TBM

Neurophysiology of pain and hypnosis for chronic pain

Tiara Dillworth, PhD,[1] M Elena Mendoza, PhD,[2] Mark P Jensen, PhD

[1]Department of Psychiatry & Behavioral Sciences, University of Washington, Box 354944, Seattle, WA 98195, USA
[2]Department of Rehabilitation Medicine, University of Washington, Box 356912, Seattle, WA 98195, USA
Correspondence to: T Dillworth
tiara@uw.edu

Cite this as: *TBM* 2012;2:65–72
doi: 10.1007/s13142-011-0084-5

ABSTRACT

In the past decade there has been a dramatic increase in (1) understanding the neurophysiological components of the pain experiences, (2) randomized clinical trials testing the efficacy of hypnotic treatments on chronic pain, and (3) laboratory research examining the effects of hypnosis on the neurophysiological processes implicated in pain. Work done in these areas has not only demonstrated the efficacy of hypnosis for treating chronic pain but is beginning to shed light on neurophysiological processes that may play a role in its effectiveness. This paper reviews a selection of published studies from these areas of research, focusing on recent findings that have the most potential to inform both clinical work and research in this area. The paper concludes with research and clinical recommendations for maximizing treatment efficacy based on the research findings that are available.

KEYWORDS

Hypnosis, Hypnotic analgesia, Chronic pain, Neurophysiology, Hypnotic suggestions

Implications

Researchers: Researchers should consider evaluating suggestion type when studying pain-related and functional outcomes and the neural networks implicated in both pain and hypnosis.

Practitioners: Hypnosis can be used as either a stand-alone or adjunct treatment for chronic pain, and different types of suggestions should be considered for improving pain and other functional outcomes.

Policymakers: Hypnosis is an important treatment to cover in policies geared to promote wellness and health of individuals with chronic pain, especially given its minimal side effects and relatively low cost to implement.

Chronic pain, defined as pain lasting longer than 6 months [1], is a complex experience that requires multifaceted approaches for both evaluation and treatment [1, 2]. Chronic pain is considered to have an underlying biological basis, for which medications and physical treatments are commonly prescribed. Medical approaches for pain relief and management include pharmacological and surgical interventions as well as physical therapy. While nonsteroidal anti-inflammatory drugs are commonly used to treat mild pain from inflammation, opioid analgesics are the mainstay of pharmacologic treatment of moderate to severe pain [2–6]. However, prolonged use of opioids may result in opioid tolerance and opioid-induced hyperalgesia, which is an increased sensitivity to pain. These problems, coupled with unpleasant medication side effects, may lead to discontinuation of treatment [7]. Depending on the patient's condition and cause of pain, surgery is typically considered for the treatment of chronic pain when it is deemed medically necessary or after other treatments have failed. These include intrathecal drug delivery [8], spinal cord stimulation [9], radiofrequency ablation [10], and chemical sympathectomy [11]. One concern is that even though surgical procedures can provide pain relief, they also may permanently damage the person's ability to perceive other sensations, such as light touch and temperature changes, and can cause different pain problems to occur.

Medical approaches for pain reduction are only one element of an interdisciplinary approach, since gains in physical and social functioning are important goals as well [12]. Psychosocial and neuropsychological models of chronic pain show that pain treatment cannot focus solely on the sensation of pain itself (e.g., pain intensity) but must also consider the affective (e.g., emotional suffering), cognitive (e.g., beliefs about pain) and behavioral (e.g., inactivity) responses which also impact the overall experience of pain [13–15]. This idea has been further supported by research evaluating the neurophysiological mechanisms implicated in pain, which will be described below. Thus, there is a need to offer treatments for chronic pain that may affect any or all components of the pain experience.

In addition to medical approaches for pain relief and management, patients with chronic pain are also seeking complementary and alternative therapies, such as hypnosis [15]. Training patients to use hypnosis is one treatment for chronic pain that has been evaluated across a variety of conditions, including fibromyalgia, low back pain, disability-related pain, cancer-related pain, arthritis, irritable bowel syndrome, and headache [16–23]. Hypnosis can be used as a stand-alone or adjunctive treatment, with some research demonstrating the ability

for hypnosis to enhance the benefits of other psychological interventions [20, 24–27] and physical interventions, including medications and standard medical care [22, 28–30]. During hypnosis, individuals are given an invitation to focus their attention through an induction, followed by suggestions for change or improvement [31]. While the format of hypnosis can vary greatly, such as the length of the induction or the types of suggestions given, overall research suggests that hypnosis is a viable treatment option for chronic pain, demonstrated through improvements in several pain-related outcomes, including pain intensity, duration, and frequency [16–18, 32]. Patients can also learn self-hypnosis, which is self-guided and can be practiced away from the clinical setting.

