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REVIEW

The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature

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ABSTRACT

Objective: Systematic review of randomized control trials (RCTs) for the effectiveness of pain neuroscience education (PNE) on pain, function, disability, psychosocial factors, movement, and healthcare utilization in individuals with chronic musculoskeletal (MSK) pain. **Data Sources:** Systematic searches were conducted on 11 databases. Secondary searching (PEARLing) was undertaken, whereby reference lists of the selected articles were reviewed for additional references not identified in the primary search. **Study Selection:** All experimental RCTs evaluating the effect of PNE on chronic MSK pain were considered for inclusion. **Additional Limitations:** Studies published in English, published within the last 20 years, and patients older than 18 years. No limitations were set on specific outcome measures. **Data Extraction:** Data were extracted using the participants, interventions, comparison, and outcomes (PICO) approach. **Data Synthesis:** Study quality of the 13 RCTs used in this review was assessed by 2 reviewers using the PEDro scale. Narrative summary of results is provided for each study in relation to outcomes measurements and effectiveness. **Conclusions:** Current evidence supports the use of PNE for chronic MSK disorders in reducing pain and improving patient knowledge of pain, improving function and lowering disability, reducing psychosocial factors, enhancing movement, and minimizing healthcare utilization.

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KEYWORDS

Chronic pain; explain pain;
pain neuroscience
education; therapeutic
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Introduction

Pain is a normal human experience and the inability to experience pain provides a significant risk to survival for any human being (Gifford, 2014; Moseley, 2003a; Moseley, 2007). Living in pain though is not a normal human experience and a powerful motivating force to seek help (Bernard and Wright, 2004; Louw, Louw, and Crous, 2009; Mortimer et al., 2003). One treatment strategy aimed at helping ease pain and often the associated suffering and disability is patient education (Brox et al., 2008; Engers et al., 2008; Heymans et al., 2005; Liddle, Gracey, and Baxter, 2007). Traditional musculoskeletal (MSK) education models have focused heavily on biomedical education focusing on anatomy, biomechanics, and pathoanatomy (Brox et al., 2008; Maier-Riehle and Härter, 2001; Moseley, 2003a, 2004). In these educational models clinicians aim to explain a pain experience to patients from a tissue perspective, be it contrasting healthy (anatomy) and injured tissues (pathoanatomy) or highlighting a mechanical deviance from normal expected patterns of movement (biomechanics) or a disease state such as degenerative changes (pathoanatomy) (Haldeman, 1990; Louw and Butler,

2011). Although these models may have clinical value in more acute phases of injury, surgical, or disease states, they lack the ability to explain complex issues associated with pain, including peripheral and central sensitization, facilitation and inhibition, neuroplasticity, immune and endocrine changes, and more, all of which have been implicated in more complex and persistent pain states (Gifford, 2014; Moseley, 2003a; Nijs et al., 2013; Woolf, 2007). Furthermore, these biomedical educational models have not only shown limited efficacy in alleviating pain and disability (Brox et al., 2008; Koes, van Tulder, van der Windt, and Bouter, 1994; Maier-Riehle and Härter, 2001; Waddell, 2004) but may even increase patient fears, anxiety, and stress, thus negatively impacted their intended outcomes (Hirsch and Liebert, 1998; Maier-Riehle and Härter, 2001; Nachemson, 1992; Poiraudau et al., 2006).

In lieu of the limited efficacy of traditional education to alleviate pain and disability, especially in persistent pain, a new model was needed and proposed (Butler and Moseley, 2003; Gifford, 1998; Gifford, 2014; Gifford and Butler, 1997; Gifford and Muncney, 1999; Moseley and Butler, 2015). People in pain are interested in learning

more about their pain (Louw, Louw, and Crous, 2009; Louw, Diener, Butler, and Puentedura, 2013; Moseley, 2003b; Rönnberg et al., 2007). This educational model of teaching people about pain biology and physiology is called therapeutic neuroscience education (Louw, Puentedura, Diener, and Peoples 2015; Zimney, Louw, and Puentedura, 2014), explain pain (Butler and Moseley, 2003; Moseley and Butler, 2015), and pain neuroscience education (PNE) (Nijs et al., 2011, 2013). PNE aims to explain to patients the biological and physiological processes involved in a pain experience and, more importantly, defocus the issues associated with the anatomical structures (Louw, Diener, Butler, and Puentedura, 2011; Moseley, 2007; Moseley, Nicholas, and Hodges, 2004; Nijs et al., 2011, 2013). Following early calls for the further study and clinical application of PNE (Gifford, 1998; Gifford and Butler, 1997) and the first conference presentation of explaining pain to patients (Gifford and Muncey, 1999), scientists used an evidence-based platform to further investigate PNE. Subsequently, various randomized controlled trials (RCT) and two systematic reviews explored the efficacy of PNE (Clarke, Ryan, and Martin, 2011; Louw, Diener, Butler, and Puentedura, 2011; Meeus et al., 2010; Moseley, 2002; Moseley, Nicholas, and Hodges, 2004; Ryan, Gray, Newton, and Granat, 2010). At the end of 2011, the systematic review of Louw, Diener, Butler, and Puentedura (2011) demonstrated for MSK pain, TNE provides compelling evidence in reducing pain, disability, pain catastrophization, and limited physical movement.

The review by Louw, Diener, Butler, and Puentedura (2011) included eight studies (Meeus et al., 2010; Moseley, 2002, 2003b, 2003c, 2004; Moseley, Nicholas, and Hodges, 2004; Ryan, Gray, Newton, and Granat, 2010; Van Oosterwijck et al., 2011), ranging in date from 2002 (Moseley, 2002) to 2011 (Van Oosterwijck et al., 2011). Since the publication of the last systematic review, various studies utilizing PNE have been published (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puentedura, 2014; Robinson and King, 2011; Van Ittersum, van Wilgen, Groothoff, and Van der Schans, 2011). This growth of additional PNE studies, along with the reflection by Moseley and Butler (2015) on 15 years of teaching people about pain begs the question if the increased research activity in PNE has resulted in any increased evidence for this educational approach? The original review was also handicapped in assessing efficacy by including lower level papers and the inability to evaluate methodologically each study in comparative fashion. The goal of this systematic review is to update and explore the efficacy of PNE as a treatment approach for people suffering MSK pain.

Methods

In line with the goal of the updated systematic review, the authors used the same methodology reported by Louw, Diener, Butler, and Puentedura (2011) as a means to add to and thus combine the cumulative evidence for PNE. The end result would be an expansion of the research results ranging from 2002 (Moseley, 2002) to the present. Additionally, the new review only included RCTs.

Search strategy

An electronic search was performed between June 2015 and August 2015, covering the last 14 years (2002–2015) from the following databases: Biomed Central, BMJ.com, CINAHL, the Cochrane Library, NLM Central Gateway, OVID, ProQuest (Digital Dissertations), PsycInfo, PubMed/Medline, ScienceDirect, and Web of Science. Each database has its own indexing terms and functions, and therefore different search strategies were developed for each database by the authors. The main search items were education, neuroscience, neurobiology, neurophysiology, pain, pain education, pain science, and therapeutic. In PubMed, medical subject headings (MeSH) terms were used where possible, with Boolean operators. The search strategies for remaining databases included synonyms of the main search items. Secondary searching (PEARLing) was undertaken, whereby reference lists of the selected articles were reviewed for additional references not identified in the primary search. The titles and abstracts of all the identified literature were screened by one primary reviewer using the inclusion criteria below. The full text of all potentially relevant articles were retrieved and screened by two reviewers using the same criteria, in order to determine the eligibility of the paper for inclusion in the review.

Inclusion criteria

All titles and abstracts were read to identify relevant papers. Papers were included in this systematic review if they met the inclusion criteria listed in Table 1. Given the heterogeneous nature of the original systematic review's outcome measures, no parameters were set on the exact measurement tools used to assess the effect of PNE on patients suffering from MSK pain. When there was uncertainty regarding the eligibility of the paper from the abstract, the full text version of the paper was retrieved and evaluated against the inclusion criteria. The full text version of all papers that met the inclusion criteria were retrieved for quality assessment and data extraction.

Table 1. Inclusion criteria used in the systematic review.

Criterion	Justification
English language	Search reviewers' primary language is English, and major journals in the subject area are published in English.
1999–2015	First study found was published in 2002.
Humans older than 18 years	Increase homogeneity of participants between studies as educational needs for infants, children, and adolescents.
MSK pain	Increase homogeneity of participants being treated with educational strategies incorporating PNE.
RCTs	Utilization of Level 1 evidence according to Centre for Evidence-based Medicine.
PNE	Increase homogeneity on type of educational intervention.
Outcomes: pain, function, psychosocial factors, movement, healthcare utilization	These are primary outcome measurements performed in the literature regarding individuals with MSK pain. No limitation was set on specific measurement tools utilized to examine effect on outcomes in these areas.

