Blended-Learning Pain Neuroscience Education for People With Chronic Spinal Pain: Randomized Controlled Multicenter Trial

Running title: Blended-Learning PNE for People With Chronic Spinal Pain

Musculoskeletal

Original Research

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ABSTRACT

Background: Available evidence favours the use of pain neuroscience education (PNE) in patients with chronic pain. However, PNE trials are often limited to small sample sizes, and despite the current digital era, the effects of blended learning PNE (e.g. the combination of online digital media with traditional educational methods) are not yet investigated.

Objective: To examine whether blended learning PNE is able to improve disability, catastrophizing, kinesiophobia and illness perceptions.

Design: A **two-centre**, triple blind RCT **(participants, statistician and outcomes assessor were blinded)**

Setting: University Hospitals of Ghent and Brussels, Belgium

Patients: 120 patients with non-specific chronic spinal pain (e.g. chronic neck and low back pain)

Intervention: 3 sessions of PNE or biomedically-focussed back/neck school education (addressing spinal anatomy and physiology).

Measurements: Self-reported questionnaires (e.g. Pain Disability Index, Pain Catastrophizing Scale, Tampa Scale for Kinesiophobia, Illness Perception Questionnaire, and Pain Vigilance and Awareness Questionnaire).

Results: None of the treatment groups showed a significant change in the perceived disability (pain disability index) due to pain (mean group difference post-education: 1.84; 95%CI: -2.80;6.47). Significant interaction effects were seen for kinesiophobia($p=.002$) and several subscales of the Illness Perception Questionnaire, including 'negative consequences'($p=.003$), 'timeline cyclical' ($p<.000$) and 'timeline acute/chronic'($p=.003$). In depth analysis revealed that only in the PNE group these outcomes significantly improved (9 to 17% improvement; $.37 \leq$ Cohen's $D \geq .86$).

Conclusions: Blended learning PNE is able to improve kinesiophobia and illness perceptions in patients with chronic spinal pain. As effect sizes remain small **to medium**, PNE should not be used as sole treatment, but rather as key element within a comprehensive active rehabilitation program. Future studies should compare the effects of blended learning PNE with offline PNE, also regarding cost-effectiveness.

Keywords:

Randomized controlled trial, Chronic Pain, Education: Clinical, Neuroscience, Low Back Pain, Neck Pain, Patient Education

INTRODUCTION

Chronic Spinal Pain (CSP) accounts for a large proportion of the chronic pain population and is generally perceived as highly disabling with tremendous personal, social and economic impact [1,2]. Within the CSP population, a minority has an explicit, identifiable cause for their pain, but the majority of people suffer without a specific underlying cause [3].

Especially in the latter group, termed non-specific CSP (nCSP), the persistence of pain may be due to other factors, including inappropriate pain cognitions and perceptions [4]. Pain cognitions and illness perceptions are identified as potential treatment barriers in these patients [5,6]. Pain Neuroscience Education (PNE) is advocated by many researchers as a strategy to improve pain perceptions and cognitions as several trials report positive effects of PNE on anxiety, stress, catastrophizing, pain and disability in different chronic pain populations, including nCSP [7–15].

The learning objectives of PNE comprise decreasing the threat value of pain, increasing the patients' knowledge of pain and reconceptualising pain. This implies improving the patient's pain or illness perceptions. Yet, studies exploring if PNE can alter these perceptions should be carried out as illness perceptions, in addition to kinesiophobia and pain catastrophizing, are strong predictors of therapy outcome [16–19]. One could hypothesize that increasing the patients' knowledge on their pain, could result in a decrease in perception of negative consequences of pain, a higher controllability of pain, a reduction in perceived symptoms, etc.

In addition, previous PNE trials focussed on patients with chronic low back pain [20], chronic fatigue syndrome [11], fibromyalgia [7], and those undergoing surgery for lumbar radiculopathy [8], but not on people having idiopathic neck pain. Neck pain is the second most common type of chronic pain [21]. Yet, PNE studies in patients with neck pain are limited to one case series report in patients with chronic whiplash-associated-disorders [22]. In this study, patients with neck pain and low back pain will be investigated as one group, as PNE education has a similar content and format in these patients.

Regarding the mode of administration, previous trials on PNE effectiveness used face-to-face sessions only [11,20], face-to-face sessions combined with an educational booklet [8,22], educational booklet only [10,23] or group education [24]. Remarkably, in this digital era, blended learning strategies for providing PNE have not yet been evaluated. Blended learning is defined as "a formal education program that combines online and face-to-face instruction", and represents a time-efficient, cost-effective approach to obtain transfer of knowledge [25]. Blended learning can, for example, be the combination of traditional classroom teaching methods with online lectures or exercises. Because of its presumed positive effect on the timing and costs of therapy, this study implemented this education approach.

Based on results of previous studies and the remaining voids, this study aimed at examining whether blended learning PNE can improve disability, pain catastrophizing, kinesiophobia, illness perceptions and pain vigilance in patients with nCSP.

