a verbal NPE intervention, 6 did not include mainly CLBP patients, and 3 were not RCTs. Hence, this review finally included 7 studies.<sup>20–26</sup> See flow diagram (Fig. 1).



**FIGURE 1.** Flow diagram. CLBP indicates chronic low back pain; NPE, neurophysiological pain education; RCT, randomized-controlled trial.

**TABLE 1.** Description of Included Studies

Studies	Setting and Sample	Intervention (s)	Comparator	Outcome	Overall Risk of Bias Judgment
Moseley <sup>22</sup>	N = 57; mean age: 43; female: 64%; duration of LBP (mo): 39 ± 18; baseline pain (SD): NRS 4.9 (1.8); RMDQ (SD): 12.4 (3.7); setting: physiotherapy clinic	Manual therapy, individualized trunk muscle training and one-on-one 1 h sessions in 4 wk of neurophysiological pain education	Medical advice by general practitioner, advised not to seek physiotherapy	Functional disability by RMDQ at baseline, just after treatment and 1 y later. Pain intensity by NRS	Low quality
Moseley <sup>20</sup>	N = 45; mean age: 40; female: 67%; duration of LBP (mo) (intervention group): 33 ± 11; baseline pain (SD): NRS 5.1 (1.6); RMDQ (SD): 12.0 (4.1); setting: physiotherapy clinic/ general practitioner	Two physiotherapy treatments per week for 4 wk, home-exercise program with trunk muscle training and individualized neurophysiological pain education	Two physiotherapy treatment per week for 4 wk, home-exercise program with trunk muscle training and neurophysiological pain education in groups	Functional disability on RMDQ at baseline, just after treatment and 1 y after. Pain intensity by NRS	Low quality
Moseley et al <sup>21</sup>	N = 58; mean age: 42; female: 57%; duration of LBP (intervention group): 29 ± 11; RMDQ (SD): 15.0 (4.0); setting: private rehabilitation clinics	3 h education session by physiotherapist with focus on pain neuroscience	3 h education session by physiotherapist with focus on anatomy of lower back, posture and endurance	Functional disability by RMDQ and secondary outcomes: pain attitudes and pain catastrophizing scale; baseline, 1 mo after treatment and 3 mo after treatment	Low quality
Pires et al <sup>11</sup>	N = 62; mean age: 51; female: 20%; duration of LBP (intervention group): 3-24 mo 20%, > 24 mo 80%; baseline pain (SD): NRS 4.3 (2.3); QBPDS (SD): 32.3 (13.9); setting: outpatient clinic	2 sessions of pain neurophysiological education session and there 12 sessions of aquatic exercise over 6 wk	12 sessions of aquatic exercise over 6 wk	Pain intensity on Visual Analog Scale and functional disability by QBPDS; secondary outcomes: Kinesiophobia by Tampa Scale of Kinesiophobia; baseline, 6 wk after treatment and 3 mo after treatment	High quality
Ryan et al <sup>24</sup>	N = 38; mean age: 46; female: 61%; duration of LBP (mo) (intervention group): 7.6 ± 7.0; baseline pain (SD): NRS 3.9 (2.6); RMDQ (SD): 10.8 (5.2); setting: 5 physiotherapy departments	Cognitive-behavioral therapy for 2 1/2 h including 1 h of biology pain education	Cognitive-behavioral therapy for 2 1/2 h including 1 h of biology pain education combined with fitness exercise classes: 6 classes for 6 wk	Pain intensity on Visual Analog Scale and functional disability by QBPDS; Secondary outcomes: Kinesiophobia by Tampa Scale of Kinesiophobia; baseline, 6 wk after treatment and 3 mo after treatment	Low quality
Télez-García et al <sup>25</sup>	N = 12; mean age: 36; female: 67%; duration of LBP (mo) (intervention group): 17 ± 9; baseline pain (SD): NRS 5.0 (2.1); RMDQ (SD): 10.3 (3.4); setting: physiotherapy clinic	Trigger point-dry needling 3 session in 3 wk combined with neuroscience education 30 min once per week for 2 wk	Trigger point-dry needling 3 session in 3 wk	Pain intensity by numerical Pain Rating Scale and functional disability by RMDQ and Ostwestry Disability Index; secondary outcomes: Kinesiophobia by Tampa Scale of Kinesiophobia and widespread pressure pain sensitivity; baseline and 1 wk after treatment	Low quality