Quality assessment

Critical appraisal of each included study was conducted by determining the level of evidence on the Australian National Health and Medical Research Council (NHMRC) Hierarchy of Evidence (National Health and Medical Research Council, 1999). This provides a broad indication of bias based on study design. Studies higher on the hierarchy potentially contain less bias than those that are lower on the hierarchy. Given the increased activity in the field of PNE, study designs other than RCT were excluded in this review because of the lower level of evidence they provide.

Methodological quality of the design and reporting of each study was assessed against the PEDro scale (Elkins et al., 2010). The PEDro scale has become widely used to rate physical therapy interventions and has been shown to have reliability and a valid measure of methodological quality of clinical trials (de Morton, 2009; Maher et al., 2003). A high-quality study was defined by the authors as scoring positive on a minimum of 50% (5/10) of the items. Each reviewer conducted an independent evaluation and PEDro scoring of the studies in the review. The Physiotherapy Evidence Database was cross-referenced for any article already having a confirmed review, and the confirm score was used if present. If differences were found between reviewers, a discussion was held to attempt consensus. Any differences that could not be agreed upon were to be evaluated by a third reviewer (E. J. Puenteadura) to come to a final judgement among all reviewers. No disagreements in PEDro scoring occurred during assessment of the articles.

Outcome assessment

Due to the heterogeneous nature of the original systematic review's outcome measures and to determine the possible influence of PNE for MSK pain, results were posted in narrative form and outcomes were defined as "positive" (experimental group obtained a significantly greater improvement than the control group); "neutral" (there were no statistically significant differences

between the groups); or "negative" (the control group obtained a significant greater improvement than the experimental group). An alpha of $p < 0.05$ was used to define a significant outcome measure. This method, used in previous systematic reviews, demonstrated four levels of scientific evidence on the quality and the outcome of the trials: (1) strong evidence: multiple, relevant, high-quality RCTs with generally consistent outcomes; (2) moderate evidence: one relevant, high-quality RCT AND one or more relevant, low-quality RCTs with generally consistent outcomes; (3) limited evidence: one relevant, high-quality RCT OR multiple relevant low-quality RCTs with generally consistent outcomes; and (4) inconclusive evidence: only one relevant, low-quality RCT, no relevant RCTs or randomized trials with inconsistent outcomes (Ezzo et al., 2000; Fernández-de-las-Peñas et al., 2006).

A study was considered "relevant" when at least one of the outcome measures concerned pain or disability. For being "generally consistent," at least 75% of the trials that analyzed the same PNE had to have the same result (positive, neutral, or negative).

Data extraction

Data were extracted by the authors using the PICO approach: *Participants*: diagnosis treated, age, sex, duration of the symptoms, type of referral source, and diagnostic criteria; *Interventions*: type, intensity, duration, educational tools/props, in combination or stand-alone physical therapy; *Comparison*: to another treatment, no treatment, or "usual" treatment; and *Outcomes*: domains and tools used to measure the effects of the intervention. Although outcomes were not specified or limited, primary outcomes in line with "relevance" stated above included pain and/or function (Stone, 2002).

Data on the effectiveness of the PNE were also extracted for each study. To determine the effect of the PNE on each outcome measure, the mean and 95% confidence intervals (CI) for the between-group differences were calculated for RCTs and comparative studies, based on the results provided in each article

Table 2. Assessment of the quality of the randomized trials ($n = 13$) using the PEDro scale.

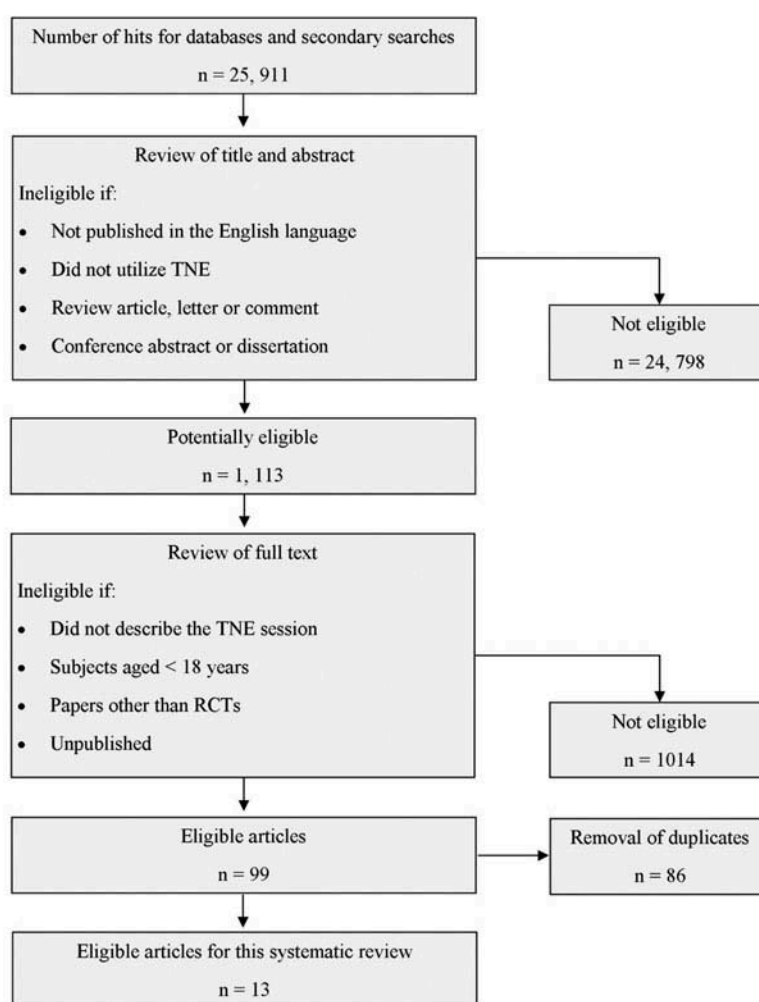
Criteria	1	2	3	4	5	6	7	8	9	10	11	Total
Moseley (2002)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10
Moseley (2003c)	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7/10
Moseley et al. (2004)	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	9/10
Ryan et al. (2010)	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	8/10
Meeus et al. (2010)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9/10
Vibe Fersum et al. (2013)	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	7/10
Gallagher et al. (2013)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10/10
Van Oosterwijck et al. (2013)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9/10
Ittersum et al. (2014)	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7/10
Louw et al. (2014)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9/10
Téllez-García et al. (2014)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10
Beltran-Alacreu et al. (2015)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10
Pires et al. (2015)	Y	Y	Y	Y	N	sN	Y	Y	Y	Y	Y	8/10

(Herbert, 2000). Moreover, the mean changes between pre- and post-treatment (and 95% CI) were calculated for the RCTs. Pain reduction of more than 20%, irrespective of the measurement tool used, was considered clinically worthwhile (Farrar et al., 2001; Ferreira et al., 2002). It was expected that there would be heterogeneity in participants, interventions, comparisons, and outcomes. Therefore, the results of the studies were synthesized in a narrative format.

Results

Search strategy yield

Initially, there were 25,911 hits gathered from databases and secondary searches for the search dates defined in the methods. After reviewing titles and abstracts, articles not meeting inclusion criteria were removed. Full text review left 99 eligible articles, after removal of duplicates there were 8 studies from the updated review

**Figure 1.** Retrieval and review process.

along with 5 eligible studies from previous review. This systematic review is based on these 13 published RCTs (Figure 1) (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Meeus et al., 2010; Moseley, 2002, 2003c; Moseley, Nicholas, and Hodges, 2004; Pires, Cruz, and Caeiro, 2015; Ryan, Gray, Newton, and Granat, 2010; Téllez-García et al., 2014; Van Oosterwijck et al., 2013; Vibe Fersum et al., 2013). The 13 RCTs comprised 734 patients.

Critical appraisal

Hierarchy of evidence

All 13 published papers were RCTs.

Methodological quality

The papers were reviewed against the PEDro scale. Agreement was obtained between reviewers and compared with the PEDro Database on each of the criteria in the PEDro scale with results listed in Table 2. All the studies scored a 6/10 or higher on the PEDro scale demonstrating good methodological quality. The blinding of subjects and those that administered the therapy were the most common criteria not met. This is partially due to the face-to-face delivery style of the intervention of PNE making it difficult to blind the person providing and receiving the PNE.

