



The influence of verbal suggestions in the management of musculoskeletal pain: a narrative review

Iván Cuyul-Vásquez, José Aguilar Barría, Natalia Foitzick Perez & Jorge Fuentes

To cite this article: Iván Cuyul-Vásquez, José Aguilar Barría, Natalia Foitzick Perez & Jorge Fuentes (2019): The influence of verbal suggestions in the management of musculoskeletal pain: a narrative review, Physical Therapy Reviews, DOI: [10.1080/10833196.2019.1639011](https://doi.org/10.1080/10833196.2019.1639011)

To link to this article: <https://doi.org/10.1080/10833196.2019.1639011>



Published online: 15 Jul 2019.



Submit your article to this journal [↗](#)



View Crossmark data [↗](#)



The influence of verbal suggestions in the management of musculoskeletal pain: a narrative review

Iván Cuyul-Vásquez^a , José Aguilar Barría^a , Natalia Foitzick Perez^a  and Jorge Fuentes^{b,c} 

^aDepartment of Therapeutic Processes, Faculty of Health Sciences, Catholic University of Temuco, Temuco, Chile; ^bClinical Research Lab, Department of Physical Therapy, Catholic University of Maule, Talca, Chile; ^cFaculty of Rehab Medicine, University of Alberta, Edmonton, Canada

ABSTRACT

Background: Pain has been considered to be the most disabling symptom of musculoskeletal disorders. It is the cause of a large number of medical consultations and high health costs around the world. Chronic back pain affects a larger population than other types of pain, with observed prevalence of between 53% and 81%; this has economic, clinical and social repercussions for the health system.

Objective: The purpose of the present article is to describe the utility and the neurobiological mechanisms of verbal suggestion as a therapeutic ally during the management of patients with musculoskeletal pain.

Important discoveries: Inducing expectations by means of verbal suggestions can activate placebo or nocebo pathways when the clinical professional uses either positive or negative words respectively. When the administration of drugs and physiotherapy interventions are accompanied by words which induce positive expectations, this may improve certain clinical parameters such as pain and/or function in people suffering low back pain. Equally important, the use of positive verbal suggestion may decrease the perception of pain in patients with osteoarthritis.

Conclusions: In the management of clinical musculoskeletal pain, the inclusion of verbal suggestion has the potential to induce expectations which may generate hypoalgesia through the placebo effect; however, more research is needed to determine the magnitude and clinical significance of this contribution.

ARTICLE HISTORY

Received 23 January 2019

Accepted 27 June 2019

KEYWORDS

Musculoskeletal pain; verbal suggestion; expectations; placebo effect

Introduction

Pain is defined as ‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage’ [1]. It has been shown that pain provokes health and socioeconomic repercussions, derived principally from the functional limitation and the disability [2]. The greatest prevalence of pain has been observed in chronic lumbar pain, reported to vary between 51 and 84%; this has generated clinical, social and economic repercussions for health systems worldwide [3]. The highest proportions of costs in treating chronic low back pain are attributable to medical-pharmacological interventions (43%) and physical therapy treatments (17%) [4]. It has been observed that health costs for the treatment of non-oncological chronic pain vary between 34 and 635 billion dollars per year in Australia and United States [3,5], annual cost higher than the treatment of heart disease, cancer and diabetes [6]. Despite all efforts, these costs are expected to increase exponentially due to the increasing number of patients that

do not respond to conventional treatments [7]. It has been observed that only 30% of patients with chronic pain respond positively to treatments like injections, surgery, implantable devices and physical rehabilitation [8]; moreover, a reduction in pain due to these interventions is not always accompanied by improvement in function [8]. The above demonstrates the imperious need to identify effective interventions or improve the effectiveness of existing treatments.