The goal of this topical review is to first give a brief review of the neurophysiological processes that underlie the experience of pain. We will then describe research that has evaluated hypnosis for chronic pain, specifically focusing on the role of suggestion type (e.g., suggestions for a reduction in pain) on pain outcomes. Next, we will discuss recent research studying the specific neurophysiological processes that are affected during hypnosis. Finally, clinical and research implications will be discussed.

NEUROPHYSIOLOGICAL MECHANISMS INVOLVED IN PAIN PERCEPTION AND REGULATION

As research has demonstrated the feasibility and efficacy of hypnosis as a stand-alone and adjunctive treatment for chronic pain, there has been a drive to better understand the potential mechanisms of hypnosis on the pain experience by examining the neurophysiological processes that are implicated in pain. Advances in brain imaging techniques over the past decade have led to a greater understanding of the supraspinal central nervous system areas (i.e., brain stem and brain) that are involved in the processing of nociception, or the information that is sent from nerve receptors that signal the possibility of injury. When physical injury occurs, nerve receptors that respond to the injury transmit information about damage (or potential damage) along specific nerve fibers (C, A delta, A beta fibers) that run to the dorsal horn in the spinal cord. Here, this information is relayed through the spinal–thalamic tract, which is a key pathway for transmitting nociceptive information to the brain. The information is then processed in multiple supraspinal areas, including the thalamus, prefrontal cortex, the anterior cingulate cortex (ACC), the primary (S1) and secondary (S2) somatosensory cortices, and the insula [33, 34].

The thalamus is considered to be the primary relay center for transmitting pain information from the periphery and spinal cord to several sites in the cortex involved in processing nociceptive information. One site is the prefrontal cortex, which is thought to encode the cognitive aspects of both acute and chronic pain, including evaluating the meaning of pain and making executive decisions regarding how best to cope with pain [33]. Another site, the ACC, is related to the affective/emotional component of pain (i.e., suffering) [33, 35] and the motivational–motor aspects of pain (e.g., preparing to do something about pain), including the initiation and facilitation of behavioral coping efforts [36, 37]. The somatosensory cortices (S1 and S2) process sensory information about nociception, including location (e.g., left hand), severity, and identification (e.g., burn). Finally, the insula is responsible for encoding a person's sense of his or her physical condition across a variety of domains as they relate to motivation (e.g., the extent to which people feel pain vs. feel physically content). In particular, the insula becomes more active when there are threats (e.g., a lack of oxygen, pain, low blood sugar) to what the body needs for survival [36, 38]. Research suggests that the insula plays a leading role in triggering the pain network and the resulting emergence of the subjective pain experience [39].

The brain areas and structures described above work closely together and along with other central nervous system structures in an integrated way to produce the experience labeled as pain [34]. These structures make up the "pain matrix," and pain is not experienced unless these supraspinal cortical areas are active. Activation of peripheral and spinal mechanisms of nociception is neither necessary nor sufficient to produce the perception of pain. Essentially, the brain holds the primary responsibility for if and how we experience pain. This helps explain why pain can be experienced even if no nociception is present (e.g., phantom limb pain). Importantly, pain can be decreased or eliminated when these processes are interrupted. As will be seen, there is evidence that hypnosis can influence each of these structures.

HYPNOSIS AND HYPNOTIC SUGGESTIONS FOR CHRONIC PAIN

As described above, hypnosis has been found to be an effective treatment for chronic pain across several conditions [15, 16]. Studies have shown that approximately 70% of individuals with chronic pain are able to experience a short-term reduction in chronic pain during a treatment session or hypnosis practice, and between 20% and 30% achieve more permanent reductions in daily pain [15, 40]. There is also evidence to suggest that hypnosis may be more effective in treating neuropathic or vascular pain and less efficacious in treating primarily musculoskeletal pain (e.g., low back pain) [15]. There are two main theories on why hypnosis may work. Trait theories [41] state that individuals vary in their level of hypnotizability, with individuals high in hypnotic suggestibility responding better to hypnotic suggestions. While there is evidence that level of suggestibility has been significantly related to hypnotic

outcomes [15, 18], studies have also found that individuals low in hypnotizability can also experience improvements in pain after hypnosis [42–44], and some research had found no association between level of hypnotizability and outcome [45, 46]. Social–cognitive theories suggest that expectancies, motivation, and environmental cues contribute to an individual's responsiveness to hypnotic suggestions and that improvements are made via cognitive changes that alter the affective components of pain [18, 45, 47, 48]. For instance, one study found treatment outcome expectancies to be moderately to strongly associated with improvements in pain intensity over time [45]. Overall, while research suggests that there is evidence to support both theories, there is a lack of consistent evidence to suggest that either theory is entirely sufficient to explain why hypnosis is effective [18]. This is an area that needs continued research.

