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Hypnosis enhances the effects of pain education in patients with chronic non-specific low back pain: a randomized controlled trial

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Conflict of Interest: RRNR is an instructor of Continous Education Courses of Clinical Hypnosis and Pain Education for chronic pain conditions. MPJ is the author of three books on hypnosis, and receives royalties for the sale of these books.
Highlights

- Hypnosis can be combined with education in patients with chronic low back pain.
- The addition of hypnosis improves pain intensity, disability, and catastrophizing.
- The beneficial effects are enhanced, at least in the short and medium-term.
- The intervention can be offered in group settings.

ABSTRACT

The potential benefits of combining pain education (PE) with clinical hypnosis (CH) has not yet been investigated in individuals with chronic pain. A total of 100 patients with chronic non-specific low back pain were randomized to receive either (1) PE alone or (2) PE plus CH. Outcomes were collected by a blinded assessor at 2 weeks and 3 months after randomization. The primary outcomes were average pain intensity, worst pain intensity (both assessed with 11-point Numerical Rating Scales), and disability (24-item Roland Morris Disability Questionnaire) at 2 weeks. At 2 weeks, participants who received PE plus CH reported lower worst pain intensity (mean difference = 1.35 points, 95% confidence interval [CI] = 0.32 to 2.37) and disability (mean difference = 2.34 points, 95% CI = 0.06 to 4.61), but not average pain intensity (mean difference = 0.67 point, 95% CI = -0.27 to 1.62), relative to participants who received PE alone. PE plus CH participants also reported more global perceived benefits at 2 weeks (mean difference = -1.98 points 95% CI = -3.21 to -0.75). At three months, participants who received PE plus CH reported lower worst pain intensity (mean difference = 1.32 points, 95% CI = 0.29 to 2.34) and catastrophizing (mean difference = 5.30 points, 95% CI = 1.20 to 9.41). No adverse effects in either treatment condition were reported. This is the first trial showing that adding hypnosis to PE results in improved outcomes over PE alone in patients with chronic non-specific low back pain. This trial was prospectively registered at clinicaltrials.gov: NCT02638753
Perspective: This study provides evidence supporting the efficacy of another treatment option for teaching patients to self-manage chronic low back pain that has a relatively low cost and that can be offered in groups.

Keywords: Education, Neurophysiology, Hypnosis, Low Back Pain, Randomized Controlled Trial
**Introduction**

Chronic non-specific low back pain is a common condition [35] which is associated with high financial costs [32; 51] and disability [3; 17]. The available biomedical interventions are typically not very effective at reducing pain or disability [18], are often associated with negative side effects [1], or involve treatment from a variety of different health care professionals, which increases costs [27]. A relatively simple intervention provided by physical therapists – patient education – has demonstrated efficacy, but its effects tend to be modest [6; 13; 37]. One particular type of education is *pain biology education*, which seeks to help patients understand the biological processes related to their pain experience [33]. This intervention has shown promise for reducing disability, catastrophizing, and increasing function [34; 42].

Hypnotic treatment for pain conditions has received more attention recently [21; 25; 30], perhaps in part of the lack of efficacy of more traditional biomedical interventions. When used for pain treatment, hypnosis typically involves an “induction” during which the clinician invites patients to experience a state of focused awareness, followed by suggestions for changes in the sensory, cognitive and emotional domains of pain experience [22].

The most recent systematic reviews conclude that hypnosis reduces pain intensity compared to usual care and when combined with other interventions for a variety of chronic conditions [2; 21; 50]. Only three studies have investigated the effects of hypnotic suggestion in patients with chronic low back pain [15; 38; 49]. Some authors have proposed that the beneficial effects of cognitive-behavioral therapy (CBT) for patients with chronic pain could be enhanced by combining CBT with hypnosis [23; 29]. Combining pain education with hypnosis has not yet been investigated, however [41].

Given these considerations, we designed the current study to evaluate the effects of adding hypnosis to pain education. We hypothesized that patients with chronic low back pain
who received pain education with hypnosis would report greater improvements in pain intensity and disability (primary outcomes) as well as patient specific function, catastrophizing, and global perceived benefits (secondary outcomes), relative to those randomized to receive pain education alone.