Educational content and delivery methods

Naming the intervention

The original systematic review (Louw, Diener, Butler, and Puenteadura, 2011) reported on the various names given to the educational intervention of explaining the biology of the pain experience to the patient with the aim at reducing pain and disability. The continued variation in the interventional name used by the various authors continues: (1) pain neurophysiology education (Pires, Cruz, and Caeiro, 2015); (2) therapeutic patient education (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015); (3) neuroscience education (Téllez-García et al., 2014); (4) pain physiology education (Meeus et al., 2010; Moseley, 2003c; Van Oosterwijck et al., 2013); (5) Pain neuroscience education (Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014); (6) neurophysiology education (Moseley, Nicholas, and Hodges, 2004); (7) pain biology education (Ryan, Gray, Newton, and Granat, 2010); and (8) neurophysiology of pain education (Moseley, 2002).

Two studies did not directly call the educational intervention a specific name but were a part of a book of metaphors and stories to help understand the biology of pain (Gallagher, McAuley, and Moseley, 2013) and the cognitive component of the education intervention (Vibe Fersum et al., 2013).

Patient characteristics

There were 734 subjects in the reviewed manuscripts with 398 of them receiving PNE (70% female). The mean age of subjects receiving educational intervention was 41.7 years (calculated from the means of the mean reported ages from each study). The youngest cohort had a mean age of 24 ± 10 years (Moseley, Nicholas, and Hodges, 2004) and the oldest cohort had 50.9 ± 6.2 years (Pires, Cruz, and Caeiro, 2015). PNE was utilized for multiple pain conditions: low back pain, chronic fatigue syndrome, fibromyalgia, lumbar radiculopathy awaiting lumbar surgery, and chronic neck pain.

Content of therapeutic neuroscience education

Specific content of each of the educational sessions can be found in Table 3. Summary of the PNE content were

- Neurophysiology of pain (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Meeus et al., 2010; Moseley, 2002, 2003c; Moseley, Nicholas, and Hodges, 2004; Pires, Cruz, and Caeiro, 2015; Ryan, Gray, Newton, and Granat, 2010; Van Oosterwijck et al., 2013; Vibe Fersum et al., 2013)
- No reference of anatomic or patho-anatomic models (Moseley, 2002, 2003c; Moseley, Nicholas, and Hodges, 2004; Téllez-García et al., 2014)
- No discussion of the emotional or behavioral aspects of pain (Moseley, 2003c; Moseley, Nicholas, and Hodges, 2004)
- Nociception and nociceptive pathways (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Moseley, 2003c; Moseley, Nicholas, and Hodges, 2004; Pires, Cruz, and Caeiro, 2015; Téllez-García et al., 2014)
- Synapses (Moseley, 2003c; Moseley, Nicholas, and Hodges, 2004)
- Action potentials (Louw, Diener, Landers, and Puenteadura, 2014)
- Spinal inhibition and facilitation (Gallagher, McAuley, and Moseley, 2013; Moseley, 2003c; Van Oosterwijck et al., 2013; Vibe Fersum et al., 2013)

Table 3. Participants, interventions, and outcomes in the reviewed studies.

Author	Participants		Interventions		Outcomes	
	Sample n	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Moseley (2002)	57	• LBP > 2 months • Women = 59% • Age (years): EG* 43 ± 7 and CG** 38 ± 7 • Duration of symptoms (months): EG = 39 ± 18 and CG 37 ± 12	Two physiotherapy sessions per week for 4 weeks; manual therapy including mobilization and manipulation, soft tissue massage, muscle and neural-mobilization techniques, but no electrophysical modalities; specific trunk stabilization program; maintain home exercises indefinitely; 1 hour educational session once a week for 4 weeks; one-on-one education format by an independent therapist; content = neurophysiology of pain with no reference to lumbar spine; accompanied by workbook with one page of revision material and three comprehensive exercises per day for 10 days	Ongoing medical care as advised by their general practitioner. No attendance of physiotherapy	• Numeric rating scale (NRS); meaningful difference set at 2 points • Roland Morris Disability Questionnaire (RMDQ); meaningful difference set at 4 points • Numbers needed to treat (NNT)	Baseline, 1 month after intervention and 1 year after intervention
Moseley (2003c)	41	• LBP > 3 months • Women = EG 67% and CG = 60% • Age (years): EG = 40 ± 7 years and CG = 42 ± 7 years • Duration of symptoms (months): EG = 33 ± 11 and CG = 30 ± 14	Individual 4 × 1 hour educational session on the physiology of pain and injury by a physiotherapist; additionally received two physiotherapy sessions per week for 4 weeks focusing on spinal stabilization exercises	Group session involved a single 4-hour session with a group of 7–10 patients provided by a physiotherapist; physiology of pain and injury; additionally received two physiotherapy sessions per week for 4 weeks focusing on spinal stabilization exercises	• Numeric rating scale (NRS) • Roland Morris Disability Questionnaire (RMDQ) • Numbers needed to treat (NNT)	Baseline, 1 month following “ongoing medical treatment” and 1 month and 2 months after educational and physiotherapy sessions

(Continued)

Table 3. (Continued).

Author	Participants		Interventions		Outcomes	
	n	Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments
Moseley et al. (2004)	58	• LBP > 6 months • Age (years): EG = 24 ± 10 and CG = 45 ± 6 • Duration of pain (months): EG = 18 ± 11 and CG = 20 ± 11	NA	Education session by a physiotherapist in one-to-one seminar format; session lasted 3 hours; diagrams and hypothetical examples used as teaching tools; at conclusion: workbook with 10 sections; patients asked to read one section per day and answer three questions on each session Neurophysiology Education No specific application was made to the lower back, or to emotional and behavioral patterns commonly associated with chronic pain such as catastrophic thought processes or fear avoidance The Nervous System Presentation of the basic structure of the nervous system, with a focus on the components of the nociception/pain pathways; this section included an outline of the functional significance of each component Synapses Presentation of how nerves "talk to each other," including the concept of "chemicals" (neurotransmitters), postsynaptic receptors, and a conceptual "volume knob" (postsynaptic excitation and inhibition), with a special focus on the "danger messenger nerve" (second order nociceptive neuron) Plasticity of the Nervous System The adaptability of the nervous system including: afferent and efferent pathways; the variable state of neural structures including normal state, peripheral, and central sensitization; receptor synthesis; axonal sprouting; the neural response to inactivity; and movement control	Education session by a physiotherapist in one-to-one seminar format; session lasted 3 hours; diagrams and hypothetical examples used as teaching tools; at conclusion: workbook with 10 sections; patients asked to read one section per day and answer three questions on each session Back Education Anatomy and physiology of the bones and joints of the lumbar spine; the intervertebral disc; the trunk and back muscles; normal spinal curves; posture and movements, including analysis of postures and activities according to intra-discal pressures and joint forces; lifting techniques and lifting loads; lifting aids and ergonomics advice; principles of stretching; and strength, endurance, and fitness training It did not include information about the nervous system, except for outlining the location and course of the spinal cord and the spinal nerve roots; it was similar to education material that has been researched elsewhere and the education components of back schools and functional restoration programs	• Roland Morris Disability Questionnaire (RMDQ) • Brief Survey of Pain Attitudes (revised) (SOPA (R)) • Pain Catastrophization Scale (PCS) • Straight Leg Raise (SLR) (inclinometer) • Forward Bending Range (Distance from longest finger to floor) • Abdominal Draw In Task (ADIT)

(Continued)

Table 3. (Continued).