Contextual factors have been defined as the physical, psychological and social elements which characterize the therapeutic encounter with the user [9,10], and include the user’s clinical history, his/her behavior and beliefs, the environment in which the attention is given, verbal suggestion and the therapeutic alliance [10]. Contextual factors can trigger expectations, memories and emotions which influence the results of treatment by triggering placebo and nocebo effects [10,11]. The verbal suggestion is a potent contextual factor present in the treatment ritual, which can influence the results of interventions

in pain-sufferers. Verbal suggestion and its effects have been strongly associated with the field of hypnosis [12]. Indeed, this concept has been understood as the mechanism which accompanies the hypnotic process and which can provoke changes in a person's sensations, perceptions, feelings or actions [13]. A similar term studied in health is 'persuasive communication' which is defined as a type of communication which seeks to convince others through the transmission of value perceptions and thus obtain changes in their ideas or behavior [14]. Verbal suggestions can generate positive or negative expectations [15]. Positive expectations have been defined as a conscious cognitive process which implies a desire for relief, positive anticipation of the treatment which can generate a placebo effect; on the other hand, negative expectations are associated with negative anticipation of the treatment in the form of anxiety, fear or repulsion and can generate a nocebo effect [16,17]. The placebo effect has been defined as an improvement in clinical symptoms due to the favorable contextual environment (e.g. enhanced therapeutic alliance), while the nocebo effect is understood as the worsening of these symptoms due to the presence of negative contextual factors in the therapeutic encounter [18,19].

When positive verbal suggestions accompany the administration of interventions attempted to manage pain, it generally gives better hypoalgesic results [20]. In fact, when verbal suggestions are used to induce positive expectations, it has been observed that similar brain areas are activated as under the administration of analgesic drugs such as remifentanyl [21]. In healthy subjects, inducing expectations by verbal suggestion has been shown to diminish the nocebo effect and promote the placebo effect [22,23]. Clinical studies in people suffering from musculoskeletal pain have also shown that positive reinforcement of treatment by verbal suggestion can be a promising, and a low-cost strategy for maximizing results [24,25]. In addition, the use of verbal suggestions as a mechanism for inducing expectations has proved useful during the administration of pills and creams for experimental pain, promoting the placebo effect and hypoalgesia [26,27]. Using verbal suggestions to increase the expectations of therapeutic benefit has been observed to produce an increase in the activity of areas of the brain involved in memory, semantic processing, emotions and analgesia, being correlated with diminished activity in areas of the brain used for processing pain [17].

The inclusion of verbal suggestions paired to positive expectations of therapeutic benefit may be seen as a low-cost strategy with potential hypoalgesic effects which could help pain-sufferers. Based on

the described above, it seems pertinent for physiotherapists to understand the relevance of this topic. Thus, the purpose of the present literature review is to describe utility and explore the neurobiological mechanisms of verbal suggestions when applied in the management of patients with musculoskeletal pain.

Materials and methods

Two independent reviewers conducted a literature search. The following databases were included; Medline, Lilacs, Cochrane Library and PEDro databases. A hand search was also performed. The strategy for the literature search involved the combination of the following keywords and MESH terms: 'Pain', 'Acute Pain', 'Pain Management', 'Musculoskeletal Pain', 'Chronic Pain', 'Pain Perception', 'Self-efficacy', 'Nocebo Effect', 'Placebo Effect', 'Verbal Suggestion', 'Persuasive Communication', 'Optimism'. The included studies were randomized clinical trials, literature reviews and systematic reviews involving verbal suggestion and its effect on pain of musculoskeletal origin, up to 5 years since being published, carried out in humans and published in English or Spanish. The articles were then filtered by their title and abstract. Articles referring only to education in the neurosciences of pain, studies in healthy subjects or animals and those published in any other language than Spanish and English were excluded.

Results

The search of the literature resulted in a total of 608 published studies. Of these, only six were deemed to fulfill the initial selection criteria. Another seven studies were selected by hand search. Thus, a total of 13 articles were analyzed. Of these, nine were reviews and four were randomized controlled trials.

Definition of verbal suggestion

The concept of verbal suggestion in the literature is ambiguous; we, therefore, suggest the following definition: a conscious or unconscious communication process by which a person who understands concepts and information about something is able to express them in such a way as to induce or foment beliefs, expectations, thoughts, emotions, behaviors and/or physical states in others.