Methods

Study Design, Setting and Participants

This trial was prospectively registered at www.clinicaltrials.gov (NCT02638753). There was no deviation from the original registered protocol. This is a 2-arm randomized controlled trial with the outcome assessor blinded to the group allocation (see Figure 1). The primary source of participants was the waiting list of the outpatient physical therapy clinic of the Universidade Cidade de São Paulo, Brazil. The interventions were conducted in classrooms of the university from February to November 2016.

Potential participants were informed that they would be randomized to receive one of “two different widely used pain education programs that have been found to be helpful for patients with chronic pain.” Patients were invited to participate if they had non-specific low back pain of at least 3 months, were aged between 18 and 80 years old, and had a minimum score of 3 on 0-10 pain numerical rating scale (NRS) of average pain intensity. Patients who were receiving physical therapy at the time of recruitment, with any contraindication to exercise, serious spinal pathologies, previous spinal surgery, nerve root compromise, cardiorespiratory illness, pregnancy, hearing problems, low back pain as secondary complaint, illiteracy, inability to attend treatment sessions, were excluded. The institutional human ethics committee of the Universidade Cidade de São Paulo approved this trial. All study participants provided written informed consent.

Randomization
A simple randomization sequence was generated using the Microsoft Excel program by one of the study investigators who was not directly involved with the study assessments or treatment. During the baseline assessment, participants received information about the study and signed a consent form to participate in the study. After the baseline assessment the therapist opened the randomization envelope and the participant was allocated into one of the two treatment groups. The allocation was concealed by using consecutively numbered, sealed, opaque envelopes. The envelopes were opened when the participants arrived for treatment, and the first session was conducted immediately after the baseline assessment that same day.

**Blinding**

The outcome assessor was blind to group allocation. Given the nature of interventions, it was not possible for the therapist or the study participants to be blind to treatment condition.

**Interventions**

Participants from both groups received pain education based on information from the *Explain Pain* book[5], and the second group received additional hypnotic suggestions. Both interventions were provided in the same group setting. The interventions were carried out in a group with up to 7 participants per class (varying from 1 to 7 participants). The frequency (four sessions, twice a week) and content of pain education were standardized in both groups. Participants from both groups received a workbook with the same pain education content given in each class. The clinician who treated the patients from both groups (RRNR) was a physical therapist with 13 years of clinical experience, including six years of experience in the delivery of pain education and clinical hypnosis for pain. The therapist was certified in hypnotherapy and received guidance from a psychologist certified by American Society of Clinical Hypnosis (ASCH).

**Pain education group (PE).** The PE classes used the same pictures, stories, metaphors and examples described in the the *Explain Pain* book[5]. Participants were
encouraged to ask questions during the classes. At the end of each class, the information presented was reviewed. A workbook was given to the participants with the same content offered during the classes, and the participants were asked to read the content after each class at home. Information provided during the classes included: pain as a normal experience (first class); components and function of the danger alarm system, and modulation of danger messages at the spinal cord level (second class); altered central nervous system alarms, and response systems in the pain experience (third class); and education and understanding that “hurt does not necessarily equal harm”, pacing and graded exposure (fourth class)[5].

**Pain education plus clinical hypnosis group (PE+CH).** Participants allocated to the PE+CH group received a total of 6 hours and fifteen minutes of treatment. The only difference between the PE and the PE+CH groups was the addition of a total 2 hours and fifteen minutes of hypnosis distributed over the 2 weeks of treatment, and a hypnosis workbook to read at home with the same hypnotic suggestions offered in the classes. In order to ensure that the content of the pain education treatment component was the same for both groups, the hypnotic suggestions were added to the pain education components. For this reason, the total duration of sessions was different between groups.

To increase acceptability of hypnosis to the participants, the pain education content was interspersed with hypnotic suggestions. For example, the participants were told, “Each hypnotic experience is intended to adjust each part of the danger alarm system.” The hypnotic inductions started with stories and metaphors related to the pain education content. After this, the participants were invited to focus their attention while looking at a spot on the wall in front of them. A brief summary of the content of each hypnotic session are described below (more detailed information about the content of the hypnotic suggestions are provided in the Supplementary Appendix):

- First class: Addressing hypnosis myths and benefits[20]. The first hypnotic experience was
intended to suggest an openness to the possibility of change. The suggestions reinforced the idea that the brain has many capacities that can be used to create comfortable experiences. Some brief suggestions explored the capacities of relaxation, dissociation (between body and mind), analgesia, and age regression to previous pleasant experiences.