METHODS

Design Overview

This multicentre randomized controlled trial took place in two centres: the University Hospitals of Ghent and Brussels. The trial was approved by the local ethics committees (University Hospital Ghent and University Hospital Brussels). All participants signed the informed consent. The data presented here comprise a part of a large randomized controlled trial. In this trial, education is followed by exercise therapy, with a follow-up period of one year. The analysis of the complete trial dataset is ongoing. The full study protocol is registered at ClinicalTrials.gov (no. NCT02098005) and is published elsewhere [26]. In the present paper, we report the effects of three sessions blended learning PNE vs. biomedical back/neck school education on self-reported questionnaires. Outcome measures were assessed at baseline, and directly after three sessions of education. In the complete RCT, physical therapy sessions (exercise therapy) was initiated two days after finalization of the third (and final) education session. The data used in this study were collected before the first physical therapy sessions took place. The trial is reported according to CONSORT guidelines (http://www.consort-statement.org) [27].

Setting and Participants

Blinding

The present study is a triple-blind randomized controlled trial. The study participants and the statistician (performing the data analyses) were blinded to the study hypothesis; and the outcomes assessor (collecting the data) was blinded for the randomization sequence. Naturally, the therapists delivering the education (in either groups) were not blinded. Yet, therapists that provided PNE did not do so in the control group and vice versa.

Studypopulation and sample size

Patients with nCSP were recruited through different sources: flyers in the Universities and University Hospitals (Ghent and Brussels), primary care practices and occupational health services, via adverts and social media. Through these flyers, people interested in study participation were asked to send an e-mail to the researchers. In the reply e-mail, they were asked to fill out an online questionnaire, which screened for all in- and exclusion criteria. People meeting all criteria were called to answer possible questions.

Inclusion criteria were: native Dutch speaker, aged between 18 and 65 years, having nCSP at least 3days/week for at least 3 months since the first symptoms. nCSP includes chronic low back pain, failed back surgery syndrome (e.g. more than three year ago, anatomically successful operation without symptom disappearance), chronic whiplash associated disorders, and chronic non-traumatic neck pain. Participants had to be available and willing to participate in educational sessions, and were not allowed to continue any other therapies (i.e. other physical therapy treatments, acupuncture, osteopathy, etc.), except for usual medication. Before every educational session, as well as every round of questionnaires, the patients were asked if they were not taking part in any other therapies. All participants always answered 'no'. Additionally, they were asked not to start new medication 6 weeks prior to and during participation in this study.

Participants were excluded if they had a specific medical condition, possibly related to their pain (e.g., neuropathic pain, a history of neck/back surgery in the past three years, osteoporotic vertebral fractures, rheumatologic diseases, etc.). Additionally, patients with chronic widespread pain syndromes (e.g. fibromyalgia, chronic fatigue syndrome) were excluded. Although these patients were excluded to obtain a homogenous population, it needs to be acknowledged that also these

patients could benefit from a pain neuroscience based program. Additionally, people living more than 50km away from the treatment location were excluded to avoid dropout.

Sample size calculations were performed with G*Power (Düsseldorf, Germany) based on the therapy effects on disability in the pilot study of Van Oosterwijck [22] (Cohen's D= .46). Calculations were based on ANOVA repeated measures (number of measurements = 2) statistics with an effect size f of 0.15, alpha set at 0.05 and a desired power of 0.90, resulting in a total of 120 people.

Randomization and interventions

Randomization

Participants were randomly assigned into the treatment groups. Randomization was performed using a stratified permuted block allocation (block size of four) at the Biostatistics Unit (Ghent University) by an independent investigator using SAS 9.4. Stratification factors were: treatment centre (Ghent or Brussels), dominant pain location (low back or neck) and gender [28,29]. Only one investigator, who was not involved in the participants recruitment, knew the randomization schedule.

Intervention

All study participants received 3 educational sessions within 2 weeks given by physical therapists with clinical experience on the matter. The format identical for both treatment groups. The first session was a group session (duration: 30 minutes to one hour) of maximal 6 participants/group led by the allocated physical therapist, using a PowerPoint presentation. Afterwards, participants had to read an educational booklet, containing the same information, at home. The second session was a home-based online e-learning module, containing 3 explanatory videos. These videos displayed the same PowerPoint presentation as the one used during the group session, with a voice-over

explaining the content of the slides. Therefore, the same topics (described below) were covered in the online session as in the group session. After each clip the participants had to complete a questionnaire which assessed their understanding and opinion on that video. The third session comprised a 30-minute one-on-one conversation focussing on the patients' personal needs: questions from the second session's questionnaires were analysed and answered; and the way of applying the knowledge into the patient's daily life was discussed. The content of the provided education (described below) rather than the format of administration differed between groups.

Experimental group

The learning objectives of PNE comprise decreasing the threat value of pain, increasing the patients' knowledge of pain and reconceptualising pain**.** In order to achieve this, the participants need to understand that all pain is produced, constructed and modulated by the brain, and that their pain symptoms often relate to hypersensitivity of the central nervous system rather than (ongoing) tissue damage. The content and pictures were based on current knowledge of the neurophysiology of pain according to Wall and Melzack [30] and on the books 'Explain Pain' [31] and 'Pijneducatie, een praktische handleiding voor (para)medici' [32]. An example of a PowerPoint used to deliver PNE can be found online (http://www.paininmotion.be/storage/app/media//materials/sem-PainPhysiologyEducationEnglish.pdf). PNE focusses solely on the nervous system and covers the general physiology of the nervous system as well as the pain system in particular by using photographs, drawings, graphs and metaphors. The content comprised the physiology of nociception and pain, all presented in layman's terms, including the following topics: the physiology of the 1) the neuron (receptor, axon, terminal), 2) the synapse (action potential, neurotransmitters, postsynaptic membrane potential, chemically driven ion channel), 3) descending nociceptive inhibition and facilitation (the influence of stress, emotions, thoughts, physical activity,…), 4) peripheral sensitization, and 5) central sensitization (receptor field growth, potentiation of the postsynaptic