Author	Participants		Interventions		Outcome instruments	Time of assessment	
	n	Sample characteristics	Diagnostic criteria	Treatment			
Ryan et al. (2010)	38	• LBP > 3 months • Education group • n = 18 • 11 women • Age (years) = 45.5 ± 9.5 • Duration of pain (months) = 13.7 ± 10.2 • Education and Exercise group • n = 20 • 14 women • Age (years) = 45.2 ± 11.9 • Duration of pain (months) = 7.6 ± 7	NA	Pain Biology Only A 2.5-hour pain biology education session Cognitive behavioral intervention focused on reshaping the participant's beliefs and attitudes about their back pain, attempting to decrease fear avoidance and harm beliefs, increase self-efficacy, and decrease avoidance behavior The biology of pain Verbal communication, prepared diagrams and free-hand drawings Additionally, all participants received "The Back Book"	Pain Biology and Exercise A 2.5- hour pain biology education session Cognitive behavioral intervention focused on reshaping the participant's beliefs and attitudes about their back pain, attempting to decrease fear avoidance and harm beliefs, increase self-efficacy, and decrease avoidance behavior The biology of pain Verbal communication, prepared diagrams and free-hand drawings Additionally, all participants received "The Back Book" Exercise component "Back to Fitness exercise classes"; six classes, one a week for 6 weeks; the classes involved circuit-based, graded, aerobic exercises with some core stability exercises The classes involved a warm-up phase (10 minutes), an aerobic phase (20–30 minutes), and a warm-down phase (10–15 minutes); the aerobic phase involved circuit-based exercise; for most exercises, there was an easy, moderate, and hard version, and the participant could choose which version to perform	• Roland Morris Disability Questionnaire (RMDQ) • Numeric Rating Scale (NRS) • Repeated sit-to-stand test • The 50-foot walk test • 5-minute walk test • Tampa Scale of Kinesiophobia (TSK-13) • Pain Self-Efficacy Questionnaire (PSEQ) • Step count (activPAL™ activity monitor)	Pre-treatment and 8 weeks later, 3 months later
Meeus et al. (2010)	46	• Chronic fatigue syndrome and wide-spread pain • Women: EG = 22 and CG = 18 • Age (years): EG = 38.3 ± 10.6 and CG = 42.3 ± 10.2	1994 Centers for Disease Control and Prevention criteria for CFS (Fukuda et al., 1994)	Pain Physiology One 30-minute interactive session Physiology of the nervous system in general and of the pain system in particular The theoretic information was illustrated with pictures and examples The objective of the education was to teach patients the function, mechanisms, and modulation of (chronic) pain, and so forth	Pacing and Self-Management One 30-minute interactive session; pacing and self-management education was provided to all participants in the control group; pacing is a strategy in which patients are encouraged to achieve an appropriate balance between activity and rest in order to avoid exacerbation and to set realistic goals for increasing activity; following this energy management strategy, patients should avoid activities at an intensity that exacerbates symptoms, or they should intersperse activities with periods of rest	• Neurophysiology of Pain Test • Pain Catastrophization Scale (PCS) • Pain Coping Inventory (PCI) • Tampa Scale of Kinesiophobia (TSK) • Pain Threshold Assessment (Fisher algometer)	Pre-treatment and immediately post-treatment

(Continued)

Table 3. (Continued).

Author	Participants			Interventions		Outcomes	
	n	Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Vibe Fersum et al. (2013)	94	• Non-specific low back pain >3 months • <i>Classification-based Cognitive Functional Therapy group (CB-CFT)</i> • 27 women and 24 men • Age (years): 41.0 ± 10.3 • <i>Manual Therapy and Exercise group (MT-EX)</i> • 21 women and 22 men • Age (years): 42.9 ± 12.5	NA	CB-CFT group A cognitive component based on findings from Orebro Musculoskeletal Pain Questionnaire Specific movement exercises as directed by the movement classification Targeted functional integration of activities in daily life Physical activity program tailored to the movement classification; initial session of 1 hour, follow-ups 30–45 minutes; patients seen weekly for first 2–3 weeks and then progressed to one session ever 2–3 weeks for 12-week intervention period; mean number of treatments 7.7 (range 4–16; SD 2.6)	MT-EX group Joint mobilization or manipulation techniques to spine or pelvis best on current manual therapy practice; general exercise of motor control exercises; motor control exercises involving isolated contractions of deep abdominal muscles in different functional positions; initial session, 1 hour, follow-ups, 30 minutes; mean number of treatments 8.0 (range 3–17; SD 2.9)	Primary outcome measures • Oswestry Disability Index (ODI) • Pain Intensity Numeric Rating Scale (PINRS) Secondary outcomes • Hopkins Symptoms Checklist (HSCL-25) • Fear-Avoidance Belief Questionnaire (FABQ) • Total lumbar spine range of motion • Patient satisfaction • Sick-leave days • Care-seeking	Baseline, post intervention and 12 months post-intervention

(Continued)

Table 3. (Continued).

Author	Participants			Interventions		Outcomes	
	n	Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Gallagher et al. (2013)	79	● Pain sufficient to disrupt activities of daily living for > than previous 3 months	NA	Booklet 1 Metaphors and stories to help understand the biology of pain Material from <i>Painful Yarns</i> : 80 pages divided in 11 sections Readability on Gunning Fog Index was 7	Booklet 2 Advice about managing pain; material drew from <i>The Back Book and Manage Your Pain</i> ; 80 pages divided in 11 sections; readability on Gunning Fog Index was 8	Primary outcome measures ● Pain Biology Questionnaire (PBQ) ● Pain Catastrophizing Scale (PCS) Secondary outcomes ● Pain (11-point numeric scale) ● Patient-Specific Functional Scale (PSFS)	Baseline, 3 weeks and 12 weeks Control group cross-over: 15 weeks and 24 weeks
		Metaphors group ● n = 40 (26 female) ● Age (years): 42 ± 11 ● Duration of pain (months): 25 ± 19					
		Advice group ● n = 39 (22 female) ● Age (years): 45 ± 11 ● Duration of pain (months): 31 ± 20					

(Continued)

Table 3. (Continued).

Author	Participants		Interventions		Outcomes	
	<i>n</i>	Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments
Van Oosterwijck et al. (2013)	30	• Fibromyalgia <i>Experimental group</i> • <i>n</i> = 15 (12 women) • Age (years): 45.8 ± 9.5 • Duration of onset (months): 156 ± 96 • <i>Control group</i> • <i>n</i> = 15 (14 female) • Age (years): 45.9 ± 11.5 • Duration of onset (months): 116 ± 46	1990 American College of Rheumatology (ACR) criteria	Experimental group received education on pain neurophysiology; received in oral format with written leaflet containing information and encouraged to take home and read several times; 1 week later second intervention delivered over the phone	Control group received education on pacing self-management techniques; received in oral format with written leaflet containing information and encouraged to take home and read several times; 1 week later second intervention delivered over the phone	<i>Primary outcome measures</i> • Spatial summation procedures (SSP) • Fibromyalgia Impact Questionnaire (FIQ) • Medical Outcomes Short Form 36 Health Status Survey (SF-36) • Pain Coping Inventory (PCI) • Pain • Catastrophizing Scale (PCS) • Pain Vigilance and Awareness Questionnaire (PVAQ) • Tampa Scale Kinesiophobia (TSK) • Neurophysiology of Pain Test <i>Secondary outcomes</i> • Pain Pressure Threshold

(Continued)

Table 3. (Continued).

Author	n	Participants		Interventions		Outcomes	
		Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Ittersum et al. (2014)	105	• Fibromyalgia <i>Pain Neuroscience Education group</i> <i>n</i> = 53 (50 female) • Age (years): 47.6 ± 9.1 • Illness duration (years): 8.5 • <i>Relaxation Education group</i> <i>n</i> = 52 (48 female) • Age (years): 45.8 ± 9.8 • Illness duration (years): 8.0	American College of Rheumatology (ACR) criteria	Pain Neuroscience Education received an educational booklet with written and illustrated information on pain physiology and the mechanisms of central sensitization; educational booklet explained structure and function of nervous system and difference between nociception and pain; central sensitization is introduced as hypersensitivity of the nervous system through metaphor; explained factors at onset and maintenance of central sensitization; three case examples used to explain how to use this information in daily life; booklet of 15 pages, and encouraged to read several times; received follow-up supporting telephone call 2 weeks post receiving information	Relaxation education group received written information on relaxation exercise and instructions on how to perform such exercises; Loeser's model of pain used to briefly explain physical and psychological factors with chronic pain; booklet 15 pages, and encouraged to read several times and apply information in daily life; received follow-up supporting telephone call 2 weeks post receiving information	Primary outcome measures • Fibromyalgia Impact Questionnaire (FIQ) Secondary outcomes • Revised Illness Perception Questionnaire for FM (IPQ-R-FM) • Pain Catastrophizing Scale (PCS) • Patient opinions about the booklet on six-point Likert scale	Baseline, 6 weeks, 6 months follow-up
Louw et al. (2014)	67	Patients with lumbar radiculopathy scheduled for lumbar surgery Experimental group • <i>n</i> = 32 • Age (years): 49.59 • Duration of symptoms (days): 91.41 Control group • <i>n</i> = 35 • Age (years): 49.65 • Duration of symptoms (days): 92.29	NA	Pre-operative neuroscience education (NE) covered: (1) decision to have lumbar surgery; (2) nervous system physiology and pathways; (3) peripheral nerve sensitization; (4) surgical experiences and environmental issues' effects on nerve sensitivity; (5) calming the nervous system; (6) recovery after lumbar surgery; (7) scientific evidence; (8) reflection and writing questions for surgeon prior to surgery. NE provided by physical therapist in one-on-one session averaging 30 minutes using pictures, examples, metaphors, and drawings; patients were given booklet that summarized educational session information and asked to read at least once before surgery; patients also received "usual care" regarding preoperative education from surgeon and staff	"Usual care" regarding preoperative education from respective surgeon and staff	Primary outcome measures • Numeric Pain Rating Scales (NPRS) • Oswestry Disability Index (ODI) Secondary outcomes • Thoughts/beliefs about surgery numeric scale (1–10) • Healthcare utilization questions	Baseline, 1, 3, 6, and 12 month(s)

(Continued)

Table 3. (Continued).