- Second class: Patients had two hypnotic experiences during the second class. The first experience was connected to the idea expressed in the Explain Pain book that “… sensors are often replaced by new and fresh ones”[5]. We offered through hypnotic suggestions that an adaptation in the sensors is possible[46]. The second hypnotic experience was related to the content of descending inhibitory modulation at the level of spinal cord. The suggestion was adapted hypnotic analgesia[20], which invites patients to experience analgesic sensations in their body.

- Third class: Patients were given two hypnotic suggestions during the third class. The first was connected to the idea that “the brain can receive amplified messages from the tissues, even when there is nothing wrong with the structure of the body”[5], and included suggestions for decreased pain unpleasantness, which invited participants to experience comfort even with the presence of some sensations in their body[20]. The second hypnotic suggestion was related to the idea of “the brain orchestra can play a different song”[5]. We offered “sensory substitution” suggestions[20], which invited participants to experience a comfortable sensation of their hands spreading to other parts of the body.

- Fourth class: During the fourth class, the participants were given three different hypnotic suggestions. The first two were related to the motor responses. The first was a “deep relaxation” suggestion[20], during which participants were invited to relax each muscle of their body. The second was an “age regression and progression” suggestion[20], during which participants were invited to bring adaptative pain responses from the past or the future into the
present. Both of these hypnotic suggestions reinforced the importance of physical movement as a way to extend the benefits. The last hypnotic experience of this class offered a metaphor to help the patients use some of the information they have learned to manage negative thoughts during the day. After each class, the participants were asked to read the hypnosis workbook and to practice self-hypnosis briefly at home. The Explain Pain workbook was also provided during the last session.

**Follow-up**

Patients were evaluated by an assessor who was blind to treatment allocation at baseline and after 2 weeks and 3 months after randomization. Patients who did not finish all interventions in 2 weeks had an opportunity to complete the sessions in the following 2 weeks. After this period, the first follow-up assessment (2 weeks follow-up) was concluded. All baseline assessments were conducted in person. Participants who completed all four sessions were evaluated in person, and participants who did not complete all four sessions were evaluated by telephone at 2 weeks. All patients were contacted at 3 months by telephone to collect follow-up data.

**Measures**

The primary outcome measures were pain intensity (average and the worst pain over the past week, measured using 0-10 pain numerical rating scales; NRS)[7; 24] and disability (measured by the 0-24 Roland–Morris Disability Questionnaire-RMDQ)[8; 43] at 2 weeks after randomization. The secondary outcome measures were: (1) pain intensity (average and worst pain)[7; 24] and disability[8; 43] assessed at 3 months after randomization; (2) catastrophizing (measured by 0-52 The Pain Catastrophizing Scale-PCS)[48]; (3) function (measured by the 0-10 The Patient-Specific Function Scale-PSFS)[7; 19]; and (4) global impression of change (measured by -5 to +5 Global Perceived Effect Scale-GPE)[28] at 2 weeks and 3 months after randomization. Sociodemographic, clinical information and
expectation of improvement with the treatment were obtained at baseline. During all telephone follow-up interviews, the occurrence of potential adverse effects was assessed by asking: “Since you started receiving this treatment, have your symptoms become worse?” To assess the expectation of improvement with the treatment, the follow question was asked: “In your opinion, what is your expectation that your symptoms will improve with this treatment (measured by the 0-10 expectation numerical rating scale)?”[11]. All outcome measures used in this trial were cross-culturally adapted into Brazilian-Portuguese and successfully tested for their measurement properties[7; 8; 19; 43; 48]. There were no changes made to the outcome measures after trial commencement.