membrane, changes at cortical and subcortical level,…). This has been used as such previously in studies examining the effects of PNE in people with chronic pain [7,11,14,20,22]. The questions asked during the online session were related to the understanding and opinion of the patient regarding the content of the video (e.g. 'Do you understand that pain and damage are not synonymous terms?', 'Do you think your neck/back is damaged at this moment?', ''Do you think that your nervous system has become more sensitive?', etc.). In the third session, the therapist and patient discussed these answers by relating them to the PNE content. At the end of the PNE education, the patients should be able to put their pain into the right perspective and to feel less threatened by **the pain, leading to** the willingness to perform physical activity with progression towards feared or avoided movements.

Control group

The biomedically-focused neck/back school was based on clinical guidelines and on studies of Glomsrod et al. and Soukup et al. [33,34]. The learning objectives of this education comprised gaining biomedically-oriented knowledge on neck and low back pain. This was done by covering the following topics: 1) the normal course and mechanical causes of back/neck pain; 2) the anatomy, physiology and biomechanics of the bones, muscles and joints of the spine and the intervertebral discs; **3)** the importance of self-care and ergonomic advise; 4) posture and movements (including description of 'good and bad' activities and postures according to pictures showing intradiscal pressure and joint forces); 5) examples of lifting techniques (using pictures of people lifting in several ways); and 6) the principles and value of different types of exercises (stretching; and strength, endurance and fitness training). It did not include information on the nervous system, except for the course and location of the spinal cord and spinal nerve roots. The questions in the online module were also related to the understanding and opinion of the patient regarding the content of the video (e.g. 'Which activities or movements are causing you pain?', 'Do you understand the importance of ergonomics?', 'What could you do to improve you posture at work?', etc.). In the third session, the

therapist and patient discussed these answers by relating them to the content of the education. Patients also got the opportunity to ask for ergonomic advice for specific activities or situations and were able to practice lifting techniques during this session.

Outcome Measures

Outcome measures were assessed at baseline, and directly after three sessions of education. Additionally, socio-demographic and medical data such as age, gender, duration of symptoms, BMI and level of education were collected at baseline. All outcome measures were web-based questionnaires, consistent with other published versions.

Primary outcome measure

Pain Disability Index

The Dutch version of the Pain Disability Index (PDI-DV) measures the impact of pain on daily life activities. This questionnaire consists of 7 items, of which the participant has to indicate the level of perceived disability during that specific activity on an 11-point Likert scale ranging from 0 = no disability **to** 10 = completely disabled. These items include family/home responsibilities, recreation, social activity, occupation, sexual behaviour, self-care, and life-supporting activities (http://www.med.umich.edu/1info/FHP/practiceguides/pain/detpdi.pdf). The sum of scores on all items leads to a total score ranging from 0-70, with higher scores indicating higher levels of perceived disability. A change in the PDI-DV score is considered clinically important when it concerns a decrease of 8.5 to 9.5 points [35]. The PDI-DV is a valid tool with good internal consistency and good test re-test reliability [36].

Secondary outcome measures

Tampa Scale for Kinesiophobia

The Dutch version of the Tampa Scale for Kinesiophobia (TSK-DV) contains 17 statements regarding fear of movement or (re)injury, each scored on a 4-points Likert-scale (1 = strongly disagree; 4 = strongly agree). Total scores range from 17 to 68, with higher scores indicating higher fear of movement [37,38] (http://www.novopsych.com/tsk-2.html). The TSK-DV has a moderate construct and criterion validity and excellent test-retest reliability [38–40]. Based on the 2-factor model as proposed by Clark et al.[41], the TSK-DV can results into two subscales: "activity avoidance" (including 8 items) and "pathological somatic focus" (including 5 items) [42].

Illness Perception Questionnaire

The Dutch version of the Revised Illness Perception Questionnaire (IPQr-DV) measures several dimensions of illness perceptions (e.g. timeline of perceived symptoms, perceived control on symptoms, consequences of pain/symptoms/illness, causes of the pain/symptoms/illness, etc.), using 37 statements which are all scored on a 5-point Likert scale ranging from 1= strongly disagree to 5= strongly agree (http://www.uib.no/ipq/pdf/IPQ-R-English.pdf). These statements lead to 7 subscales. The subscales "acute/chronic timeline" (5 items) and "cyclical timeline" (4 items) assess the participant's beliefs about the course of their pain and the time scale of symptoms. The subscale "consequences" (6 items) assesses beliefs regarding the impact of the illness on quality of life and functional capacity. The subscales "personal control" (6 items) and "treatment control" (5 items) measure the perceived influence of own behaviour and treatment efficacy. The subscale "emotional representations" (6 items) assesses emotional responses generated by the illness. The subscale "illness coherence" (5 items) assesses to which degree a participant has a coherent understanding of his/her illness [43,44]. Higher scores relate to strongly held beliefs about the controllability of the illness,

the personal understanding of the condition, the number of symptoms attributed to the illness, the negative consequences of the illness, the chronicity of the condition, and the cyclical nature of the condition. Therefore, depending on the aspect of illness perceptions, the interpretation of scores will differ (e.g. a higher perceived controllability of the illness is positive, while higher negative consequences is a negative outcome). The IPQr-DV has a good test-retest reliability, factor structure, and predictive validity in different patient populations [44].