As stated above, hypnosis can vary considerably in how it is presented [15]. One way in which it can vary is by the suggestions used when treating chronic pain. When hypnosis is used as a treatment for chronic pain, suggestions for change or improvement may target several pain-related outcomes, including decreasing pain, increasing comfort, improving one's ability to ignore or shift attention away from pain, or changing the sensation of pain to another sensation, such as tingling or numbness [31]. Additionally, suggestions may focus on improvements in other areas of life that can be influenced by or that influence pain, such as improved self-efficacy, changes in beliefs or attitudes, increased activity, or improved sleep quality. Studies evaluating hypnosis for chronic pain have used different combinations of these types of suggestions, with overall findings demonstrating hypnosis to be at least as effective as other active treatments (e.g., relaxation, biofeedback), and advantageous when compared to treatment as usual [15–18].

More recently, research has begun to focus on the role of the specific types of suggestions used in hypnosis. A recent review [49] found that in studies that utilized only pain-specific suggestions (e.g., reduction in pain intensity) [20, 22, 27, 42, 50–55], hypnosis was overall more effective than control groups in improving pain outcomes, including pain severity [27], intensity [22, 50, 51], and duration [50, 51]. Hypnosis with only pain-specific suggestions was found to be at least as effective in improving pain intensity when compared to active treatments, including cognitive behavior therapy [27], biofeedback [42], and autogenic training [52, 55]. Some studies have found hypnosis to be significantly more effective compared to active treatments in improving outcomes such as increased use of coping strategies (when compared to autogenic training) [56] and sleep (when compared to relaxation) [57].

Only two studies evaluating hypnosis for chronic pain were found that used nonpain-related suggestions exclusively (e.g., improved fatigue, self-confidence, feeling healthier) [21, 26]. One study found hypnosis to be significantly more effective in improving pain intensity and decreasing pain medication use compared to relaxation and a control group at a 4-week follow-up. By the 8-week follow-up, both hypnosis and relaxation were more effective than the control group (but equal to each other), and all three groups had equal outcomes 6 months after treatment ended [21]. Another study found significantly greater improvements in severe pain when patients were given a combination of hypnosis and biofeedback compared to each treatment alone [26]. Thus, despite a lack of pain-specific suggestions, there is some evidence that suggestions for improvements in other areas of life can positively influence pain intensity.

In studies that have used a combination of pain-specific and nonpain-related suggestions, the majority of findings have shown that hypnosis is more effective than both active and control treatments across several different pain outcomes, including pain intensity [45, 57–64], pain sensation [59, 60], perceived control over pain [65]. pain interference [45], and decreased use of pain medications [57, 64]. Additionally, improvements have been found other outcomes, including emotional distress and sleep [57, 63]. The effect on pain outcomes appears to be more consistent when a combination of suggestions is given than when hypnosis includes only either pain-specific or nonpain-related suggestions [16]. When considering biopsychosocial and neuropsychological models of pain, using a combination of pain-specific and nonpain-related suggestions may be more effective because these suggestions can target not only pain itself, but emotional (e.g., suggestions for improved mood), cognitive (e.g., suggestions for increased self-efficacy), and behavioral (e.g., suggestions for improved sleep) factors that play an important role in the pain experience. This implies that a combination of suggestions, which can be tailored to the individual, covering improvements in pain (e.g., reduction in pain severity), improvements in other pain-related outcomes (e.g., changing attitudes about pain), and improvements in other areas of life (e.g., improved stress management) may provide the most relief from the effects of chronic pain [16]. This is an area of research that needs further research.

NEUROPHYSIOLOGICAL EFFECTS OF HYPNOSIS

Given the evidence that hypnosis can be effective in improving pain outcomes, coupled with research evaluating the neurophysiological components implicated in pain, recent reviews and research [32, 34, 66] have evaluated studies exploring the neurophysiological effects of hypnosis. These studies have concluded that hypnosis can impact pain by affecting a number of different neurophysiological processes that make up the pain matrix, rather than by

influencing a single mechanism or process. Specifically, research indicates that hypnosis can impact activity in: (1) the periphery and spinal cord [67–69], (2) the thalamus [65, 70, 71], (3) the sensory cortices [72, 73], (4) the insula [70, 71, 73], (5) the ACC [35, 70, 71, 73–75], and (6) the prefrontal cortex [70, 71, 73, 76]. Given the extensiveness of these previous reviews, this section will briefly review past research that has examined the neurophysiological effects of hypnotic analgesia, specifically focused on the role of suggestion type [35, 72, 77]. Additionally, three studies that were not included in these previous reviews will be discussed, including one recent study evaluating the neurophysiological mechanisms associated with hypnotic induction and two studies that studied the neural processes correlated with suggestions [73, 76, 78].