**Sample Size**

We designed the study to detect a between-group differences of at least 1 point in pain intensity measured by the NRS, with an estimated standard deviation of 2 points, and a between-group difference of 4 points for disability measured by the RMDQ, with an estimated standard deviation of 5 points[9; 36]. The specifications were: a power of 80%, an alpha coefficient of .05, and a possible loss to follow-up of up to 15%[39]. Therefore, a total of 100 participants were enrolled into the study. The estimates for powering the study were lower than the minimal clinical important difference for patients with low back pain[44]. The rationale for powering the study to detect a change in pain that is less than the minimally clinically important difference was that most published clinical trials of pain education have not achieved this effect size. Therefore, we designed the study to be sufficiently powered to be able to detect at least the effect sizes shown in earlier studies.

**Statistical Analyses**

Statistical analyses were conducted using intention-to-treat principles. The between-group differences and their respective 95% confidence intervals were calculated using linear mixed models. We also estimated the number needed to treat for the primary outcomes by
dichotomizing patients who had reached the minimal clinically important difference compared with those who had not reached minimal clinically important difference. The cutoffs used for determining minimal clinically important differences in pain intensity (a reduction of at least 2 points or 30% on the NRS scale, relative to baseline) and disability (a reduction of at least 5 points or 30% on the RMDQ, relative to baseline) was determined based on previous studies relating these scales to global assessments of change[4; 12; 14]. We used SPSS 22 for Mac for all statistical analyses.

Results

Two hundred and seventy patients who were seeking care for low back pain at the physical therapy clinic from February to November, 2016, were approached for possible participation. Forty-three (16%) of these declined participation, 127 (47%) were excluded and 100 (37%) were eligible and agreed to participate (see Figure 1). The primary reasons for exclusion were inability to attend treatment sessions (n=33), low back pain as secondary complaint (n=25), presence of an acute low back pain episode (n=17), being less than 18 years old or more than 80 years old (n=13), receiving physical therapy at the time of recruitment (n=12), having hearing problems (n=8), being illiterate (n=6), having a history of previous spinal surgery (n=4), presence of signs of nerve root compression (n=3), having no interest in hypnosis (n=2), having no interest in pain education (n=2), the presence of cardiorespiratory illness (n=1) and pregnancy (n=1).

All patients received the treatments as allocated. In the PE group, 86% (n=43) of the patients attended all classes, 8% (n=4) attended three classes, 4% (n=2) two classes and 2% (n=1) only one class of the program. In the PE+CH group, 88% (n=44) attended all four classes, 2% (n=1) three classes, 2% (n=1) two classes, and 8% (n=4) attended only one class of the program. Overall follow-up response rates were 99% (n=99) at both 2 weeks and 3
months. One of the patients in the PE+CH group dropped out the study and was lost to follow-up.

The baseline sociodemographic and clinical characteristics were similar in both groups (see Table 1). Most participants in both groups were women, with secondary level education, with a median duration of pain of 4 years and with moderate levels of average pain intensity and disability. Participants in both groups started treatment with a high expectation of improvement.

**Primary Outcomes**

There was no significant differences between the groups in average pain intensity at 2 weeks (mean difference [MD] = 0.67 point, 95% CI = -0.27 to 1.62) or 3 months (MD = 0.09 point, 95% CI = -0.85 to 1.04). However, patients enrolled in the PE+CH group reported lower worst pain intensity at both 2 weeks (MD = 1.35 points, 95% CI = 0.32 to 2.37) and 3 months (MD = 1.32 points, 95% CI = 0.29 to 2.34). They also reported significantly greater reductions in disability at 2 weeks (MD = 2.34 points, 95% CI = 0.06 to 4.61) (see Table 2).

**Secondary Outcomes**

With respect to the secondary outcomes, there was significant difference in favour of the PE+CH group for catastrophizing at 3 months (MD = 6.78 points, 95% CI = 2.08 to 11.48) and global perceived benefits at 2 weeks (MD = 1.98 points, 95% CI = -3.25 to -0.71) (see Table 2). The number needed to treat (NNT) were 2.9 (95% CI = 0.3 to 0.7) for the worst pain intensity and 5.1 (95% CI = 0.4 to 1.0) for disability at 2 weeks in favor of the PE+CH group.