Neurobiology of verbal suggestion

Verbal suggestions have been shown to produce positive therapeutic results in terms of hypoalgesia

when used to induce a placebo effect through expectations of pain relief [16,17,25]. The generation of the placebo effect has been associated with the release of endogenous opiates, cannabinoids, dopamine, oxytocin and vasopressin; the nocebo effect has been associated with the activity of cholecystokinin, deactivation of the opioid system and cyclooxygenase activation [16]. When verbal suggestions are used to induce expectations of therapeutic benefit, motivations, and anticipatory ideas about less pain, an increase in the activity of the opioid and dopaminergic systems has been observed. Other ways of producing the placebo effect, such as conditioning, has been associated with a greater release of endocannabinoids [17].

The process of informing the patient that he/she is being given a powerful analgesic can create treatment expectations which could generate analgesia mediated by placebo; on the other hand, communicating the possibility of a negative effect of the treatment may compromise its effectiveness, inducing hyperalgesia mediated by nocebo [10]. An increase in the dopaminergic activity has been observed of the nucleus accumbens during the communication of verbal suggestion messages [10,17], with a subsequent increase in the release of endogenous opioids in the areas of the brain associated with the interpretation of verbal suggestions, associative learning and the formulation of expectations [10,17]. Analgesia obtained by the placebo effect as a result of the inducement of expectations through verbal suggestion may produce a reduction in neuron activity in regions associated with the cognitive-emotional processing of pain and an increase in those areas associated with the maintenance of instructed beliefs [10,17,19]. The dorsolateral prefrontal cortex, the nucleus accumbens and the dopaminergic system appear to play important roles in reward learning when expectations are induced through verbal suggestion [19].

Effects of verbal suggestion in pain sufferers

The combination of positive verbal suggestions and a high level of professional empathy can favor the analgesic effect significantly [10,15]. Conversely, it has been observed that when verbal communication is neutral, not provoking positive expectations, with low levels of empathy, the pain of musculoskeletal origin may become worse [10,15]. Negative verbal suggestions (e.g. 'this procedure may cause a slight increase in pain') tend to be correlated with poor outcomes [16]. A meta-analysis aimed to study the effectiveness of verbal suggestions in acute experimental and chronic clinical pain concluded that mechanisms associated with conditioning and verbal

suggestion can produce moderate to large effects in acute experimental pain, however, these effects were shown to be small in patients with chronic pain [28]. These results contrast with other evidence showing that verbal suggestion alone may have strong effects on chronic pain outcomes [29]. Therefore, some controversy exists about the magnitude of the effect of verbal suggestions on pain modulation in the clinical setting.

For example, an experimental study in 485 subjects with osteoarthritis of the knee sought to assess the relationship between the expectations triggered by verbal suggestions about acupuncture, and the self-efficacy measured in terms of pain management and pain reduction [25]. The acupuncturists were 'trained' to communicate either positively or neutrally. The participants were divided and randomly assigned into two groups: therapists who used positive verbal suggestions combined with the application of simulated acupuncture using a technique not focused on specific points for pain reduction; and therapists who used neutral communication with the application of classic acupuncture focused on specific points for pain reduction. The results showed that the subjects who received a positive communication style along with positive verbal suggestions presented lower pain perception. This change was observed even 3 months after. In the same way, other authors who investigated the influence of contextual factors in patients with osteoarthritis [20,30] noted that the communication style, a patient-clinician interaction based on empathy, the validation of the patients' experiences and the provision of clear information can prevent negative treatment outcomes, can encourage patients to adhere physical exercise programs, and thus support greater self-efficacy, physical function and less pain in these patients. In addition, the type of expectations elicited by verbal suggestions seems to produce a differential effect. For example, in people with osteoarthritis who are going to undergo arthroplasty, the use of verbal suggestions, aimed to evoke realistic expectations, diminishes residual pain and functional deficit as compared with the induction of expectations associated with early symptomatic and functional recovery [31].