(Continued)

TABLE 1. (continued)

Studies	Setting and Sample	Intervention (s)	Comparator	Outcome	Overall Risk of Bias Judgment
Wälti et al <sup>26</sup>	N = 28; mean age: 42; female: 9%; duration: > 3 mo LBP; baseline pain (SD): NRS 4.9 (1.6); RMDQ (SD): 10.2 (4.4); setting: health care center	Two sessions of physiotherapy per week over 8 wk. Home exercises guided by a web-based home training interface. This treatment was combined multimodal treatment consisting of education on the neurophysiology of pain, sensory retraining and motor retraining	Two sessions of physiotherapy per week during 8 wk. Home exercises guided by a web-based home training interface	Pain intensity by numerical Pain Rating Scale; secondary outcomes: functional disability by RMDQ, patient-specific function Scale and fear avoidance by fear avoidance beliefs questionnaire, movement control impairment, sick leave and analgesic intake; baseline and 3 mo after treatment	Low quality

LBP indicates low back pain; NRS, Numerical Rating Scale; QBPDS, Quebec Back Pain Disability Scale; RMDQ, Roland Morris Disability Questionnaire.

**Description of Included Studies**

For characteristics of included studies (Table 1). Description of included studies. Four studies compared NPE combined with other treatments (physiotherapy, cognitive-behavioral

therapy [CBT]) with other treatment alone.<sup>23-26</sup> One study compared NPE with endurance training combined with education in anatomy and posture.<sup>21</sup> One study compared a mixture of manual therapy, individualized trunk muscle training and

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data addressed (attrition bias)	Selective reporting (reporting bias) (primary outcomes)	Selective reporting (reporting bias) (secondary outcomes)	Other sources of bias
Moseley 2002	+	?	-	+	+	+	?	?	?
Moseley 2003	+	?	-	+	+	?	?	?	+
Moseley 2004	?	-	+	-	-	?	-	-	+
Pires 2015	+	+	-	+	+	+	+	+	+
Ryan 2010	?	+	-	+	+	+	+	+	-
Tellez Garcia 2015	+	+	-	+	+	+	+	+	-
Wälti 2015	+	+	-	?	?	?	?	?	-

FIGURE 2. Risk of bias summery. - indicates high risk; ?, uncertain; +, low risk.

NPE with advice at a general practitioner,<sup>22</sup> and 1 study compared group NPE with individualized NPE.<sup>20</sup>

### Risk of Bias in Included Studies

The final results of the risk of bias are shown in Figure 2. All studies were described as randomized; however, only 3 of them used a clearly described and adequate randomization procedure in combination with adequate concealment of treatment allocation.<sup>23,25,26</sup> It was not possible to blind participants but assessors were blinded to outcome data in 5 studies.<sup>20,22–25</sup> The risk of bias associated with selective reporting was low in 3 studies,<sup>23–25</sup> unclear in a further 3<sup>20,22,26</sup> and high in 1 study.<sup>21</sup> Generally, the studies were very small, and only 1 included a sample size calculation.<sup>23</sup>

### Effect of Intervention

See Appendix B, (Supplemental Digital Content 2, <http://links.lww.com/CJP/A477>) showing the meta-analysis results, forest plots.

### Pain

There were 5 studies (212 participants) reporting treatment effect of NPE on pain intensity on a 0 to 10 scale (Table 2). Analyses were performed on the original metric. The meta-analysis on pain showed statistically significant lower pain in the NPE group compared with the control group after treatment; WMD at  $-1.03$  (95% CI,  $-0.55$  to  $-1.52$ ) with very low heterogeneity ( $I^2 = 3.26\%$ ). The prediction interval, showing the interval for the potential effect of the treatment when applied in a new study, showed pain reduction between 0.25 and 1.82 on a 0 to 10 scale.