Pain Catastrophizing Scale

The Dutch Version of the Pain Catastrophizing Scale (PCS-DV) assesses catastrophic thoughts regarding pain (**http://sullivan-painresearch.mcgill.ca/pdf/pcs/PCSManual_English.pdf**), and contains 13 statements that describe different thoughts and feelings that one may experience when having pain. The participant is asked to score those statements on a 5-point Likert-scale (0 = not at all; 4 = all the time). Summing these scores leads to a total score or three subscales: rumination (4 statements), magnification (3 statements) and helplessness (6 statements). Higher scores indicate a higher degree of catastrophic thoughts regarding pain [45]. The PCS-DV has adequate reliability in various subgroups of musculoskeletal disorders [46] and has good criterion and construct validity [46,47].

Pain Vigilance and Awareness Questionnaire

The Dutch version of the Pain Vigilance and Awareness Questionnaire (PVAQ-DV) measures the patient's awareness/attention to pain in 16 statements, which are scored on a 6-point Likert scale (0 = Never; 5 = Always). Summing these scores, leads to a total score, which ranges from 0 to 80 with higher scores indicating a higher degree of pain awareness/attention. The questionnaire correlates highly with constructs like the PCS and general body vigilance [48]. The PVAQ-DV has good internal consistency and test-retest reliability, validity and reliability in several chronic pain populations [48–50].

Statistical Analysis

Data were analysed using SPSS 22.0 (SPSS Inc. Headquarters, Chicago, Illinois, USA). All data were analysed using the intention-to-treat principle (i.e., first-observation-carried-forward). This approach was used to handle missing data, as removing dropouts would lead to biased results. We chose the most conservative way to handle dropouts, because there were only two moments of assessment and both moments were very close to each other, leading to the assumption that baseline values of the dropouts would be most representative. Effectiveness of interventions was analysed using ANCOVA analyses with time as within-subject factor, treatment group as between-subject factor, and gender and age as covariate. However, as both covariates did not interact significantly in any variable, the analysis was performed again without covariates. The assumption of homogeneity and sphericity was checked by Levene's and Mauchly's test respectively. When the assumption of sphericity was violated, Greenhouse-Geisser corrections were used. Significant interaction effects were evaluated using Bonferroni post-hoc analysis. Cohen's D effect sizes were calculated. The Minimal Important Differences were calculated using the method described by Armijo-Olivo et al.[51].

Role of the Funding Source

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RESULTS

One-hundred-twenty patients with nCSP were included in this study. Participants were recruited from January 2014 to January 2016. Nine persons dropped out before completion of the second round of questionnaires (post-education), due to a busy job, personal life or participation in another treatment. Participants' baseline characteristics are presented in table 1. Figure 1 comprises the CONSORT flow diagram.

Primary Outcomes

There were no significant interaction or main effects for the PDI-DV. Detailed results are displayed in table 2.

Secondary Outcomes

Significant interaction effects were seen for the TSK-DV (p=.002). Post-hoc analysis showed that only in the PNE group kinesiophobia reduced significantly (12% improvement; Cohen's D = .56 **–** medium effect size), leading to significantly lower scores than the controls. Similar results were found for the two subscales of the TSK-DV: 'activity avoidance' and 'pathological somatic focus' only reduced significantly in the PNE group (respectively 11 and 13% improvement; Cohen's D = .38 and .46 – small to marginal medium effect size). Detailed results are displayed in table 2.

Regarding the IPQr-DV, subscales 'negative consequences' (p=.003), 'timeline cyclical' (p<.000) and 'timeline acute/chronic' (p=.003) showed significant interaction effects. Post-hoc analysis showed that following subscales only improved in the PNE group: 'negative consequences (13% improvement; Cohen's D = .42 **–** small effect size) and 'timeline cyclical' (9% increase; Cohen's D = .37

– small effect size); all leading to a significant better score in the PNE group post-education. Additionally, both groups showed a significant reduction of the ' timeline acute/chronic' subscale, but this reduction was greater in the PNE group (17% improvement; Cohen's D = .86 – large effect **size**), leading to a significant lower post-education score than the control group. For other IPQr subscales, only a significant main effect of time was seen ($p \leq .004$), except for the 'emotional representation subscale', which showed no significant interaction of main effects. Detailed results are displayed in table 2.

Also, a main effect of time was found for the PCS subscales helplessness (p=.003) and rumination (p=.033) as well as the total score (p=.010); but no significant interaction or main effects for the PCS magnification subscale. Last, a main effect of time was found for the PVAQ total score (p=.002), but no differences between groups were found (p=.798). Detailed results are displayed in table 2.

DISCUSSION

This study aimed at investigating the effects of PNE using a blended learning approach in people with nCSP. While PNE was not able to reduce perceived disability, results indicate that PNE, and not back/neck school, is capable of reducing kinesiophobia, the perceived negative consequences and the perceived chronicity in patients with nCSP. Moreover, PNE was shown to increase the perceived symptom fluctuations in patients with nCSP. Last, neither therapy was able to reduce pain catastrophizing **(**PCS) or hypervigilance (PVAQ).