McGeown and colleagues specifically focused on the neural correlates of hypnotic induction [76]. fMRI was used to measure high and low hypnotizable participants (i.e., individuals who do not typically respond to hypnotic suggestions) during a hypnotic induction and out of hypnosis. Results found that those high in hypnotizability showed reductions in brain activity in the anterior "default mode" network, which includes the prefrontal cortex, whereas participants low in hypnotizability did not. The "default mode" network includes the pattern of spontaneous brain activity that occurs during a normal resting state [79]. This pattern of neural activity during a resting state is associated with the "mind wandering," whereas reductions in activity in the default mode during a hypnotic induction may suggest an increased focus or preparedness for whatever may follow next, which in the case of hypnosis would be hypnotic suggestions. In contrast to previous research, no increases in activation were found. The authors suggest that this observation may be specific to the hypnotic induction and not necessarily to the entire hypnotic experience, especially for individuals who are highly hypnotizable. While this study suggests that there is a reduction in prefrontal activity during the induction, this study was not designed to determine whether or not this reduction actually affected responsiveness to suggestions and which neural pathways may be implicated during hypnotic suggestions.

There is a dearth of research studying the role of suggestions, more specifically suggestion type, on various neurophysiological pathways implicated in pain. In the research that has been conducted, one study found that suggestions for decreasing pain unpleasantness were associated with decreased activity in the ACC, which is associated with the affective component of pain. In contrast, changes in activity in the ACC were not found for suggestions to decrease pain intensity. Suggestions for decreasing pain unpleasantness did not result in changes in activity in the somatosensory cortices, which process sensory information about nociception (e.g., pain severity) [35]. However, another study found that suggestions specific to decreasing pain intensity were associated with decreased activity in the S1 cortex, with a similar pattern for the S2 cortex but no decreased activity in the ACC [72]. One study gave suggestions for varying levels of pain with or without a hypnotic induction by asking patients with fibromyalgia to visualize a dial turning their pain up or down (i.e., high vs. low pain intensity). Results found that neural structures commonly associated with the "pain matrix," including the cerebellum, ACC, insula, and right prefrontal cortex, were activated after the suggestions were given; however, greater activation was seen after the hypnotic induction compared to the nonhypnotized condition in these structures. Patients also reported a greater decrease in pain after the "low" pain suggestion when the suggestion followed a hypnotic induction. These results suggest that hypnosis may alter responsiveness to suggestions via changes in brain activity found after a hypnotic induction [77].

One recent study by Raij and colleagues [78] evaluated brain activation using fMRI during suggestions for pain (e.g., increasing pain on back of left hand), holding the pain level for 30 s (e.g., pain will remain stable), followed by pain relief (e.g., pain goes completely away) given multiple times over the course of 12 min. During the periods of suggestions for increasing pain, activation was found in several areas, including the right inferior frontal gyrus, insula, ACC, prefrontal cortex, temporal lobes, supplementary motor cortices, premotor cortices, and the right dorsolateral prefrontal cortex (DLPFC). During the period participants were asked to continue feeling the pain, more activation was seen in the S2 cortex, which was significantly related to the amount of subjective pain reported. Structures that were activated during pain initiation, with the exception of the insula, were also active during pain maintenance. Overall, these results demonstrate the role of cognitive (e.g., DLPFC) and emotional–motivational (e.g., ACC, insula) structures on initiation and maintenance of pain.

Another recent study by Nusbaum and colleagues [73] in patients with chronic back pain evaluated the neural networks activated during normal alertness and hypnosis for both direct analgesic suggestions (i.e., to alter the intensity and location of pain) and indirect suggestions (i.e., referencing general well-being with no mention of the pain). Using positron emission tomography, participants were given either direct or indirect suggestions first during normal alertness and then followed by a hypnotic induction. Neural activity was compared in two primary ways: (1) normal alertness vs. hypnosis, regardless of suggestion type, and (2) direct vs. indirect suggestions, regardless of hypnotic condition (i.e., normal alertness or hypnosis). Imaging showed shared and unique activation and deactivation for both types of comparisons. Based on the imaging results, the findings indicated that sugges-

tions given during normal alertness activated a cognitive–sensory network, including the temporal cortices and cerebellum, whereas suggestions given during hypnosis-activated brain regions associated with an emotional-weighted neural network, including areas such as the medial prefrontal cortex and anterior insula. Comparing direct and indirect suggestions, results found direct suggestions activated areas in the frontotemporal network, whereas indirect suggestions activated more widespread areas. These finding suggest the possibility that direct suggestions may work via networks involved in cognitive processes, while indirect suggestions may influence outcomes via an emotional-weighted network.

Comparing improvements in pain intensity, results found that both types of suggestions significantly decreased pain intensity after hypnosis. However, only direct suggestions were found to decrease pain intensity after normal alertness. Results also showed that the decrease in pain intensity was significantly greater after hypnosis than after normal alertness. The authors hypothesized that hypnosis had a greater effect with both types of suggestions due to the emotional-weighted network involved in both hypnosis and with indirect suggestions.