The effect at 3 months follow-up was measured in 3 studies ( $n = 116$ ) and showed similar results; WMD  $-1.09$  (95% CI,  $-2.17$  to  $0.00$ ) with low to moderate heterogeneity ( $I^2 = 43.1\%$ ). Only 2 studies had long-term follow-up at 1 year after the intervention and no meta-analyses were performed.<sup>20,22</sup>

### Disability

The effect of NPE on disability was measured in all 7 studies ( $n = 313$ ); the Roland Morris Disability Questionnaire (RMDQ) was used in 6 studies and the Quebec Back Pain Disability Scale (QBPDS) was used in the seventh (Table 2). There was statistically significant lower disability score in the NPE group after treatment SMD  $-0.47$  (95% CI,  $-0.80$  to  $-0.13$ ) with low heterogeneity ( $I^2 = 38.3\%$ ). Using the approach from Bliddal and Christensen<sup>18</sup> the included studies had a mean disability score of 13.75 (SD, 4.94) on a 0 to 23 scale; this effect corresponds to a difference of  $-1.00$  (95% CI,  $-1.72$  to  $-0.29$ ) on a 0 to 10 scale in favor of NPE.

The effect at 3 months follow-up was measured in 4 studies ( $n = 170$ ) showing a slightly lower effect size SMD  $-0.38$  (95% CI,  $-0.74$  to  $-0.02$ ) with low heterogeneity ( $I^2 = 24.1\%$ ), corresponding to a difference of  $-0.82$  (95% CI,  $-1.56$  to  $-0.05$ ) on a 0 to 10 scale in favor of NPE.

### Behavioral Attitudes

Four studies included outcomes measuring different behavioral attitudes: Fear Avoidance Belief Questionnaire (FABQ), Pain Catastrophizing Scale (PCS), Survey of Pain Attitudes (SOPA), and Tampa Scale of Kinesiophobia (TSK). As these outcomes reflect very different aspects of patients' attitudes towards movement and pain, results were not pooled in a meta-analysis.

However TSK was measured in 3 studies and the results from this subgroup of studies were combined.<sup>11,24,25</sup>

There was statistically nonsignificant lower TSK-score in the NPE group after treatment WMD  $-5.73$  (95% CI,  $-13.06$  to  $2.14$ ), with high heterogeneity ( $I^2 = 91.0\%$ ).

The effect at 3 months follow-up was measured on TSK in 2 studies<sup>11,24</sup> showing a nonsignificant lower WMD  $-0.94$  (95% CI,  $-6.28$  to  $4.40$ ) in favor of NPE, with substantial heterogeneity ( $I^2 = 62.1\%$ ).

Outcomes that reflect the overall improvement and the ability to return to work were not addressed in the included studies.

### Subgroup Analysis

There was a tendency towards a larger effect on both pain and disability when more focused and intensive NPE education was delivered (NPE education alone, individual education and education of longer duration and involving more sessions), but no significant differences between subgroups were found. However, the heterogeneity for the analysis of pain was very low and none of the covariates reduces the overall heterogeneity. Heterogeneity was larger, when analyzing disability outcomes and including covariates on both NPE intensity and delivery mode reduced heterogeneity indicating better effect in more intense and focused NPE intervention.

### The GRADE Approach

Using the GRADE approach, we found moderate quality evidence that NPE has a moderate effect on pain immediately after the intervention. The quality of evidence was downgraded with one due to risk of bias in the included studies. Furthermore, we found low quality of evidence that NPE has a moderate effect on pain at 3 months follow-up and on disability immediately after the intervention and at 3 months follow-up. The evidence was downgraded by 2 due to imprecision and risk of bias. There was only low to very low evidence on behavioral attitude (TSK) just after treatment and 3 months later (Table 2).

## DISCUSSION

The main result of this review was moderate quality evidence that NPE has an effect on pain relief for patients with CLBP just after intervention. The review found low quality of evidence that NPE has an effect on disability just after the intervention and on pain and disability at 3-month follow-up. For the TSK, there was a nonsignificant effect, with low to very low quality of evidence. Finally there was no difference between the effects of different types of NPE.

### Outcomes

It was not possible to investigate the role of baseline status and patient characteristics, such as age, sex, BMI, and education because of the lack of information from the included studies and low heterogeneity between trials.