Author	Participants		Interventions		Outcomes	
	Sample characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Téllez-García et al. (2014)	<i>n</i> 12 - Chronic non-specific low back pain <i>TRP-DN group</i> <i>n</i> = 6 (4 female) - Age (years): 37 ± 13 - Time with pain (months): 19 ± 8 <i>TRP-DN+EDU group</i> <i>n</i> = 6 (4 female) - Age (years): 36 ± 5 - Time with pain (months): 17 ± 9	NA	Neuroscience education group (TRP-DN + EDU) received 30-minute education sessions, once per week for the last two sessions (treatment session 2 and 3) after TRP-DN treatment (as performed in control group); face-to-face individual instruction on neurophysiology of pain with no particular reference to the lumbar spine; informed about the role of beliefs and attitudes toward their pain; PowerPoint presentation based on <i>Explain Pain</i> was used; during the session, patients were encouraged to ask questions to individualize information; written information about pain physiology concepts were provided as homework between sessions	Clinician with 10 years experienced in technique delivered trigger point-dry needling (TRP-DN) done to active trigger points in gluteus medius and quadratus lumborum; position was side lying, with depth of needle insertion approximately 20–25 mm and moved in multi-directions until first local twitch response was obtained; needling performed with up and down movement 5–8 mm with no rotation at approximately 1 Hz for 25–30 seconds; treatment done one time per week over 3 weeks	Primary outcome measures - Roland-Morris Disability Questionnaire (RMDQ) - Oswestry Low Back Pain Disability Index (ODI) - Numerical Pain Rate Scale (NPRS) - Tampa Scale of Kinesiophobia (TSK) - Pressure pain threshold (PPT)	Baseline, 1 week after last intervention

(Continued)

Table 3. (Continued).

Author	Participants			Interventions		Outcomes	
	Sample n	Characteristics	Diagnostic criteria	Treatment	Control	Outcome instruments	Time of assessment
Beltran-Alacreu et al. (2015)	45	- Non-specific chronic neck pain Experimental group 1 - n = 15 (13 female) - Age (years): 40.9 ± 16.2 - Pain duration (months): 54.9 ± 57.1 Experimental group 2 - n = 15 (10 female) - Age (years): 39.8 ± 13.4 - Pain duration (months): 83.4 (94.1) Control group - n = 15 (12 female) - Age (years): 43.5 ± 15.9 - Pain duration (months): 95.8 ± 77.5	NA	Experimental group 1 (Exp1) Eight one-on-one sessions over 1 month; same treatment as control group with addition of pain neuroscience education in two sessions; neuroscience education based on biobehavioral approach divided into three parts: cognitive, operant, and respondent; neuroscience education duration was approximately 20 minutes for each of two sessions; first session on initial visit covering cognitive part; use of PowerPoint with diagrams, images, and texts with education along with information booklet reviewing relevant content of education from first session; second session on fifth visit reviewing first session and operant and respondent parts. Operant section explained self-treatment techniques and coping strategies to reduce attention to pain. Experimental group 2 (Exp2) Received same intervention as Experimental group 1 with addition of therapeutic exercise program; exercise program based on neck stabilization exercises for deep neck flexors and extensors and neural self-mobilizations; progressive exercise program was added in sessions 5–8; with integration of exercise treatment during treatment session manual therapy, time was halved; patients asked to perform exercises once per day at home	Eight one-on-one sessions over 1 month; manual therapy techniques with specific passive movements of cervical facet joints; global mobilization of cervical spine and high-velocity technique to dorsal spine	Primary outcome measure - Neck Disability Index (NDI) Secondary outcomes - Tampa Scale of Kinesiophobia (TSK) - Fear Avoidance Beliefs Questionnaire (FABQ) - Neck Flexor Muscle Endurance (NFME) test - Visual Analog Fatigue Scale (VAFS)	Baseline, 4, 8, 16 weeks
Pires et al. (2015)	62	- Chronic low back pain Education group - n = 30 (20 female) - Age (years): 50.9 ± 6.2 Control group - n = 32 (20 female) - Age (years): 51.0 ± 6.3	NA	Completed aquatic exercises program similar to control with addition of pain neurophysiology program; two group sessions, 90 minutes each; topics addressed: acute pain origin in nervous system, transition from acute to chronic pain, central sensitization, role of brain in pain perception, cognitive and behavioral responses related to pain, flare-up management and pacing; metaphors and pictures used throughout the session	Six-week program of 12 biweekly sessions of aquatic exercise; groups of 6–9 participants lasting 30–50 minutes; three phases: (1) warm-up; (2) specific exercises; (3) warm-down	Primary outcome measures - Visual Analogue Scale (VAS) - Quebec Back Pain Disability Scale Secondary outcomes - Tampa Scale of Kinesiophobia (TSK)	Baseline, 6 weeks after beginning program and 3 months follow-up

*EG, experimental group; **CG, control group.

- Peripheral sensitization (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Moseley, 2003c; Van Oosterwijck et al., 2013; Vibe Fersum et al., 2013)
- Central sensitization (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Moseley, 2003c; Moseley, Nicholas, and Hodges, 2004; Pires, Cruz, and Caeiro, 2015; Vibe Fersum et al., 2013)
- Plasticity of the nervous system (Gallagher, McAuley, and Moseley, 2013; Louw, Diener, Landers, and Puenteadura, 2014; Moseley, 2003c; Moseley, Nicholas, and Hodges, 2004; Van Oosterwijck et al., 2013)
- Psychosocial factors and beliefs contributing to pain (Beltran-Alacreu, Lopez-de-Urvalde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Gallagher, McAuley, and Moseley, 2013; Pires, Cruz, and Caeiro, 2015; Téllez-García et al., 2014; Vibe Fersum et al., 2013)

The book *Explain Pain* by Butler and Moseley (2003) was directly referenced in six of the studies (Meeus et al., 2010; Pires et al., 2015; Ryan, Gray, Newton, and Granat, 2010; Téllez-García et al., 2014; Van Oosterwijck et al., 2013).

Professionals performing PNE

Physical therapists have been the delivery professional of PNE in all of the studies found in this review. In one study, utilizing booklets, the lead author was an occupational therapist, but no direct education (other than the book, authored by a physical therapist) was provided (Gallagher, McAuley, and Moseley, 2013).

Duration and frequency of PNE

The time and frequency of delivery was varied with a shift toward shorter durations found more common in the more recent studies. Longest duration of the documented sessions was 4 hours (Moseley, 2003c) in one session, with shortest duration being around 30 minutes (Louw, Diener, Landers, and Puenteadura, 2014; Meeus et al., 2010; Téllez-García et al., 2014; Van Oosterwijck et al., 2013). Shortest frequency was one time educational session (Moseley, Nicholas, and Hodges, 2004; Pires, Cruz, and Caeiro, 2015) with other studies utilizing education spread out over multiple episodes during the course of treatment.

Educational format and tools

The primary format for delivery of PNE was verbal one-on-one between patient and provider; two studies utilized group sessions (Moseley, 2003c; Pires, Cruz, and Caeiro, 2015) and one study did not have any face-to-face contact and only the information from a book that was read by the subjects (Gallagher, McAuley, and Moseley, 2013). The one-on-one sessions were most often described in terms of conversational, with encouragement for subjects to ask questions, so material could be individualized and not a straight lecture format. Various teaching aids were used during the delivery of the education consisting of prepared pictures, PowerPoint presentations, drawings, examples, metaphors, and books complementing the in person education information.

Adjunct treatment to PNE

Different study methodologies were used in the studies under review. The use of PNE was used in conjunction with other active movement-based therapy interventions in many of the studies. The list of other therapeutic activities used with PNE consisted of:

- Mobilization and manipulation (Moseley, 2002)
- Soft tissue massage (Moseley, 2002)
- Muscle and neural mobilization (Beltran-Alacreu, Lopez-de-Urvalde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Moseley, 2002)
- Trunk stabilization (Moseley, 2002, 2003c; Ryan, Gray, Newton, and Granat, 2010)
- Circuit-based aerobic exercise (Ryan, Gray, Newton, and Granat, 2010)
- Movement exercises (Vibe Fersum et al., 2013)
- Paced/graded exposure with activities of daily (Meeus et al., 2010; Vibe Fersum et al., 2013)
- Trigger point dry needling (Téllez-García et al., 2014)
- Neck stabilization exercises (Beltran-Alacreu, Lopez-de-Urvalde-Villanueva, Fernandez-Carnero, and La Touche, 2015)
- Aquatic exercise program (Pires, Cruz, and Caeiro, 2015)
- None (PNE only) (Ittersum et al., 2014; Louw, Diener, Landers, and Puenteadura, 2014; Moseley, Nicholas, and Hodges, 2004; Van Oosterwijck et al., 2013)

Outcome measures

Many different outcome measurement tools were used across the studies (Table 3) and assessed at various time points post-intervention. Measurements periods varied from immediate post-intervention to 1 year follow-up. We used the grouping of each of the outcomes

measurements into the four categories established in the initial systematic review: pain, function, psychosocial factors, and movement along with adding a fifth category of healthcare utilization.