The expectation of improvement between the groups were very similar at 2 weeks (MD = -0.00 point, 95% CI = -0.70 to 0.68) and at 3 months follow-ups (MD = -0.23 point, 95% CI = -0.92 to 0.46).
Participants in both groups reported similar frequency of home practice at 3 months (never or little: 14% in the PE and 20% in the PE+CH group; somewhat: 50% in the PE and 40% in the PE+CH group; much: 36% in the PE and 38% in the PE+CH group).

Adverse Effects

The percentage of patients who reported increased pain at 3 month follow-up was 12% (n=6) in the PE group, and 8% (n=4) in the PE+CH group (a non-significant difference; chi-square = 0.40, p = 0.53). No serious adverse effects were reported.

Discussion

To our knowledge, this is the first randomized controlled trial that has investigated the beneficial effects of combining clinical hypnosis with pain education for patients with chronic pain. We found that the addition of clinical hypnosis to pain education resulted in improved outcomes of worst pain intensity, disability and global perceived benefits in the short-term, compared to pain education alone. Moreover, adding pain education to clinical hypnosis maintained its superiority over pain education alone for reducing the worst pain intensity at medium-term, and also showed additional benefits in reducing catastrophizing at medium-term.

We prospectively registered the worst pain intensity as a primary outcome because similar hypnotic suggestions have been shown to influence this outcome in other chronic pain conditions[23]. Jensen and colleagues compared clinical hypnosis with cognitive restructuring and did not find a statistically significant difference in the average pain intensity, but detected a statistical difference in the worst pain intensity[23]. The reasons for finding significant effects for worst pain intensity but not for average pain intensity are not entirely clear. It is possible that when rating average pain intensity, patients might consider different cognitive
and emotional references than when rating worst pain intensity. Also, worst pain intensity
tends to be more strongly correlated with pain interference (mood, social relationships,
walking, work and enjoyment of life) than average pain[10]. Recently, a study showed that a
scale for measuring pain intensity may reflect patients’ perceptions about pain interference
and beliefs about their pain, and not only pain intensity[26]. In our study, patients who
received clinical hypnosis also evidenced a larger reduction in catastrophizing. There is
evidence that catastrophizing may, at least in part, influence pain intensity in chronic pain
conditions[30; 40]. Overall, the findings suggest the possibility that a greater variety of pain
experience domains might be influenced by clinical hypnosis than pain education alone.
Future studies could shed some light on this by testing the causal mechanisms that underlie
the effect of clinical hypnosis on different pain-related outcomes, including worst pain
intensity.

Previous studies that have evaluated the efficacy of hypnosis treatment (alone) for
chronic low back pain found no additional benefits for pain intensity, relative to other active
psychosocial pain treatments such as pain education, biofeedback, and relaxation[15; 38; 49].
The current findings suggest the possibility that combining different psychosocial
interventions may boost their overall efficacy. However, it is important to keep in mind that
the component parts of combination treatments may influence efficacy[23; 29; 31; 47]. For
example, exercise therapy has been shown to reduce the beneficial effects of pain
neuroscience education in patients with chronic low back pain[47]. On the other hand, there is
also evidence that hypnosis can increase the beneficial effects of cognitive behavioral therapy
for reducing worst pain intensity in patients with chronic pain and multiple sclerosis[23].
Research is needed to help determine which treatment combinations are most effective for
most patients.

This study has some important limitations that should be considered when interpreting
the results. As is the case with all psychosocial interventions, neither the therapist nor the
patients were blind to treatment condition. Thus, although the pain educational content and
pain education treatment time were the same in both treatment conditions, the participants in
the pain education plus hypnosis condition received more therapist attention overall, because
of the additional time needed for hypnosis. Further studies could compare the effects of pain
education plus hypnosis with pain education plus another intervention to control the potential
effects of therapy time. In addition, a single therapist who was aware of the study hypotheses
conducted the interventions; further research is therefore needed to determine if the current
findings generalize to other therapists, including those who might not be aware of the study
hypotheses.