Other clinical trials have investigated how conditioning and verbal suggestions can elicit the placebo effect in people with low back pain [24, 32]. For example, a recent study conducted in 48 patients with chronic low back pain attempted to show that a placebo solution could have hypoalgesic effects on experimental and clinical pain through the use of conditioning and verbal suggestion [32]. The participants were assigned into four groups: neutral instruction without conditioning, neutral instruction

with conditioning, verbal suggestion without conditioning and verbal suggestion with conditioning. The conditioning was carried out by applying a painful electric stimulus to the subject's index finger, which was manipulated so that the intensity was reduced to 50% after the subject had ingested the placebo solution. In the verbal suggestion groups, the participants were told: '*you will be given a highly effective treatment for chronic low back pain, which will improve physical function and movement through an opioid solution*'. After the conditioning and verbal suggestion, all the subjects were subjected to two sessions of four exercises before and after ingestion of the placebo solution. The results showed a significant reduction in pain and increased function of the lumbar spine after ingestion of the placebo solution in the groups with conditioning and verbal suggestion. Conversely, the group with neutral instruction without conditioning reported higher pain levels, regardless they had received the placebo. An interesting trial in physiotherapy aimed to examine the impact of words used during the application of therapeutic ultrasound (US) in acute low back pain [24]. In this randomized trial, 67 participants were allocated into three groups: traditional US explanation (e.g. control), inflated US explanation and extra-inflated US explanation. All participants received the same active US parameters. Outcome measures included pain intensity, lumbar flexion and straight leg raise. Although no differences were found for leg pain and flexion among groups, both the inflated and extra-inflated explanation about the properties of the US were able to show statistically significant improvement in the straight leg raise when compared to the control group. In addition, participants in the extra-inflated US explanation group were 4.4. times more likely to improve beyond the minimal detectable change that participants in the control group. In this study, the words that the therapist choose to describe the US treatment was able to produce relevant changes in objective outcomes in subjects suffering from acute low back pain. Thus, different informational or verbal contexts about the characteristics of physiotherapy interventions, may impact treatment effectiveness. It is plausible, that during the application of physiotherapy interventions, the use of enhanced informative contexts may be paired with positive suggestions, and possibly greater expectations of therapeutic benefits. However, this needs to be confirmed with additional research in this field.

Discussion

The purpose of this review was to describe the utility and the neurobiological mechanisms of verbal

suggestions when interventions for the management of musculoskeletal pain are applied. The results of the search showed emerging interest in elucidating its effects. However, it is worth mentioning that among the thirteen selected articles, only four were randomized studies.

Overall, the results of this review indicated that verbal suggestion, as a mechanism for inducing positive expectations, has a positive impact on pain treatment in subjects with osteoarthritis and with acute or chronic low back pain [24,25,30,32]. Yet, definitive conclusions about the impact of verbal suggestions in the management of pain cannot be reached with such a small amount (4) of clinical trials.

Regarding the underlying mechanisms of verbal suggestions, Morral et al. and Rossetini et al. reported that people with clinical pain presented greater activity in the areas of the brain responsible for the semantic and cognitive-emotional processing of pain when a verbal suggestion is interpreted [10,17]. The same effect has been shown in healthy subjects under an experimental pain [33]. The boost of expectations of therapeutic benefit is the mechanism which would explain the analgesic responses of verbal suggestion in both, healthy subjects subjected to experimental pain and in subjects with clinical musculoskeletal pain [10,16,22–24,34]. For example, recent evidence in healthy subjects under an experimentally-induced mechanical pain found that active TENS applied using an informational context aimed to encourage positive suggestions (i.e. 'this intervention is very effective to promote pain relief in general and we hope to reduce your perception of mechanically induced pain') is able to produce a significant reduction of pain ($P < 0.03$) and increase in pressure pain thresholds ($P < 0.02$) when compared to the same TENS associated to negative expectations (i.e. 'this intervention is ineffective to promote pain relief and we hope that your mechanically induced pain perception increases temporarily') [35].

Despite some agreement in the literature about the positive impact of verbal suggestions in pain modulation, a certain inconsistency in the magnitude of the analgesic response has been observed, especially in subjects responding to the placebo [29]. It has been suggested that the variability in analgesic response to verbal suggestions is modulated by personal beliefs, expectations and treatment history [36,37]. The results of this review do not allow us to draw conclusions in this matter; however, the treatment history appears to have a significant influence on the effectiveness of verbal suggestion, as seen in the treatment of people with pain, as well as in sports performance [28,32,38]. In this regard, it has

been shown that previous negative experiences with certain treatments reduce the magnitude of the hypoalgesic effect of verbal suggestion, which justifies the exploration of this issue during the clinical interview before treatment is selected [28].