Outcomes related to pain

- Pain rating (Numeric Pain Rating Scales or Visual Analog Scale) (Gallagher, McAuley, and Moseley, 2013; Louw, Diener, Landers, and Puente-dura, 2014; Moseley, 2002; Pires, Cruz, and Caeiro, 2015; Ryan, Gray, Newton, and Granat, 2010; Vibe Fersum et al., 2013)
- Pain knowledge (Neurophysiology of Pain Questionnaire or Pain Biology Questionnaire) (Meeus et al., 2010; Van Oosterwijck et al., 2013)
- Pain Vigilance and Awareness Questionnaire (Van Oosterwijck et al., 2013)
- Pressure Pain Threshold (Meeus et al., 2010; Téllez-García et al., 2014; Van Oosterwijck et al., 2013)
- Spatial summation procedure (Van Oosterwijck et al., 2013)

Outcomes related to function and disability

- Roland Morris Disability Questionnaire (Moseley, 2002, 2003c; Ryan, Gray, Newton, and Granat, 2010; Téllez-García et al., 2014)
- Oswestry Disability Index (Louw, Diener, Landers, and Puente-dura, 2014; Téllez-García et al., 2014; Vibe Fersum et al., 2013)
- Neck Disability Index (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015)
- Fibromyalgia Impact Questionnaire (Ittersum et al., 2014; Van Oosterwijck et al., 2013)
- Revised Illness Perception Questionnaire for Fibromyalgia (Ittersum et al., 2014)
- Short Form 36 Health Status Survey (Van Oosterwijck et al., 2013)
- Quebec Back Pain Disability (Pires, Cruz, and Caeiro, 2015)
- Patient-Specific Functional Scale (Gallagher, McAuley, and Moseley, 2013)

Outcomes related to psychosocial factors

- Tampa Scale of Kinesiophobia (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Meeus et al., 2010; Pires, Cruz, and Caeiro, 2015; Van Oosterwijck et al., 2013)
- Pain Catastrophization Scale (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Moseley, Nicholas, and Hodges, 2004)

- Pain Coping Inventory (Meeus et al., 2010; Van Oosterwijck et al., 2013)
- Survey of Pain Attitudes (revised) (Moseley, Nicholas, and Hodges, 2004)
- Pain Self-Efficacy Questionnaire (Ryan, Gray, Newton, and Granat, 2010)
- Hopkins Symptoms Checklist (Vibe Fersum et al., 2013)
- Fear Avoidance Beliefs Questionnaire (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Vibe Fersum et al., 2013)
- Beliefs about surgery (Louw, Diener, Landers, and Puente-dura, 2014)

Outcomes related to movement

- Straight leg range of motion (Moseley, Nicholas, and Hodges, 2004)
- Lumbar range of motion (Moseley, Nicholas, and Hodges, 2004; Vibe Fersum et al., 2013)
- Abdominal draw in task (Moseley, Nicholas, and Hodges, 2004)
- Repeated sit to stand test (Ryan, Gray, Newton, and Granat, 2010)
- 50-foot walk test (Ryan, Gray, Newton, and Granat, 2010)
- 5-minute walk test (Ryan, Gray, Newton, and Granat, 2010)
- Step count (Ryan, Gray, Newton, and Granat, 2010)
- Neck flexor muscle endurance test (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015)
- Visual Analog Fatigue Scale (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015)

Outcomes related to healthcare utilization

- Healthcare center visits (Moseley, 2002)
- Sick-leave days (Vibe Fersum et al., 2013)
- Care-seeking (Vibe Fersum et al., 2013)
- Healthcare utilization questions (Louw, Diener, Landers, and Puente-dura, 2014)

Effectiveness of PNE

Results could not be pooled for all the studies due to the variability in outcome measurement tools and differing control groups. Results of outcomes are summarized in Table 4.

Table 4. Effectiveness of PNE on pain, disability, anxiety, and stress for MSK conditions.

Outcome	Meeus										Louw et al. (2014)	Téllez-García et al. (2014)	Beltran-Alacreu et al. (2015)	Pires et al. (2015)
	Moseley (2002)	Moseley (2003c)	Moseley et al. (2004)	Ryan et al. (2010)	Meeus et al. (2010)	Vibe Fersum et al. (2013)	Gallagher et al. (2013)	Van Oosterwijk et al. (2013)	Ittersum et al. (2014)					
Decrease in pain ratings	+	+		+	0	+	0	+		0	0		+	
Increase pain tolerance					+		+	+						
Increase knowledge of pain						+		+	0	0	0	+	0	
Improve function and disability	+	+	+	0			0	+						
Decrease fear of movement				0	0	+		0	0		+	+	0	
Decrease pain catastrophization			+		+		+							
Develop strategies to cope with pain					0			0						
Develop healthy attitudes regarding pain			+	0						+				
Decrease anxiety and/or depression symptoms						+						+		
Improve physical movement and performance			+	0	0									
Decrease health care utilization	+				+					+				
positive effectiveness; 0, no effectiveness.														

+, positive effectiveness; 0, no effectiveness.

PNE addressing pain

Ten of the 13 studies evaluated the effect of PNE on pain of the subjects.

- (1) The mean improvement of pain at 1 month was 1.5 on the NRS (95% CI: 0.7–2.3) for those receiving the intervention over those in the control group. This difference was shown to have a significant treatment effect ($p < 0.01$) with a number needed to treat to gain clinical significance at 3 (95% CI: 2–8). At 1 year follow-up, this difference maintained in regards to improvement with pain 1.9 (95% CI: 1–2.8) with number needed to treat of 2 (95% CI: 1–4) (Moseley, 2002).
- (2) Significant decrease in pain on NRS from 5-week “on-going usual treatment” to end of 4-week treatment intervention and 12-month follow-up. Individual education group showed treatment effect of 3.1 (95% CI: 1.8–4.2) on NRS at conclusion of 4-week intervention and group education group showed 2.7 (95% CI: 1.6–3.9) reduction on NRS. The difference between pre-treatment and post-treatment between independent and group treatment was 1.0 (95% CI: 0.3–2.0) (Moseley, 2003c).
- (3) There was a significant time and group interaction from pre-test to post-1-month follow-up for PNE group over control group of exercise and traditional education group with decrease in NRS. This difference leveled off at the 3 months post-intervention time measurement point (Ryan, Gray, Newton, and Granat, 2010).
- (4) Pressure pain threshold decreased in both groups over time but no between-group differences were found at the end of the intervention. Significant difference in pain neuroscience knowledge in experimental group over control group ($p < 0.001$) was found (Meeus et al., 2010).
- (5) Both treatment groups showed significant improvement with respect to improved pain ratings with the PNE group showing statistically ($p < 0.001$) superior outcomes compared with traditional therapy group at 3 and 12 months follow-up. The mean difference between groups for 3 and 12 months, respectively, for PINRS were 2.1 (95% CI: 2.7–1.4) and 1.3 (95% CI: 2.1–0.5) (Vibe Fersum et al., 2013).
- (6) Analysis showed that both groups improved over time in NRS but there was no significant

effect between groups in regards to pain with reading either the PNE book or control book. Increased knowledge about pain biology in the experimental group over advice group ($p < 0.01$) was seen with an effect size of Cohen $d = 1.7$ (Gallagher, McAuley, and Moseley, 2013).