Before discussing these positive results, they need to be put into the right perspective. Although p-values indicate a significant positive effect in favour of PNE, the obtained effect sizes and actual

percentages of improvement remain small to moderate (except for the large effect size in IPQr 'Timeline acute/chronic'). Additionally, only the TSK-DV (total score and subscales) group differences post education exceeded the minimal important difference. Therefore, it becomes clear that PNE alone is unable to substantially improve pain cognitions and perceptions in people with nCSP. Hence, it should be recommended to evaluate the effect of PNE over a longer period (e.g., in order to look for actual behavioural changes), and not to use PNE as a solitary therapy, but rather in combination with other treatment modalities to remove barriers, improve expectations and alliance and thus enhance their effect [13,14,52].

Previous studies investigating PNE have reported an improvement in function and disability, which was not seen here (e.g. PDI-DV scores did not change in either group). It should be noted that in these previous studies a different questionnaire was used to quantify disability, i.e., the Roland Morris Disability Questionnaire and the Neck Disability Index respectively [20,22,52]. These questionnaires are more specific to the particular patient populations, while we used a more general questionnaire (PDI-DV), as the included population comprised both people with chronic neck and low back pain.

However, when looking at kinesiophobia, the present study results are consistent with previous research showing that PNE is able to reduce kinesiophobia in people with chronic whiplash-associated-disorders and chronic low back pain [20,22,52]. Kinesiophobia often occurs from an ignorance regarding **and a biomedical focus towards** pain symptoms[53]. PNE tries to address both elements by providing patients with a clear, understandable and valid explanation for the symptoms and by teaching the patients about the role of the nervous system in explaining their symptoms. Patients with nCSP often believe that pain is resulting from and related to tissue damage, while research has shown that radiological imaging findings are often unrelated to the pain problem[3]. PNE helps these

patients to understand the underlying mechanisms of their pain problem; by explaining that pain is a result of a hypersensitive pain system rather than the result of a damaged spine. PNE also focusses on the positive influence of physical activity on pain. The combination of both (insight into the underlying mechanisms of pain and the value of physical activity) allows them to move the spine without being afraid of creating more damage, possibly resulting in a decrease in kinesiophobia. Although several pain cognitions and perceptions improved in both study groups, only PNE was capable to reduce kinesiophobia, a result that was not seen for biomedically-focussed back/neck school. This is a significant finding as kinesiophobia has been defined as a strong predictor for chronification in people with low back pain [54] and neck pain [55], and a decrease in kinesiophobia is related to larger improvements in pain and disability [56] and better therapy outcome[17]**.** Additionally, a decrease in kinesiophobia has been identified as mediating factor in increasing participation in daily and social life activities, implying that a reduction might enhance an active rehabilitation in nCSP [57].

The effect of PNE on altering pain or illness perceptions has received little attention in the literature so far. This study shows that PNE can the perceived chronicity and negative consequences of the illness in a positive way. This is not an odd finding, as PNE aims at giving a patient insight into the exact underlying mechanisms of pain and its sustaining and influencing factors. This helps patients to put the pain into the right perspective, possibly helping them to relativize the symptoms and the related consequences. This is an important finding as an improvement in perceptions and beliefs regarding an illness is related to better therapy outcome[18,19]. One particular finding was that PNE can significantly increase the perceived fluctuations of symptoms, indicating that PNE leads to stronger beliefs of unpredictability and cyclicity of the illness [48]. In this particular study, it is important to interpret the increase of this subscale within the content of PNE. PNE teaches patients that it is normal that chronic pain has a fluctuating and unpredictable nature and are taught how to cope with

it. Therefore, a significant increase in this subscale could represent the increased knowledge and acceptance, rather than a negative outcome of PNE.

Either way, PNE imparts a change in pain cognitions and perceptions by redefining pain. Due to this reconceptualization, participants may be more open to activities and movements that they feared prior to the education, they may be more keen to challenge catastrophic thoughts regarding pain and their perceptions may be changed into more correct ones. All those effects may possibly lead to less attention for pain. These positive effects of PNE are important as patients may see themselves as less disabled, leading to an increase in activities [58–60], while the presence of catastrophic thoughts and kinesiophobia is associated with pain persistence and avoidance behaviour [61–64]. Given the evidence for the importance of physical activity and exercises in the management of nCSP [65–67], PNE becomes an essential part of nCSP interventions.

Strengths, limitations and recommendations for further research

Although this is the first sufficiently powered study with a large sample size to investigate the effects of PNE in patients with nCSP, effect sizes small to moderate, which might raise the concern of limited clinical utility. Still, the TSK-DV scores exceed the minimal detectable difference, and IPQr 'Timeline acute/chronic' shows even a large effect size. Also, lack of larger effect sizes and significant effects in the primary outcome variable might be due to the short follow-up period, the choice of outcome measures, or their sensitivity for change. Future researchers might want to use outcome measures more specific to the study population like the Roland Morris Disability Questionnaire for patients with chronic low back pain and the Neck Disability Index for patients with chronic neck pain. Nevertheless, some people might need more than three sessions of PNE, as not everyone is open to new insights and beliefs regarding pain and some might need more time or a more individual

approach. In clinical practice, the physical therapist therefore needs to make sure that PNE is tailored to the individual patient. Moreover, PNE should not be used as sole treatment modality, but rather combined with other treatment strategies to enhance their (synergistic) effect. This has already been investigated in a small study with positive results [13,14], but should be considered for consolidation in further research with large sample sizes and sufficient power.