NPE showed a low to moderate effect in reducing pain and disability and a small but nonsignificant effect in reducing behavioral outcomes. In the light of the complexity in treating patients with chronic pain, a mean reduction of  $\sim 1$  on a Visual Analog Scale (VAS) from 0 to 10 may be a positive result but also highlights the importance of seeing NPE as only a part of a complex biopsychosocial intervention for this group of patients.

These results are comparable to the effectiveness of different physical activity for adults with chronic pain evaluated in an overview of Cochrane Reviews. The overview found favorable but small-to-moderate effects in

TABLE 2. Summary of Findings

Quality Assessment						No. Patients		Effect (95% CI)	Quality	Importance
	No of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Neurophysiological Pain Education			
Pain (follow-up: median 4 wk) Pain measured on a VAS scale from 0-10 (10 worst) (5 studies)	Randomized trials	Serious*†	Not serious	Not serious	Not serious	106/212 (50.0%)	WMD -1.03 (-1.52 to -0.55)	⊕⊕⊕○ Moderate	Important	
Pain (follow-up: median 3 mo) Pain measured on a VAS scale from 0-10 (10 worst) (3 studies)	Randomized trials	Serious‡§	Not serious	Not serious	Serious	62/116 (53.4%)	WMD -1.09 (-2.17 to 0.00)	⊕⊕○○ Low	Important	
Disability (follow-up: median 4 wk) Disability measured on various different scales and transformed to NRS scale from 0-10 (10 worst) (6 studies)	Randomized trials	Serious*†	Not serious	Not serious	Serious	127/253 (50.2%)	WMD -1.00 (-1.72 to -0.29)	⊕⊕○○ Low	Important	
Disability (follow-up: median 3 mo) Disability measured on various different scales and transformed to NRS scale from 0-10 (10 worst) (4 studies)	Randomized trials	Serious*†	Not serious	Not serious	Serious	90/178 (50.6%)	WMD -0.82 (-1.56 to -0.05)	⊕⊕○○ Low	Important	
Behavioral attitude (Tampa Scale of Kinesiophobia) (follow-up: median 4 weeks) Behavioral attitude measured on Tampa Scale of Kinesiophobia (17-68) (68 worst) (3 studies)	Randomized trials	Serious*¶#	Serious**	Not serious	Serious	56/112 (50.0%)	WMD -5.73 (-13.60 to 2.14)	⊕○○○ Very low	Important	
Tampa Scale of Kinesiophobia (follow-up: median 3 mo) Behavioral attitude measured on Tampa Scale of Kinesiophobia (17-68) (68 worst) (2 studies)	Randomized trials	Serious*#	Not serious	Not serious	Serious	50/100 (50.0%)	WMD -0.94 (-6.28 to 4.40)	⊕⊕○○ Low	Important	

\*Selective reporting bias: no registered protocol, unclear in choice of reported results.

†Concealment bias: explanation of the concealment missing.

‡No blinding of outcome assessors.

§Other sources of bias: baseline difference between groups.

||Wide 95% CI.

¶Other sources of bias: high dropout.

#No blinding of assessor.

\*\*High heterogeneity.

CI indicates confidence interval; VAS, Visual Analog Scale; WMD, weighted mean difference.

reducing pain severity and improving physical function.<sup>27</sup> Furthermore, a Cochrane review by Henschke et al<sup>28</sup> found moderate effect on short-term pain relief of CBT for patients with CLBP, but found no effect on functional status compared with usual care.

Comparing the effect of NPE on pain with other kinds of intervention (eg, analgesics, exercise, and acupuncture) for patients with LBP the same picture appears. Most treatments have only a small effect on patients with LBP.<sup>29</sup> It could be argued that it is very difficult to change pain in patients with CLBP, and other outcomes should be considered as primary ones. However, our meta-analyses relating to disability and behavioral attitude do not produce better results.

### Strength and Limitations

This review shows improved data collection and analysis compared with previous ones.<sup>13–15</sup> Applying the GRADE approach, which considers limitations in the trials as well as inconsistency, imprecision, and indirectness, a change in judgment of the strength of evidence, has been made.