Despite the study’s limitations, it also has some important strengths. The trial was
prospectively registered, used true randomization, concealed allocation, used outcome
assessors who were blind to treatment condition, used an intent-to-treat analysis and had very
high follow-up rates. In addition, a high percentage (87%) of attendance in all treatment
interventions was observed. The interventions were clearly defined and standardized, and
conducted by a therapist who had several years of experience delivering both interventions.
The participants were seeking physical therapy services and were very similar to patients
from previous clinical trials in back pain[16; 45], which increases the external validity of the
study. Moreover, the expectation of improvement with the treatments was similar in both
groups and at all assessment points. Thus, patient expectancies, either due to their beliefs
about hypnosis or as might have been influenced by the therapist, do not appear to have had a
biasing effect on the findings.

Summary and conclusions

The findings from this study indicate that clinical hypnosis enhances the effects of
pain education, at least in the short and medium-term. The study findings provide support for
another option for the management of chronic low back pain; a treatment option that has a relatively low cost (compared to many other pain treatments) and that can be offered in group settings.

Disclosures

Mr. Rizzo’s masters scholarship was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brazil. Other than this, none of the authors received any funding to finance the research reported here. RRNR is an instructor of Continuous Education Courses of Clinical Hypnosis and Pain Education for chronic pain conditions. MPJ is the author of three books on hypnosis, and receives royalties for the sale of these books.

Acknowledgments

We thank the guidance of Stephen Paul Adler who is a psychologist and hypnotherapist certified by the American Society of Clinical Hypnosis (ASCH).
References


Figure 1. Participants’ Flow Diagram. All patients received the treatments as allocated. Overall follow-up response rates were 99% (n=99) at both 2-weeks and 3-months.
### Table 1. Demographic and Clinical Characteristics of the Participants at Baseline (N=100)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pain Education (PE) (N=50)</th>
<th>PE plus Hypnosis (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>36 (72)</td>
<td>44 (88)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.4 (12.60)</td>
<td>51.7 (14.46)</td>
</tr>
<tr>
<td>Duration of pain (months)</td>
<td>50 (102)</td>
<td>48 (98)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.99 (12.94)</td>
<td>71.44 (15.55)</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>1.64 (0.06)</td>
<td>1.62 (0.06)</td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>17 (34)</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Married</td>
<td>27 (54)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>Divorced</td>
<td>6 (12)</td>
<td>15 (30)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Education status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>10 (20)</td>
<td>18 (36)</td>
</tr>
<tr>
<td>Secondary school</td>
<td>22 (44)</td>
<td>25 (50)</td>
</tr>
<tr>
<td>University</td>
<td>18 (36)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Use of medication</td>
<td>31 (62)</td>
<td>32 (64)</td>
</tr>
<tr>
<td>Physically active</td>
<td>17 (34)</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Smoker</td>
<td>7 (14)</td>
<td>10 (20)</td>
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<tr>
<td>Work compensation</td>
<td>1 (2)</td>
<td>3 (6)</td>
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<tr>
<td>Treatment expectation (0-10)</td>
<td>8.46 (1.69)</td>
<td>8.37 (1.85)</td>
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<tr>
<td>NRS average (0-10)</td>
<td>7.20 (1.61)</td>
<td>6.63 (1.57)</td>
</tr>
<tr>
<td>NRS worse (0-10)</td>
<td>8.18 (1.57)</td>
<td>8.31 (1.41)</td>
</tr>
<tr>
<td>RMDQ (0-24)</td>
<td>13.44 (5.02)</td>
<td>14.88 (5.10)</td>
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<tr>
<td>PCS (0-52)</td>
<td>28.16 (12.83)</td>
<td>28.92 (13.75)</td>
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<tr>
<td>PSFS (0-10)</td>
<td>3.63 (1.80)</td>
<td>4.38 (1.89)</td>
</tr>
<tr>
<td>GPE (-5 to +5)</td>
<td>-2.34 (2.67)</td>
<td>-2.29 (2.78)</td>
</tr>
</tbody>
</table>