Further research should also consider long-term follow-up to investigate whether positive results of PNE remain over time, as recently shown in a trial of presurgical PNE in people with lumbar radiculopathy [8]. Also, in this study patients with chronic low back pain and chronic neck pain were investigated as one group to comply with the a priori defined power. Future research should focus specifically at patients with chronic neck pain as PNE has not been investigated as such in this population. Additionally, this study only focussed on subjective self-reported questionnaires, but further research should also consider objective outcome measures for pain and function. Last, this study provides evidence that blended learning can be used in a PNE educational setting. However, as there was no control group that received PNE without an online component, no assumptions can be made on the specific effectiveness of blended learning itself. Therefore, future research might focus on the best treatment modalities to deliver PNE by comparing different approaches.

Next to the large sample size (n=120) and adequate power, this study was conducted as multi-centric, which is a considerable strength. Other study strengths include the balanced treatment arms, triple blind randomized design, use of reliable and valid outcomes and the a priori study protocol publication [68]. In addition, this is the first study to examine the effects of blended learning PNE.

CONCLUSION

PNE, and not neck/back school education, is able to improve kinesiophobia, beliefs regarding the negative impact of the illness on quality of life and functional capacity, and beliefs regarding the chronicity of pain and the time scale of illness symptoms. However, none of the educational programs of this study was able to decrease the participants perceived disability due to pain. Nevertheless, as kinesiophobia in particular is generally considered to be a strong predictor and mediator of chronic pain, PNE is preferred as education approach for people with nCSP.

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Ethics Approval

The trial was approved by the local ethics committees at University Hospital Ghent and University Hospital Brussels.

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Clinical Trial Registration

The full study protocol (of which the present trial is a part) is registered in the Clinical Trials Registry of the National Institutes of Health (ClinicalTrials.gov identifier: NCT02098005).

Disclosure and Presentations

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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Table 1. Baseline Characteristics of Participants With Chronic Spinal Pain (N=120) [a]

Baseline Characteristic	**Experimental Group (n=60)**	**Control Group (n=60)**
Dominant pain problem (no. of participants with NP/LBP)	32/28	32/28
Diagnostics[b]		
Chronic LBP	26 (43.3)	28 (46.7)

Chronic failed back surgery syndrome	2 (3.3)	0 (0)
Chronic idiopathic NP	24 (40.0)	27 (45.0)
Chronic whiplash-associated disorders	8 (13.3)	5 (8.3)
Sex (no. of women/men)	38/22	35/25
Duration of pain, mo[c]	97.00 (154.50)	67.00 (132.00)
Body mass, kg[c]	66.00 (17.75)	70.00 (18.00)
Body height, cm[d]	172.86±8.86	171.52±10.65
Educational level (no of participants with no degree/lower secondary/higher secondary/higher education)	0/4/11/45	0/8/13/39
Working h/wk[c]	40.00 (13.25)	40.00 (14.00)
Age, y[c]	37.50 (24.30)	42.00 (21.00)
Age, y (minimum–maximum)	20–65	19–65
PDI-DV Total score[c]	21.64 (14.69)	21.58 (13.43)
PDI-DV Subitems		
Family/Home Responsibilities[c]	3.67 (2.63)	4.00 (2.39)
Recreation[c]	4.78 (2.55)	4.70 (2.57)

Social activity[c]	2.77 (2.61)	2.72 (2.74)
Occupation[c]	4.04 (2.72)	4.07 (2.56)
Sexual behavior[c]	2.67 (2.73)	2.30 (2.58)
Self-care[c]	1.68 (2.43)	1.65 (2.07)
Life-support activities[c]	2.17 (2.37)	2.15 (2.48)
TSK-DV score		
Total[c]	34.37 (7.09)	36.72 (6.85)
Activity avoidance[d]	15.80±4.57	17.08±4.48
Pathological somatic focus[d]	9.50±2.84	10.70±3.07
IPQr-DV score		
Timeline[c]	23.85 (4.18)	23.23 (3.61)
Consequence[c]	16.52 (4.94)	16.65 (4.55)
Personal control[c]	20.18 (4.11)	20.85 (4.21)
Treatment control[c]	16.83 (2.56)	17.23 (2.94)
Illness coherence[c]	17.05 (2.48)	16.45 (2.56)
Timeline cyclical[c]	13.10 (3.39)	13.17 (3.00)
Emotional representations[c]	14.93 (4.27)	14.53 (5.20)
PCS-DV score		
Total[c]	16.53 (9.75)	16.85 (10.54)

Subscale rumination[c]	6.52 (4.11)	6.50 (4.18)
Subscale magnification[c]	2.45 (2.20)	2.75 (2.28)
Subscale helplessness[c]	7.57 (4.64)	7.60 (5.29)
PVAQ-DV score[c]	36.90 (11.91)	35.77 (12.66)

[a] IPQr-DV= Dutch version of the Revised Illness Perception Questionnaire, LBP=low back pain, NP=neck pain, PCS-DV= Dutch version of the Pain Catastrophizing Scale, PDI-DV=Dutch version of the Pain Disability Index, PVAQ-DV= Dutch version of the Pain Vigilance and Awareness Questionnaire, TSK-DV= Dutch version of the Tampa Scale for Kinesiophobia.