In sum, research has demonstrated that hypnosis can impact several different neurophysiological processes, many of which are implicated in the experience of pain. As described above, pain is a complex experience that involves cognitive, affective, and sensory components that may also be activated during hypnosis. What is not yet known is whether the neurophysiological changes observed following hypnosis that are associated with improvements in pain represent key biological mechanisms of hypnosis, or if they are simply by products of hypnosis and pain relief.

DISCUSSION

Clinical Implications

There are a number of important clinical implications of the research findings regarding the effects and mechanisms of hypnosis. First, given the strong evidence that hypnosis is an effective treatment for chronic pain, coupled with its cost-effectiveness and minimal side effects [80, 81], it can be concluded that hypnosis is a reasonable approach for clinicians to use for helping patients better manage with chronic pain. Second, given evidence that adding hypnosis to other treatments, such as CBT [25] or cognitive therapy [24], may enhance the efficacy of those treatments, hypnosis can be considered a reasonable adjunct to other psychological interventions. Therefore, clinicians who treat patients with chronic pain would do well to consider learning and incorporating hypnotic techniques into their practice.

A third clinical implication is that when using hypnosis or teaching patients self-hypnosis for pain management, clinicians should use a *variety* of suggestions that target improvement in the multiple components of pain (e.g., sensory, affective, cognitive, motivational) [82]. Jensen [34, 83] provided an extensive list of suggestions based on the neurophysiological processes associated with both pain and hypnosis. For example, suggestions targeting the somatosensory cortex may focus on directly decreasing pain intensity, whereas suggestions affecting the ACC might include positive changes in the affective response to pain. The prefrontal cortex may be targeted with suggestions to change the meaning of pain or focus on meaningful or enjoyable activities. Suggestions can also target the many functional domains that can be negative affected by pain (e.g., sleep quality, physical activity, depression).

Another important consideration when choosing suggestions is the goal of treatment. While one goal may be to decrease the intensity of pain, an arguably important (if not more important) goal of treatment may be to increase quality of life, return to work, or improve function in daily activities regardless of pain level [84–86]. However, although hypnosis has now demonstrated efficacy for pain reduction, there are very few studies that have tested the efficacy of hypnotic suggestions for improving other outcomes that are affected by pain, such as return to work, increased social activity, improved sleep quality, or improved physical functioning. Given evidence that hypnosis can enhance the efficacy of CBT interventions that target behavioral change in nonpain populations [87], there is good reason to expect that hypnosis and hypnotic suggestions could enhance functional outcomes. Suggestions may also be directed towards improvement with physical interventions, such as better adherence to medications or increased motivation to participate in physical therapy. The literature is full of examples of hypnotic suggestions that can be used to target many different outcomes. Two excellent resources for exploring the many different possible suggestions include Cory Hammond's *Handbook of hypnotic suggestions and metaphors* [88] and the collected papers of Milton H. Erickson on hypnosis [89–93]. Thus, suggestions for increasing activity, improving motivation to return to work or participate in rehabilitation therapies, or feeling more connected with a social network may play a critical role achieving successful outcomes with chronic pain populations [15].

Research Implications

While research has demonstrated activity in various areas of the nervous system and neurophysiological processes that are implicated in both pain and hypnosis, more research is needed to further evaluate how specific types of hypnotic suggestions may serve to improve pain outcomes as well as further our understanding of the neurophysiological mechanisms at work. Studies have made beginning

steps in pursuing this type of research [35, 72, 73, 77]. As we learn more about the pain mechanisms that are specific to an individual's pain experience, we may be able to test specific suggestions that target those neural pathways [34]. There may be ways to maximize on both the cognitive–sensory and emotion-weighted networks implicated in both hypnosis and suggestion type. For instance, a recent study compared hypnosis to cognitive restructuring (CR) and a combination treatment in which CR was conducted in the context of hypnosis. Hypnosis consisted of suggestions for improving pain-related outcomes and the option of also have two additional suggestions chosen by the participant, such as increased energy or improved sleep. CR focused on reducing catastrophizing cognitions, which have been associated with worse pain outcomes [94]. The novel treatment condition combined both CR and hypnosis by giving participants suggestions during hypnosis for increasing acceptability regarding the ambiguity of pain sensations, increasing pain-related self-efficacy, automatically monitoring and restructuring catastrophizing cognitions into more realistic and reassuring thoughts, and increasing a sense of control over pain. Results showed hypnosis to be more effective than CR in reducing pain intensity. Both CR and hypnosis were found to significantly decrease pain catastrophizing. Interestingly, the strongest effects for reducing pain intensity and pain-related catastrophizing were found after the combination hypnosis–CR treatment. It may be that this combination treatment affected a broader neural network, resulting in larger effects than either CR or hypnosis alone. Future research could evaluate which neural networks are at play during these types of suggestions.