The importance of verbal suggestion may be appreciated when it is compared to other information delivery mechanisms such as therapeutic education. A systematic review focused on determining the effectiveness of long-term pain management education programs in people with osteoarthritis [39] concluded that these interventions produce small benefits in terms of pain, functionality and the typical symptoms of osteoarthritis. However, verbal suggestions in the form of advice and information could improve the efficacy of traditional education since its application requires less time and has been associated with better adherence to physical exercise, analgesia and functional programs [30]. The long-term effects of verbal suggestion alone, or as a complement to traditional education, have not been described either in review articles or experimental studies.

The health professional can unconsciously trigger a nocebo effect by generating negative expectations through verbal suggestion, which may compromise the therapeutic results of rehabilitation [40,41]. Thus, when treatment is given with negative verbal suggestions (e.g. this procedure may be associated with an increase in your pain level), the perceived pain is exacerbated by the conduct of anticipatory anxiety which produces hyperalgesia through the release of cytokines [42,43]. Nocebo and placebo effects are inherent in clinical practice, and the health professional may trigger them by any type of verbal or contextual interaction [44]. It is therefore recommended that verbal suggestion should be applied on a neurophysiological basis, consciously and ethically [10,16].

There is little research into verbal suggestion in subjects with clinical pain when physiotherapy interventions are applied [17,45]. In addition, the experimental studies included in this review presented some methodological limitations. Some important flaws included the absence of a control group and of the lack of blinding for participants. Other limitations from the experimental studies included in this review involve the poor analysis of the participants' treatment histories; and heterogeneity of the interventions in terms of complexity, treatment session frequency and the type of health professional administering the treatment [15,32]. The conclusions and/or results of this review must be treated with caution since the risk of bias was not fully assessed in included the studies. Finally, the absence of a consistent definition for the concept of verbal

suggestion in the field of health may have limited the scope of the searches, and therefore affecting the number of selected studies in this review.

Conclusion

Positive verbal suggestions have the potential to induce expectations which could be useful, via the placebo phenomenon, to improving the effectiveness of intervention strategies in people with musculoskeletal pain. Although the evidence provided by the literature seems to be promising, more research is still needed to reach definitive conclusions as well as to determine the magnitude of this effect and its clinical significance.

Disclosure statement

No potential conflict of interest was reported by the authors.

Notes on contributors

José Aguilar Barría is graduated from Temuco Catholic University with the title of physiotherapist. E-mail: jaguilar2014@alu.uct.cl; LinkedIn: <https://www.linkedin.com/in/jos%C3%A9-aguilar-barr%C3%ADa-74a656179/>

Natalia Foitzick Pérez is graduated from Temuco Catholic University with the title of physiotherapist. E-mail: nfoitzick2014@alu.uct.cl, LinkedIn: <https://www.linkedin.com/in/natalia-foitzick-978657179>.

Jorge Fuentes is an adjunct professor at Catholic University of Maule and University of Alberta. He investigates pain, context and placebo. E-mail: jorgef@ualberta.ca. Researchgate: https://www.researchgate.net/profile/Jorge_Fuentes2

Iván Cuyul Vásquez is an adjunct professor at Temuco Catholic University and a postgraduate student in the master's degree in Kinesiology at Maule Catholic University. He is currently investigating the influence of contextual effect and therapeutic exercise in the rehabilitation of people with chronic pain. E-mail: icuyul@uct.cl; LinkedIn: <https://www.linkedin.com/in/ivan-cuyul-b6561168>; Researchgate: https://www.researchgate.net/profile/Ivan_Cuyul_Vasquez

ORCID

Iván Cuyul-Vásquez  <http://orcid.org/0000-0002-0511-0503>

José Aguilar Barría  <http://orcid.org/0000-0002-5253-0631>

Natalia Foitzick Pérez  <http://orcid.org/0000-0002-8356-0059>

Jorge Fuentes  <https://orcid.org/0000-0003-0626-3656>

References

- [1] Williams AC de C, Craig KD. Updating the definition of pain. *Pain*. 2016;157:2420–2423.