[b] Values are presented as number (percentage) of participants.

[c] Values are presented as median (interquartile range) for continuous data that were observed to be not normally distributed.

[d] Values are presented as mean±SD for continuous normally distributed data.

Table 2. Effectiveness of Blended-Learning Pain Neuroscience Education (PNE) in Participants With Chronic Spinal Pain (N=120)[a]

Questionnaire	Measurement	Experimental Group (n=60)	Control Group (n=60)	Mean Group Difference (95% CI)	Minimal Important Difference	ANOVA (*P*)		Bonferroni Post Hoc Analysis (*P*)	
						Interaction Effect (*P*)	Main Effect of Group		
PDI-DV score	Baseline	21.64±14.69	21.58±13.43	−0.22 (−5.29 to 4.86)	7.04	.241	.704	N/A	
	Posteducation	20.90±12.31	22.73±13.21	1.84 (−2.80 to 6.47)					
	Cohen *d*	0.07	0.09						
TSK-DV score									
Total	Baseline	34.37±7.09	36.72±6.85	0.07 (−0.17 to 4.87)	**3.49**	**.002**		Time	**<.001**[b]
	Posteducation	30.32±7.25	35.73±6.86	5.42 (2.86 to				Group	Posteducation: **<.001**
	Cohen *d*	0.56	0.14						

				7.97)					
Activity avoidance	Baseline	15.80±4.57	17.08±4.48	1.28 (−0.35 to 2.92)	**2.26**	**.048**		Time	**.001**[b]
	Posteducation	14.12±4.26	16.77±4.14	2.65 (1.13 to 4.17)				Group	Posteducation: **.001**
	Cohen *d*	0.38	0.07						
Pathological somatic focus	Baseline	9.50±2.84	10.70±3.07	1.20 (0.13 to 2.27)	**1.48**	**.026**		Time	**<.001**[b]
	Posteducation	8.25±2.54	10.45±2.92	2.20 (1.21 to 3.19)				Group	Posteducation: **<.001**
	Cohen *d*	0.46	0.08						
IPQr-DV score									
Timeline acute/chronic	Baseline	23.85±4.18	23.23±3.61	0.39 (−2.03 to 0.79)	1.95	**<.001**		Time	**<.001**[b,c]
	Posteduc	19.92±5.	21.58±3	1.67				Gro	Posteduc

	ation	10	.92	(0.02 to 3.31)				up	ation: **.047**
	Cohen *d*	**0.86**	0.42						
Consequence	Baseline	16.52±4.94	16.65±4.55	0.88 (−1.58 to 1.85	2.37	**.003**		Time	**<.001**[b]
	Posteducation	14.55±4.35	16.45±4.50	1.90 (0.30 to 3.50)				Group	Posteducation: **.020**
	Cohen *d*	0.42	0.06						
Personal control	Baseline	20.18±4.11	20.85±4.21	0.38 (−0.84 to 2.17)	2.08	.160	.740	N/A	
	Posteducation	22.43±3.16	22.15±2.94	−0.28 (−1.39 to 0.82)					
	Cohen *d*	0.61	0.36						
Treatment control	Baseline	16.83±2.56	17.23±2.94	0.43 (−0.60 to 1.40)	1.38	.175	.832	N/A	
	Posteducation	17.92±2.31	17.68±2.12	−0.23 (−1.04					

	Cohen *d*	0.44	0.18	to 0.57)					
Illness coherence	Baseline	17.05±2.48	16.45±2.56	0.20 (−1.51 to 0.31)	1.26	.641	.234	N/A	
	Posteducation	17.58±2.38	17.18±2.84	−0.40 (−1.35 to 0.55)					
	Cohen *d*	0.23	0.27						
Timeline cyclical	Baseline	13.10±3.39	13.17±3.00	0.91 (−1.09 to 1.22)	1.60	**.003**		Time	**<.001**[b]
	Posteducation	14.32±3.09	12.95±3.38	−1.37 (−2.54 to −0.20)				Group	Posteducation: **.023**
	Cohen *d*	0.37	0.07						
Emotional representations	Baseline	14.93±4.27	14.53±5.20	0.65 (−2.12 to 1.32)	2.38	.958	.636	N/A	
	Posteducation	15.33±4.23	14.97±5.24	−0.37 (−2.09					

	Cohen *d*	0.09	0.08	to 1.36)				
PCS-DV score								
Rumination	Baseline	6.52±4.11	6.50±4.18	−0.17 (−1.52 to 1.48)	2.07	.536	.778	N/A
	Posteducation	6.08±3.75	5.72±4.03	−0.37 (−1.77 to 1.04)				
	Cohen *d*	0.11	0.19					
Magnification	Baseline	2.45±2.20	2.75±2.28	0.30 (−0.51 to 1.11)	1.12	.272	.827	N/A
	Posteducation	2.55±2.20	2.40±2.07	−0.15 (−0.92 to 0.62)				
	Cohen *d*	0.05	0.16					
Helplessness	Baseline	7.57±4.64	7.60±5.29	0.97 (−1.77 to 1.83)	2.49	.862	.984	N/A