More research is also needed on the role of suggestion on other functional outcomes, such as return to work, increased activity, or daily functioning. While the primary outcomes of research in this area have reported on pain-specific outcomes (e.g., pain intensity), other types of functional outcomes are commonly not evaluated or reported. As suggested above, a decrease in pain intensity may not be the only important outcome. Evaluating suggestions that may increase, for example, a patient's desire to participate in an exercise program has the potential to not only influence pain-specific outcomes but other outcomes important for daily functioning. Future research should consider these types of outcomes both in terms of choosing suggestions to be given during hypnosis and for measuring whether or not a treatment has made significant improvements.

As has been discussed elsewhere, there is also a need for standardized procedures for testing the effects of hypnosis as well as publishing or making easily available the hypnotic protocols used [16–18, 95]. As described above, studies have included pain-specific suggestions, nonpain-related suggestions, neither type, or both. More recent research has also included posthypnotic suggestions, such as suggestions to use pain as a cue to take a deep breath, relax, or think of good memories [58, 59], or suggestions for the benefits of hypnosis to continue beyond the hypnotic session [24, 45, 65]. More research is needed to better understand how suggestion types impact pain and related outcomes. Being specific as to the types of suggestions used and their relation to changes in pain-related outcomes also allows for easier replication and extension of future research [16, 95].

Finally, there is a need for more research to study the mechanisms (why it works) and moderators (for whom it works) of hypnosis. Trait theories argue that it is related to hypnotizability and the state of hypnosis, whereas social–cognitive models state that it is because of expectancies, motivation, and environmental cues. However, neither model has garnered overwhelming support in clinical studies [18, 45, 46]. Additional models may need to be developed to better answer these questions, and research will be needed to test these new models. There is also limited knowledge about how different physical interventions may impact hypnosis. For instance, it is currently unknown whether different medications interact (if at all) with hypnosis, or if participation in a physical intervention (e.g., physical therapy) in addition to hypnosis improves both pain and other functional outcomes. These are areas of study open to future research.

SUMMARY AND CONCLUSION

The marked increase in research studying the mechanisms and efficacy of hypnosis for chronic pain management in the past decade has yielded important findings that have important implications for chronic pain treatment. Although response to hypnosis and training in self-hypnosis is variable (i.e., not all patients benefit), the available evidence indicates that hypnosis can significantly reduce average daily pain and result in benefits in other pain-related outcome domains for many individuals. Hypnosis may also work synergistically with other psychological and physical interventions to enhance their efficacy. The evidence showing that hypnosis can impact pain via multiple mechanisms indicates that clinicians using hypnosis should provide a variety of hypnotic suggestions for their patients with chronic pain in order to maximize the chances of success. More research is needed to help identify the potential moderators of hypnotic treatment and suggestions (e.g., the extent to which a formal hypnotic induction is necessary for positive outcomes, the ideal "dose" or number of sessions needed) to help (1) understand the mechanisms of hypnotic analgesia and (2) create an empirical basis for making hypnotic treatments even more effective. Ultimately, the findings suggest that individuals with chronic pain will be better served if their treatment

providers incorporate hypnotic procedures into their treatment protocols.

Acknowledgments: Second author's participation was funded by the Spanish Foundation of Science and Technology (Spanish Ministry of Science and Innovation).