- [2] Woolf AD, Erwin J, March L. The need to address the burden of musculoskeletal conditions. *Best Pract Res Clin Rheumatol*. 2012;26:183–224.
- [3] Henschke N, Kamper SJ, Maher CG. The epidemiology and economic consequences of pain. *Mayo Clin Proc*. 2015;90:139–147.
- [4] Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *Spine J*. 2008;8:8–20.
- [5] MBF Foundation. The high price of pain: the economic impact of persistent pain in Australia. Access Economics Pty Limited (MBF Foundation); 2007. <https://apo.org.au/node/3054>
- [6] Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012;13:715–724.
- [7] O'Brien T, Breivik H. The impact of chronic pain-European patients' perspective over 12 months. *Scand J Pain*. 2012;3:23–29.
- [8] Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. *Lancet (London, England)*. 2011;377:2226–2235.
- [9] Di Blasi Z, Harkness E, Ernst E, et al. Influence of context effects on health outcomes: a systematic review. *Lancet (London, England)*. 2001;357:757–762.
- [10] Rossetini G, Carlino E, Testa M. Clinical relevance of contextual factors as triggers of placebo and nocebo effects in musculoskeletal pain. *BMC Musculoskelet Disord*. 2018;19:27.
- [11] Wager TD, Atlas LY. The neuroscience of placebo effects: connecting context, learning and health. *Nat Rev Neurosci*. 2015;16:403–418.
- [12] Larra Bujalance FJ, Aguayo LV, Fernández JA. Hipermnesia bajo condiciones de vigilia e hipnosis. *Clínica Salud*. 2003;14:203–220.
- [13] Lynn SJ, Kirsch I. Teorías Hipnosis. *Papeles del Psicólogo*. 2005;25(89):9–15. <https://www.redalyc.org/pdf/778/77808903.pdf>
- [14] Falk E, Scholz C. Persuasion, influence, and value: perspectives from communication and social neuroscience. *Annu Rev Psychol*. 2018;69:329–356.
- [15] Mistiaen P, van Osch M, van Vliet L, et al. The effect of patient-practitioner communication on pain: a systematic review. *Eur J Pain*. 2016;20:675–688.
- [16] Testa M, Rossetini G. Enhance placebo, avoid nocebo: how contextual factors affect physiotherapy outcomes. *Man Ther*. 2016;24:65–74.
- [17] Morral A, Urrutia G, Bonfill X. Placebo effect and therapeutic context: a challenge in clinical research. *Med Clin (Barc)*. 2017;149:26–31.
- [18] Colloca L, Miller FG. The Nocebo effect and its relevance for clinical practice. *Psychosom Med*. 2011;73:598–603.
- [19] Koban L, Jepma M, Geuter S, et al. What's in a word? How instructions, suggestions, and social information change pain and emotion. *Neurosci Biobehav Rev*. 2017;81:29–42.
- [20] Dieppe P, Goldingay S, Greville-Harris M. The power and value of placebo and nocebo in painful osteoarthritis. *Osteoarthr Cartil*. 2016;24:1850–1857.
- [21] Petrovic P, Kalso E, Petersson KM, et al. A prefrontal non-opioid mechanism in placebo analgesia. *Pain*. 2010;150:59–65.
- [22] Peerdeman KJ, van Laarhoven AIM, Donders ART, et al. Inducing expectations for health: effects of verbal suggestion and imagery on pain, itch, and fatigue as indicators of physical sensitivity. *PLoS One*. 2015;10:e0139563.
- [23] Bartels DJP, van Laarhoven AIM, Stroo M, et al. Minimizing nocebo effects by conditioning with verbal suggestion: a randomized clinical trial in healthy humans. *PLoS One*. 2017;12:e0182959.
- [24] Louw A, Zimney K, Landers MR, et al. A randomised controlled trial of 'clockwise' ultrasound for low back pain. *S Afr J Physiother*. 2016;72:306.