Categorical variables are expressed as number (%), continuous variables are expressed as mean (SD), and duration pain is expressed as median (interquartile range). NRS = Pain Numerical Rating Scale; RMDQ = Roland Morris Disability Questionnaire; PCS = Pain Catastrophizing Scale; PSFS = Patient-Specific Function Scale; GPE = Global Perceived Effect Scale.
Table 2. Primary and secondary outcomes - Mean change by treatment group: unadjusted mean differences (SD). Mean (95% CI) differences between treatment groups: adjusted mean differences.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unadjusted Mean Outcome (SD)</th>
<th>Adjusted Treatment Effect (95% CI)</th>
<th>PE vs. PE plus Hypnosis Adjusted Mean Difference (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity average - NRS (0-10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7.2 (1.61)</td>
<td>6.6 (1.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>5.6 (2.21)</td>
<td>4.4 (2.14)</td>
<td>0.67 (-0.27 to 1.62)</td>
<td>0.16</td>
</tr>
<tr>
<td>3 months</td>
<td>5.1 (2.48)</td>
<td>4.4 (2.93)</td>
<td>0.09 (-0.85 to 1.04)</td>
<td>0.84</td>
</tr>
<tr>
<td>Pain intensity worse - NRS (0-10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>8.1 (1.57)</td>
<td>8.3 (1.41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>6.8 (2.49)</td>
<td>5.5 (2.06)</td>
<td>1.35 (0.32 to 2.37)</td>
<td>0.01*</td>
</tr>
<tr>
<td>3 months</td>
<td>6.1 (2.63)</td>
<td>4.9 (3.14)</td>
<td>1.32 (0.29 to 2.34)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Disability - RMDQ (0-24)</td>
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<tr>
<td>Baseline</td>
<td>13.4 (5.02)</td>
<td>14.8 (5.10)</td>
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<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>9.6 (6.45)</td>
<td>8.9 (6.40)</td>
<td>2.34 (0.06 to 4.61)</td>
<td>0.04*</td>
</tr>
<tr>
<td>3 months</td>
<td>7.6 (7.09)</td>
<td>7.2 (7.24)</td>
<td>2.07 (-0.19 to 4.35)</td>
<td>0.07</td>
</tr>
<tr>
<td>Catastrophizing - PCS (0-52)</td>
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<tr>
<td>Baseline</td>
<td>28.1 (12.83)</td>
<td>28.9 (13.75)</td>
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<tr>
<td>2 weeks</td>
<td>17.9 (14.43)</td>
<td>16.2 (11.00)</td>
<td>2.38 (-1.72 to 6.48)</td>
<td>0.25</td>
</tr>
<tr>
<td>3 months</td>
<td>14.3 (14.89)</td>
<td>9.8 (9.22)</td>
<td>5.30 (1.20 to 9.41)</td>
<td>0.01*</td>
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<tr>
<td>Function - PSFS (0-10)</td>
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<tr>
<td>Baseline</td>
<td>3.6 (1.80)</td>
<td>4.3 (1.89)</td>
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</tr>
<tr>
<td>2 weeks</td>
<td>5.4 (2.28)</td>
<td>6.0 (1.90)</td>
<td>0.08 (-0.84 to 1.00)</td>
<td>0.86</td>
</tr>
<tr>
<td>3 months</td>
<td>5.7 (2.30)</td>
<td>6.2 (2.58)</td>
<td>0.16 (-0.75 to 1.09)</td>
<td>0.72</td>
</tr>
<tr>
<td>Global Perceived Effect - GPE (-5 to +5)</td>
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<tr>
<td>Baseline</td>
<td>-2.3 (2.67)</td>
<td>-2.2 (2.78)</td>
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<tr>
<td>2 weeks</td>
<td>0.5 (3.35)</td>
<td>2.6 (2.08)</td>
<td>-1.98 (-3.21 to -0.75)</td>
<td>0.002*</td>
</tr>
<tr>
<td>3 months</td>
<td>1.8 (2.65)</td>
<td>2.4 (2.60)</td>
<td>-0.47 (-1.69 to 0.75)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Primary outcomes are highlighted in gray. PE = Pain Education; NRS = Numerical Rating Scale; RMDQ = Roland Morris Disability Questionnaire; PSFS = Patient-Specific Function Scale; GPE = Global Perceived Effect. Positive scores treatment effect favor pain neurophysiology education plus hypnosis for outcomes of pain intensity, disability, catastrophizing and function. Negative scores favor the pain neurophysiology education plus...
hypnosis for the outcome of global perceived effect. CI=95% confidence interval.

SD=Standard Deviation

* P < 0.05