1. Keefe FJ. Behavioral assessment and treatment of chronic pain: current status and future directions. *J Consult Clin Psychol*. 1982; 50(6):896-911.
2. DuPen A, Shen D, Ersek M. Mechanisms of opioid-induced tolerance and hyperalgesia. *Pain Management Nursing*. 2007; 8 (3):113-121.
3. Trescot AM, Boswell MV, Atluri SL, et al. Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician*. 2006; 9(1):1-39.
4. Bruera E, Kim HN. Cancer pain. *JAMA*. 2003; 290(18):2476-2479.
5. Dews TE, Mekhail N. Safe use of opioids in chronic noncancer pain. *Cleveland Clinic Journal of Medicine*. 2004; 71(11):897-904.
6. Gammaitoni AR, Fine P, Alvarez N, McPherson ML, Bergmark S. Clinical application of opioid equianalgesic data. *The Clinical Journal of Pain*. 2003; 19(5):286-297.
7. Varrassi G, Muller-Schwefe G, Pergolizzi J, et al. Pharmacological treatment of chronic pain—the need for CHANGE. *Current Medical Research and Opinion*. 2010; 26(5):1231-1245.
8. Duarte, R. V., Raphael, J. H., Sparkes, E., Southall, J. L., Lemarchand, K., & Ashford, R. L. (2011). Long-term intrathecal drug administration for chronic nonmalignant pain. *Journal of Neurosurgical Anesthesiology* (in press).
9. Mailis-Gagnon, A., Furlan, A. D., Sandoval, J. A., & Taylor, R. (2004). Spinal cord stimulation for chronic pain. *Cochrane Database Systematic Reviews* (3), CD003783.
10. Soloman M, Mekhail MN, Mekhail N. Radiofrequency treatment in chronic pain. *Expert Rev Neurother*. 2010; 10(3):469-474.
11. Ilfeld BM, Shuster JJ, Theriaque DW, et al. Long-term pain, stiffness, and functional disability after total knee arthroplasty with and without an extended ambulatory continuous femoral nerve block: a prospective, 1-year follow-up of a multicenter, randomized, triple-masked, placebo-controlled trial. *Regional Anesthesia and Pain Medicine*. 2011; 36(2):116-120.
12. Willimann P. Pharmacological treatment of chronic pain. *Ther Umsch*. 2011; 68(9):512-516.
13. Jensen MP. Psychosocial approaches to pain management: an organizational framework. *Pain*. 2011; 152(4):717-725.
14. Jensen MP, Turner JA, Romano JM, Karoly P. Coping with chronic pain: a critical review of the literature. *Pain*. 1991; 47(3):249-283.
15. Stoelb BL, Molton IR, Jensen MP, Patterson DR. The efficacy of hypnotic analgesia in adults: a review of the literature. *Contemp Hypn*. 2009; 26(1):24-39.
16. Dillworth T, Jensen MP. The role of suggestions in hypnosis for chronic pain: a review of the literature. *Open Pain Journal*. 2010; 3(1):39-51.
17. Jensen MP, Patterson DR. Hypnotic treatment of chronic pain. *Journal of Behavioral Medicine*. 2006; 29(1):95-124.
18. Patterson DR, Jensen MP. Hypnosis and clinical pain. *Psychol Bull*. 2003; 129(4):495-521.
19. Spinhoven P, Linssen AC. Education and self-hypnosis in the management of low back pain: a component analysis. *Br J Clin Psychol*. 1989; 28(Pt 2):145-153.
20. Spiegel D, Bloom JR. Group therapy and hypnosis reduce metastatic breast carcinoma pain. *Psychosomatic Medicine*. 1983; 45(4):333-339.
21. Gay MC, Philippot P, Luminet O. Differential effectiveness of psychological interventions for reducing osteoarthritis pain: a comparison of Erikson [correction of Erickson] hypnosis and Jacobson relaxation. *European Journal of Pain*. 2002; 6(1):1-16.
22. Roberts L, Wilson S, Singh S, Roalfe A, Greenfield S. Gut-directed hypnotherapy for irritable bowel syndrome: piloting a primary care-based randomised controlled trial. *Br J Gen Pract*. 2006; 56 (523):115-121.
23. Tan G, Fukui T, Jensen MP, Thornby J, Waldman KL. Hypnosis treatment for chronic low back pain. *Int J Clin Exp Hypn*. 2010; 58 (1):53-68.
24. Jensen MP, Ehde DM, Gertz KJ, et al. Effects of self-hypnosis training and cognitive restructuring on daily pain intensity and catastrophizing in individuals with multiple sclerosis and chronic pain. *Int J Clin Exp Hypn*. 2011; 59(1):45-63.
25. Kirsch I. Response expectancy as a determinant of hypnotic behavior. *Am Psychol*. 1985; 40:1189-1202.
26. Melzack R, Perry C. Self-regulation of pain: the use of alpha-feedback and hypnotic training for the control of chronic pain. *Exp Neurol*. 1975; 46(3):452-469.
27. Edelson J, Fitzpatrick JL. A comparison of cognitive-behavioral and hypnotic treatments of chronic pain. *J Clin Psychol*. 1989; 45 (2):316-323.
28. Walker WR. Hypnosis as an adjunct in management of pain. *Southern Medical Journal*. 1980; 73(3):362-364.
29. Thornberry T, Schaeffer J, Wright PD, Haley MC, Kirsh KL. An exploration of the utility of hypnosis in pain management among rural pain patients. *Palliative & Supportive Care*. 2007; 5(2):147-152.