- [25] Hsiao-Wei Lo G, Balasubramanyam AS, Barbo A, et al. Link between positive clinician-conveyed expectations of treatment effect and pain reduction in knee osteoarthritis, mediated by patient self-efficacy. *Arthritis Care Res (Hoboken)*. 2016;68:952–957.
- [26] Koban L, Brass M, Lynn MT, et al. Placebo analgesia affects brain correlates of error processing. *PLoS One*. 2012;7:e49784.
- [27] Geuter S, Eippert F, Hindi Attar C, et al. Cortical and subcortical responses to high and low effective placebo treatments. *Neuroimage*. 2013;67:227–236.
- [28] Peerdeman KJ, Van Laarhoven AIM, Keij SM, et al. Relieving patients' pain with expectation interventions: a meta-analysis. *Pain*. 2016;157:1179–1191.
- [29] Müller M, Kamping S, Benrath J, et al. Treatment history and placebo responses to experimental and clinical pain in chronic pain patients. *Eur J Pain*. 2016;20:1530–1541.
- [30] Hurley M, Dickson K, Walsh N, et al. Exercise interventions and patient beliefs for people with chronic hip and knee pain: a mixed methods review. *Cochrane Database Syst Rev*. 2013;4:CD010842.
- [31] Husain A, Lee GC. Establishing realistic patient expectations following total knee arthroplasty. *J Am Acad Orthop Surg*. 2015;23:707–713.
- [32] Klinger R, Kothe R, Schmitz J, et al. Placebo effects of a sham opioid solution: a randomized controlled study in patients with chronic low back pain. *Pain*. 2017;158:1893–1902.
- [33] Richter M, Eck J, Straube T, et al. Do words hurt? Brain activation during the processing of pain-related words. *Pain*. 2010;148:198–205.
- [34] Pazzaglia C, Testani E, Giordano R, et al. Expectation to feel more pain disrupts the habituation of laser-pain rating and laser-evoked potential amplitudes. *Neuroscience*. 2016;333:244–251.
- [35] Agripino MEDJ, Lima L V., Freitas IF, et al. Influence of therapeutic approach in the TENS-induced hypoalgesia. *Clin J Pain*. 2016;32:594–601.
- [36] Carlino E, Benedetti F. Different contexts, different pains, different experiences. *Neuroscience*. 2016;338:19–26.
- [37] Geurts JW, Willems PC, Lockwood C, et al. Patient expectations for management of chronic non-cancer pain: a systematic review. *Heal Expect*. 2017;20:1201–1217.
- [38] Mothes H, Leukel C, Jo H-G, et al. Expectations affect psychological and neurophysiological benefits even after a single bout of exercise. *J Behav Med*. 2017;40:293–306.
- [39] Kroon FP, van der Burg LR, Buchbinder R, Osborne RH, Johnston R V, Pitt V. Self-management education programmes for osteoarthritis. *Cochrane Database Syst Rev*. 2014;2014(1):CD008963. doi:10.1002/14651858.CD008963.pub2

- [40] Jensen KB, Kaptchuk TJ, Kirsch I, et al. Nonconscious activation of placebo and nocebo pain responses. *Proc Natl Acad Sci USA*. 2012;109:15959–15964.
- [41] Cormier S, Lavigne GL, Choinière M, et al. Expectations predict chronic pain treatment outcomes. *Pain*. 2016;157:329–338.
- [42] Benedetti F, Amanzio M. The placebo response: how words and rituals change the patient's brain. *Patient Educ Couns*. 2011;84:413–419.
- [43] Carlino E, Frisaldi E, Benedetti F. Pain and the context. *Nat Rev Rheumatol*. 2014;10:348–355.
- [44] Finniss DG, Kaptchuk TJ, Miller F, et al. Biological, clinical, and ethical advances of placebo effects. *Lancet*. 2010;375:686–695.
- [45] Bräscher A-K, Witthöft M, Becker S. The underestimated significance of conditioning in placebo hypoalgesia and nocebo hyperalgesia. *Pain Res Manag*. 2018;2018:6841985.