In total, 7 RCTs were included in this systematic review. However, the total sample size was small and there was imprecision in the estimates. Therefore the overall evidence was downgraded. Furthermore, downgrading was necessary due to risk of bias, mainly seen by selective reporting and lack of adequate concealment procedures.

Identifying only 7 RCTs, and most of them of low quality, was unexpected because of the importance and popularity of the area. It could be argued that the inclusion criteria were too strict and the search in databases not sufficient. However, our review gave the same picture as an earlier one<sup>13</sup> with regard to the effect of NPE on patients with CLBP. In this review we expanded the inclusion criteria to include studies in which only 50% of the included participants had CLBP. However, this did not result in more studies.

The study population was surprisingly homogeneous with regard to age, sex, and time lived with LBP but information such as education, social status, or BMI was not sufficiently reported in most studies. It was thus not possible to perform subgroup analyses on the patient characteristics. It is important to emphasize that the included patients in this review had quite low baseline pain and disability compared with CLBP patients seen in hospital settings. Helping those who are more disabled, distressed, or medication-dependent is much more challenging, and it would be interesting to see if a more disabled group of patients led to similar conclusions.

Most of the included studies used NPE as a supplement to another intervention and compared with intervention alone. Simply by adding NPE to an already existing active intervention the results indicate that it is possible to decrease pain and disability. Hence in this setting even a small relative effect on pain and disability is an interesting change in results.

The decision to restrict inclusion to studies in English, Swedish, Norwegian, or Danish can be a limitation; however, we found no published RCTs in NPE for CLBP in any language other than English.

We may have missed relevant RCTs including NPE as a part of an intervention, as NPE is described differently and it is challenging to differentiate between NPE and education in anatomy of the back or CBT if the intervention was not sufficiently described.

In the included studies it was possible to make a meta-analysis of outcomes (pain and disability) only just after the intervention and at 3-month follow-up.

Finally pooling data from studies with judged differences in quality may be a problem. When more high-quality studies, with larger sample sizes, are published, an updated meta-analysis would be appropriate.

### Clinical Implications

The NPE intervention may be useful in a clinical context as it is simple to combine it with other interventions, it requires no equipment and has no side effects for the patient. Furthermore, verbal NPE makes it possible to be patient-specific and condition-specific and to answer urgent questions. In most studies included in this review NPE was given as a supplement only to other interventions. It is interesting that a simple supplement with no side effects can produce a small but significant change in pain and disability.

There was a tendency towards a larger effect on both pain and disability when the NPE was more intensive. For example individual sessions and longer duration education seem to be more effective. This means that the therapist can argue for educating patients in one-on-one sessions in order to achieve the best effect. Considering the individual and complex processing of pain, it is not surprising that one-on-one educational sessions produced superior results.<sup>30,31</sup>

In a clinical setting time consuming and expensive interventions is a challenge, but considering the huge health care cost of CLBP, it could be relevant to evaluate the cost-effectiveness of NPE offered to patients with CLBP.

An easier and cheaper education style is video, booklets, and pamphlets. A study by Gallagher et al<sup>32</sup> found that written material that explains key biological concepts of pain increases knowledge of pain biology and decreases catastrophic thoughts. A limitation of our review is that it includes only verbal NPE.

Even though NPE seems simple to implement in the clinic, how clinicians understand and teach pain neuroscience is an important problem. Pain neuroscience is complex and even today not fully understood. It is important that clinicians who teach pain neuroscience have a good understanding of the theory behind pain neuroscience.<sup>31,33</sup> Furthermore they should have caring, insightful, and pedagogical skills so that individual patients get the most benefit from clinicians training and understanding

### CONCLUSIONS

There was moderate evidence supporting the conclusion that, just after the intervention, NPE has a small to moderate effect on pain for CLBP patients. There was low evidence of small to moderate effect on disability just after the intervention and of small to moderate effect of pain and disability at 3-month follow-up. It was not possible to make firm conclusions on the superiority of any of the types of NPE for CLBP patients, but there was a tendency towards a larger effect when more focused and intensive NPE education was delivered.

Larger studies, and those with longer follow-up periods, are needed to investigate the benefits of NPE for CLBP patients. Furthermore, studies are needed for further interpretation of the biology and physiology of pain, and how pain should be communicated to the right group of patients.

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