- (7) Spatial summation procedure showed no significant differences at 2 weeks post-intervention with PNE compared with control, but there was a significant difference at 3 months ($p = 0.041$). There was no significant difference in pressure pain threshold or Pain vigilance and Awareness Questionnaire between groups over assessment periods. Neurophysiology of pain test showed significant increase in response with experimental group ($p < 0.001$) but not control group ($p = 0.150$) (Van Oosterwijck et al., 2013).
- (8) There was no significant effect for low back or leg pain between PNE group and control group over the 12-month time. Overall time effects for decreased pain for both groups were significant ($p < 0.002$). There was short term (1 month follow-up) effect with significant decrease in pain for low back and leg ($p < 0.046$) but plateaued over the 3, 6, and 12 months follow-up (Louw, Diener, Landers, and Puenteadura, 2014).
- (9) No group interaction for pain intensity was found between trigger point dry needling group with PNE (–3.6 (95% CI: –6.0 to –1.1)) or without PNE (–4.2 (95% CI: –6.6 to –1.7)) but time interaction was found significant for both groups ($p < 0.002$). There was no group interaction differences for pressure pain threshold measurements but there was significant time interaction post-treatment at all three measurement points (Téllez-García et al., 2014).
- (10) Statistical differences were found for overall group interaction by time and also between-group interaction at 3 months follow-up favoring the PNE group but none at 6 weeks follow-up on the visual analog scale. Visual analog change at 3 months for education group compared with control group was -25.4 ± 26.7 and -6.6 ± 30.7 , respectively (Pires, Cruz, and Caeiro, 2015).

PNE addressing function

Twelve of the 13 studies addressed function through various functional measurement tools. Six studies

looked at general functional improvement scores through use of Roland Morris Disability Questionnaire (RMDQ) (Moseley, 2002; Moseley, Nicholas, and Hodges, 2004; Ryan, Gray, Newton, and Granat, 2010; Téllez-García et al., 2014) or Short Form 36 Health Status Survey (SF-36) (Van Oosterwijck et al., 2013). Eight of the studies used more specific questionnaires based on diagnostic or functional status. The diagnostic or specific functional measurement tools used were (1) Oswestry Disability Index (ODI) (Louw, Diener, Landers, and Puentedura, 2014; Téllez-García et al., 2014; Vibe Fersum et al., 2013); (2) Neck Disability Index (NDI) (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015); (3) Patient-Specific Functional Scale (PSFS) (Gallagher, McAuley, and Moseley, 2013); (4) Fibromyalgia Impact Questionnaire (FIQ) (Van Oosterwijck et al., 2013); (5) Revised Illness Perception Questionnaire for Fibromyalgia (IPQ-R_FM) (Ittersum et al., 2014); and (6) Quebec Back Pain Disability Scale (Pires, Cruz, and Caeiro, 2015).

- (1) Both groups improved in regards to disability with mean improvement of the intervention group over control of 3.9 points on the RMDQ (95% CI: 2.0–5.8). With number needed to treat of 2 (95% CI: 2–5) for the RMDQ (Moseley, 2002).
- (2) Between-group change favored the intervention group with a mean effect of 2.4 (95% CI: 0.8–4.2) on the RMDQ (Moseley, 2003c).
- (3) Experimental group improved in RMDQ by 2 points (95% CI: 0.4–3.6) compared with control group post-treatment (Moseley, Nicholas, and Hodges, 2004).
- (4) There was a non-significant trend toward a more favorable outcome with experimental group in improvement of RMDQ ($p = 0.127$) (Ryan, Gray, Newton, and Granat, 2010).
- (5) Both groups showed significant improvement over time with treatment for ODI scores. The group receiving PNE had a significant ($p < 0.001$) mean difference improvement of -9.7 (95% CI: -12.7 to -6.7) at 3 months and -8.2 (95% CI: -12.6 to -3.8) at 12 months compared with the other group ODI score. The group receiving PNE showed an overall ODI improvement over 12 months of 13.7 (95% CI: 11.4 – 16.1 ; $p < 0.001$) (Vibe Fersum et al., 2013).
- (6) Both groups improved over time in regards to disability as measured through PSFS, but no differential effect between groups was

found ($p = 0.07$) (Gallagher, McAuley, and Moseley, 2013).

- (7) Significant between-group differences were found in favor of experimental group for SF-36 physical functioning ($p = 0.046$), general health perceptions ($p < 0.001$), and vitality ($p = 0.047$) subscores. A large effect size (Cohen d) was found for the SF-36 health perceptions scale ($d = -0.98$). The remaining SF-36 subscores and FIQ did not show significant effects for between-group differences (Van Oosterwijck et al., 2013).
- (8) No significant effects were found between groups for FIQ, and all effect sizes for FIQ domains were small. Illness perception as measured through IPQ-R_FM did not show any statistically different effects between groups (Ittersum et al., 2014).
- (9) There was no significant between-group interaction ($p > 0.167$), both groups showed improvement over time in regards to function as measured with ODI ($p < 0.002$) (Louw, Diener, Landers, and Puentedura, 2014).
- (10) ODI scores showed no significant group interaction changes for ODI ($p = 0.542$) or RMDQ ($p = 0.111$). There was a main effect for time for both groups for ODI ($p < 0.001$) and RMDQ ($p < 0.001$) (Téllez-García et al., 2014).
- (11) NDI showed significant improvement ($p < 0.01$) for both experimental groups compared with control group at the 4, 8, and 16 weeks follow-ups (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015).
- (12) Functional disability showed significant ($p < 0.05$) group by time interaction but no statistically significant between-groups difference at 6 weeks ($p = 0.83$) or 3 months ($p = 0.09$). A greater percent of participants in PNE reported benefits from treatment for functional disability at both measurement points with only the 3 months follow-up showing significant ($p = 0.034$) findings (Pires, Cruz, and Caeiro, 2015).

PNE addressing psychosocial factors

Outcomes related to psychosocial factors were measured in 11 of the 13 studies. Researchers choose a mixture of validated tests consisting: (1) Pain Catastrophizing Scale (PCS) (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Meeus et al., 2010; Moseley, Nicholas, and Hodges, 2004; Van Oosterwijck

et al., 2013); (2) Pain Coping Index (PCI) (Meeus et al., 2010; Van Oosterwijck et al., 2013); (3) Tampa Scale of Kinesiophobia (TSK) (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Meeus et al., 2010; Pires, Cruz, and Caeiro, 2015; Ryan, Gray, Newton, and Granat, 2010; Téllez-García et al., 2014; Van Oosterwijck et al., 2013); (4) Pain Self-Efficacy Questionnaire (PSEQ) (Ryan, Gray, Newton, and Granat, 2010); (5) Fear Avoidance Beliefs Questionnaire (FABQ) (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015; Vibe Fersum et al., 2013); (6) Survey of Pain Attitudes (revised) (SOPA(R)) (Moseley, Nicholas, and Hodges, 2004); (7) Hopkins Symptoms Checklist (HSCL-25) (Vibe Fersum et al., 2013); and (8) Beliefs about surgery questionnaire (Louw, Diener, Landers, and Puentedura, 2014).

- (1) Both SOPA(R) and PCS were better in the experimental group compared with control group ($p < 0.001$ for both). Effect size for SOPA(R) total was 9.0 (95% CI: 6.5–11.5) and for PCS was 6.0 (95% CI: 3.8–8.2) (Moseley, Nicholas, and Hodges, 2004).
- (2) No statistically significant effect for PSEQ or TSK-13 was found (Ryan, Gray, Newton, and Granat, 2010).
- (3) Significant reduction ($p = 0.009$) in PCS for ruminating scale in the PNE group compared with control, coping strategies (PCI) trended toward significance with “distraction” ($p = 0.021$) and worrying ($p = 0.011$). The TSK did not reach significance levels when comparing groups (Meeus et al., 2010).
- (4) FABQ for physical subscales showed significant changes favoring experimental group at 3 months: -3.6 (95% CI: -5.3 to -1.9 ; $p < 0.001$) and at 12 months -4.7 (95% CI: -6.5 to -3.0 ; $p < 0.001$). Work subscale of the FABQ also showed favorable results toward experimental group at both time measurement intervals -5.7 (95% CI: -7.8 to -3.6 ; $p < 0.001$) and -5.6 (95% CI: -8.7 to -2.5 , $p < 0.001$), respectively. The HSCL-25 also showed significant results at 3 months: -0.12 (95% CI: -0.19 to -0.04) and at 12 months: -0.13 (95% CI: -0.22 to -0.04) in favor of the experimental group (Vibe Fersum et al., 2013).
- (5) A large significant shift ($p < 0.01$) in PCS scores was found in pain metaphor group compared with control advice group initially and at 3 months follow-up, with large effect size at 3 months follow-up (Cohen $d = 0.7$).

When the control group was crossed over to metaphor group, it also showed significant ($p < 0.01$) improvements in PCS (Gallagher, McAuley, and Moseley, 2013).