	Posteducation	6.73±4.99	6.67±4.75	−0.07 (−1.83 to 1.70)				
	Cohen *d*	0.17	0.18					
Total	Baseline	16.53±9.75	16.85±10.54	0.87 (−3.35 to 3.99)	5.08	.464	.938	N/A
	Posteducation	15.37±9.74	14.78±9.48	−0.58 (−4.06 to 2.89)				
	Cohen *d*	0.12	0.21					
PVAQ score	Baseline	36.90±11.91	35.77±12.66	0.62 (−5.58 to 3.31)	6.15	.463	.798	N/A
	Posteducation	33.72±11.13	33.78±13.16	0.07 (−4.34 to 4.47)				
	Cohen *d*	0.28	0.23					

[a] All questionnaires represented secondary outcome measures, except for the Dutch version of the Pain Disability Index (PDI-DV), which represented a primary outcome measure. Baseline and posteducation measurements for the experimental and control groups are reported as mean±standard deviation. Cohen *d* is a measure of effect size (0.20=small, 0.50=medium, 0.80=large). Bold type indicates large effect sizes (exceeding the minimal important difference) and significant *P* values. ANOVA=analysis of variance, PDI-DV= Dutch version of the Pain Disbility Index, IPQr-DV= Dutch

version of the Revised Illness Perception Questionnaire, N/A=not applicable, PCS-DV= Dutch version of the Pain Catastrophizing Scale, PVAQ-DV= Dutch version of the Pain Vigilance and Awareness Questionnaire, TSK-DV= Dutch version of the Tampa Scale for Kinesiophobia.

[b] Significant difference in the PNE (experimental) group.

[c] Significant difference in the control group

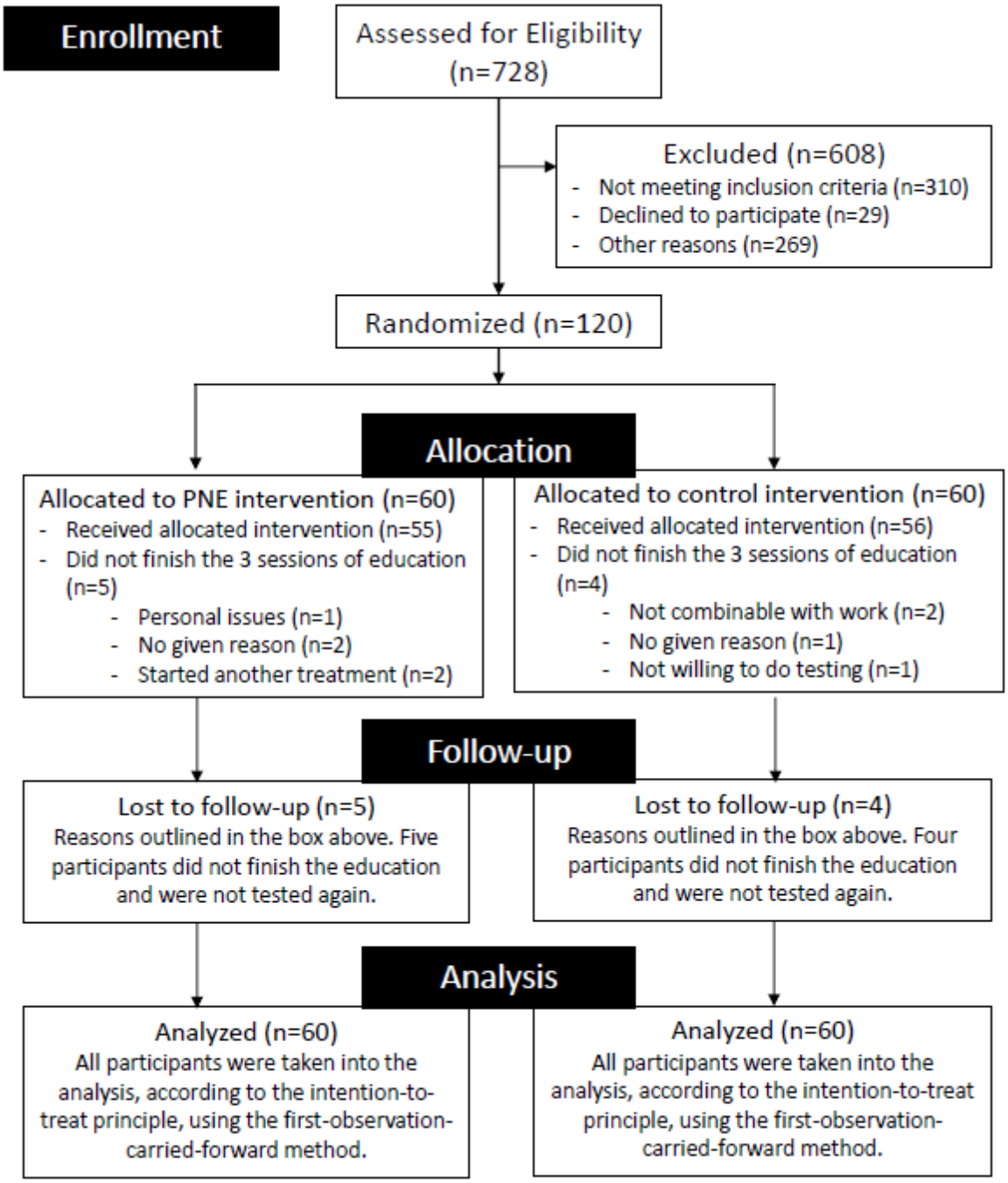

Figure. Study flow diagram. PNE=pain neuroscience education.