- (6) Mean scores of PCI and TSK decreased with treatment as they did not reach significance for between-group differences (Van Oosterwijck et al., 2013).
- (7) In regards to PCS, there were no between-group or within-group changes found (Ittersum et al., 2014).
- (8) Main effect for more favorable post-operative opinion in experimental group over control group was found on three questions: “fully prepared for surgery” ($p = 0.01$), “preoperative education prepared well” ($p = 0.001$), and “met expectations” ($p = 0.042$) (Louw, Diener, Landers, and Puentedura, 2014).
- (9) Treatment with PNE had greater reduction ($p = 0.008$) of kinesiophobia than those treated without PNE. Between-group change was in favor of PNE on TSK (-12.7 (95% CI: -21.3 to -4.0)) (Téllez-García et al., 2014).
- (10) With TSK there were significant effects ($p < 0.05$) for post-treatment, 8 and 16 weeks for favoring experimental 1 to control. Also, similar significant effects of TSK favoring experimental 2 versus control at 8 and 16 weeks were found. There were no differences in TSK when comparing the two experimental groups. Effect size of experimental group 1 for TSK was $d = 1.22$, while it was $d = 1.02$ for experimental group 2. Significance ($p < 0.5$) for FABQ was similarly in favor of experimental group 1 and 2 over control with difference between the two experimental groups. Effect size for experimental 1 was $d = 0.78$ and for experimental 2 was $d = 1.13$ (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015).
- (11) No statistical interaction was found with TSK (Pires, Cruz, and Caeiro, 2015).

PNE addressing movement

Four of the studies looked specifically at an impairment in movement. All four studies chose different physical performance tasks to study effects.

- (1) Forward bending and straight leg raise were improved more in the experimental group over the control group ($p < 0.001$ for both). Abdominal “drawing-in” task did not show

- between-group differences (Moseley, Nicholas, and Hodges, 2004).
- (2) Physical performance measurements of repeated sit-to-stand test, 50-foot walk test, and 5-minute walk test did not show any significant changes between the experimental and control group (Ryan, Gray, Newton, and Granat, 2010).
 - (3) No significant changes between the experimental and control group were found at 3 months (Vibe Fersum et al., 2013).
 - (4) Visual Analog Fatigue Scale (VAFS) and Neck Flexor Muscle Endurance Test (NFME) showed significant effects ($p < 0.05$) at 8 and 16 weeks follow-up. Experimental group 1 was significant ($p < 0.01$) for VAFS and NFME. In experimental group 2, the NFME test was significant ($p < 0.01$) but not for VAFS (Beltran-Alacreu, Lopez-de-Uralde-Villanueva, Fernandez-Carnero, and La Touche, 2015).

PNE addressing healthcare utilization

Three studies explored changes in healthcare utilization following PNE. Each study utilized different outcome measurements for their study design.

- (1) At 1 year follow-up, experimental group made 3.6 ± 2 (mean $\pm$ SD) healthcare center visits for low back pain, which was statistically less ($p < 0.001$) than the control group who made 13.2 ± 5 visits (Moseley, 2002).
- (2) Reduction of sick-leave days extracted from the Orebro Screening Questionnaire was observed with significance ($p < 0.01$) toward the experimental group ($z = 2.95$). Also improved ($p < 0.001$) reduction in care-seeking after intervention was noticed ($z = 4.79$) (Vibe Fersum et al., 2013).
- (3) Overall reduction in healthcare costs for medical treatment at 1 year follow-up was less for experimental group (mean = \$22678.57, SD = \$3135.30) compared with control group (mean = \$4833.48, SD = \$3256.00) ($z = -2.700$, $p = 0.007$) (Louw, Diener, Landers, and Puentedura, 2014).

Discussion

The results of this updated systematic review of PNE for MSK pain provide supporting evidence for PNE improving pain ratings, pain knowledge, disability, pain catastrophization, fear-avoidance, attitudes and

behaviors regarding pain, physical movement, and healthcare utilization (Ezzo et al., 2000; Fernández-de-las-Peñas et al., 2006). These positive results need, however, to be considered in lieu of the heterogeneous nature of the studies included in this systematic review. It is also important to recognize that no PNE study showed any outcome to be worse than the control groups, thus implying a significant risk-benefit ratio in favor of PNE. In comparison with the previous two systematic reviews, however, the quality of the studies, number of studies, and total number of patients ($n = 734$) are substantially increased (Clarke, Ryan, and Martin, 2011; Louw, Diener, Butler, and Puentedura, 2011). This increase not only reflects the increased activity in this field of study but also impacts the conclusions that can be made in regards to the efficacy of PNE. For example, in the systematic review by Louw, Diener, Butler, and Puentedura (2011) which included lower-level studies (pseudo-RCT, case-control), the efficacy of PNE addressing pain was reported as “compelling,” whereas the current review using higher-level RCTs showcases a similar and even increased effect on reducing pain ratings.

Various noteworthy observations can be made. First, only three studies reported 1 year outcomes, and interestingly, also reported on healthcare utilization (Louw, Diener, Landers, and Puentedura, 2014; Moseley, 2002; Vibe Fersum et al., 2013). All three studies showed a significant reduction of healthcare utilization 1 year after PNE. Given the various concerns regarding healthcare cost in general, there is an ever-increasing request for treatments that are cheaper, easily accessible, and have long-lasting efficacy. Pain is complex, and with well-documented issues such as central sensitization, neuroplasticity, changes in endogenous mechanisms, etc., using pain ratings alone as a measure of improvement seems illogical. Even though evidence supports the reduction over time of pain with the utilization of PNE, a sudden, total resolution of pain is biologically questionable. The concept of reconceptualizing pain, a cornerstone of PNE, aims to have patients see their pain differently. This implies that even though they still experience pain, they think differently about it, equating it to sensitization of the nervous system versus the health of the tissues. Furthermore, this reconceptualization imparts a message of “despite the pain,” it is worthwhile to move, exercise, engage, and continue in daily activities and not necessary to seek additional care for the sensitization (pain). This behavior change is the key to changing any patient’s healthcare status, that is, smoking, weight gain, etc. In line with the results from this systematic review and the three RCTs being discussed, it is argued

that true behavior change is reflected in healthcare utilization. Given the relative low cost of “only” educational sessions with a physical therapist, the ability to have such a huge impact, especially 1 year, out needs mention. In contrast, these three studies also highlight the need for more long-term studies on the efficacy of PNE to measure its true impact. To date, the authors are only aware of one PNE study extending beyond 1 year outcome, with Louw, Diener, Landers, and Puentedura (2014) measuring 3-year outcomes of preoperative PNE for patients undergoing surgery for lumbar radiculopathy.

The second observation highlights the possible differences between education-only approaches of PNE versus PNE combined with a movement-based strategy such as exercise and/or manual therapy. In five studies, patients received education-only intervention (Gallagher, McAuley, and Moseley, 2013; Ittersum et al., 2014; Louw, Diener, Landers, and Puentedura, 2014; Moseley, Nicholas, and Hodges, 2004; Van Oosterwijck et al., 2013). None of these studies had any ability to decrease pain ratings, whereas five of the six studies that combined PNE with a physical intervention were able to produce a significant reduction in pain ratings. In line with the definition of PNE and the argument that PNE “biologizes” pain, teaching patients about the biology and physiology of a pain experience would make sense. Education-alone may not be sufficient for change. This is important as many clinicians may be under the impression that PNE is education-only intervention. Additionally, it has been reported that some clinicians see PNE and pain science as “hands-off” versus “hands-on.” This review strongly suggests that the combination of PNE with movements, be it passive and/or active, may be a key in the success of PNE. Further studies are needed to explore this finding.

Various issues in regards to questions and potential future avenues associated with PNE research are found in the results of this systematic review. The obvious shortcoming is the heterogenous studies regarding design, patient populations, outcome measures, educational delivery methods, etc. By standardization of these factors, subsequent reviews and meta-analysis may shed further light on the efficacy of PNE. An interesting observation is that three studies examined and showed an increase in pain knowledge, yet this increased knowledge of pain has yet to be shown to correlate to decreased pain and disability. Of the three studies that reported increased knowledge of pain, it is, however, interesting to note that both Meeus et al. (2010) and Gallagher, McAuley, and Moseley (2013) showed an increase in pain knowledge as well as a positive effect of their PNE on pain catastrophization. This increase of

pain knowledge and its potential effect warrants further investigation. Additionally, in line with current trends of MSK pain treatments, such as low back pain, is there a need to explore sub-grouping of patients? Both groups made meaningful changes in regards to various outcome measures. Apart from PNE alone not being effective in reducing pain ratings, the current review does not show any meaningful trends beyond this and warrants further investigation.

Conclusion

Strong evidence supports the use of PNE for MSK disorders in reducing pain ratings, limited knowledge of pain, disability, pain catastrophization, fear-avoidance, unhealthy attitudes and behaviors regarding pain, limited physical movement and healthcare utilization (Ezzo et al., 2000; Fernández-de-las-Peñas et al., 2006).

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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