30. Klapow JC, Patterson DR, Edwards WT. Hypnosis as an adjunct to medical care in the management of Burger's disease: a case report. *Am J Clin Hypn*. 1996; 38(4):271-276.
31. Erickson MH, Rossi EL. Two level communication and the microdynamics of trance and suggestion. *Am J Clin Hypn*. 1976; 18(3):153-171.
32. Jensen MP. Hypnosis for chronic pain management: a new hope. *Pain*. 2009; 146(3):235-237.
33. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. *European Journal of Pain*. 2005; 9(4):463-484.
34. Jensen MP. The neurophysiology of pain perception and hypnotic analgesia: implications for clinical practice. *Am J Clin Hypn*. 2008; 51(2):123-148.
35. Rainville P, Duncan GH, Price DD, Carrier B, Bushnell MC. Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science*. 1997; 277(5328):968-971.
36. Craig AD. Interoception and emotion: a neuroanatomical perspective. In: Lewis M, Havilan-Jones JM, Barrett LF, eds. *Handbook of emotion*. 3rd ed. New York: Guilford Press; 2008:272-288.
37. Rainville P. Brain mechanisms of pain affect and pain modulation. *Curr Opin Neurobiol*. 2002; 12(2):195-204.
38. Byers MR, Bonica JJ. Peripheral pain mechanisms and nociceptor plasticity. In: Loeser JD, Butler SH, Chapman CR, Turk DC, eds. *Bonica's management of pain*. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins; 2001:26-72.
39. Isnard J, Magnin M, Jung J, Mauguiere F, Garcia-Larrea L. Does the insula tell our brain that we are in pain? *Pain*. 2011; 152(4):946-951.
40. Jensen MP, Hakimian S, Sherlin LH, Fregni F. New insights into neuromodulatory approaches for the treatment of pain. *The Journal of Pain*. 2008; 9(3):193-199.
41. Hilgard ER, Hilgard JR. *Hypnosis in the relief of pain*. Los Altos: W. Kaufmann; 1975.
42. Andreychuk T, Skriver C. Hypnosis and biofeedback in the treatment of migraine headache. *Int J Clin Exp Hypn*. 1975; 23 (3):172-183.
43. Friedman H, Taub HA. Brief psychological training procedures in migraine treatment. *Am J Clin Hypn*. 1984;26(3):187-200.
44. Holroyd J. Hypnosis treatment of clinical pain: understanding why hypnosis is useful. *Int J Clin Exp Hypn*. 1996;44(1):33-51.
45. Jensen MP, Barber J, Romano JM, et al. A comparison of self-hypnosis versus progressive muscle relaxation in patients with multiple sclerosis and chronic pain. *Int J Clin Exp Hypn*. 2009; 57 (2):198-221.
46. Jensen MP, Hanley MA, Engel JM, et al. Hypnotic analgesia for chronic pain in persons with disabilities: a case series. *Int J Clin Exp Hypn*. 2005;53(2): 198-228.
47. Spanos NP, Chaves JF. *Hypnosis: the cognitive-behavioral perspective*. Buffalo: Prometheus Books; 1989.
48. Chaves JF. Hypnosis in pain management. In: Rhue JW, Lynn SJ, Kirsch I, eds. *Handbook of clinical hypnosis*. Washington, DC: American Psychological Association; 1993.
49. Dillworth T, Jensen MP. The role of suggestions in hypnosis for chronic pain: a review of the literature. *The Open Pain Journal*. 2009; 3(1):39-51.
50. Melis PM, Rooimans W, Spierings EL, Hoogduin CA. Treatment of chronic tension-type headache with hypnotherapy: a single-blind time controlled study. *Headache*. 1991; 31(10):686-689.
51. Simon EP, Lewis DM. Medical hypnosis for temporomandibular disorders: treatment efficacy and medical utilization outcome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 2000; 90(1):54-63.
52. Spinhoven P, Linssen AC, Van Dyck R, Zitman FG. Autogenic training and self-hypnosis in the control of tension headache. *General Hospital Psychiatry*. 1992; 14(6):408-415.
53. ter Kuile MM, Spinhoven P, Linssen AC, Zitman FG, Van Dyck R, Rooijmans HG. Autogenic training and cognitive self-hypnosis for the treatment of recurrent headaches in three different subject groups. *Pain*. 1994; 58(3):331-340.
54. Winocur E, Gavish A, Emodi-Perlman A, Halachmi M, Eli I. Hypnorelaxation as treatment for myofascial pain disorder: a

comparative study. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 2002; 93(4):429-434.
55. Zitman FG, van Dyck R, Spinhoven P, Linssen AC. Hypnosis and autogenic training in the treatment of tension headaches: a two-phase constructive design study with follow-up. *J Psychosom Res*. 1992; 36(3):219-228.
56. ter Kuile BH, Spinhoven P, Linssen AC, van Houwelingen HC. Cognitive coping and appraisal processes in the treatment of chronic headache. *Pain*. 1995; 64:257-264.
57. McCauley JD, Thelen MH, Frank RG, Willard RR, Callen KE. Hypnosis compared to relaxation in the outpatient management of chronic low back pain. *Archives of Physical Medicine and Rehabilitation*. 1983; 64(11):548-552.
58. Abrahamsen R, Baad-Hansen L, Svensson P. Hypnosis in the management of persistent idiopathic orofacial pain—clinical and psychosocial findings. *Pain*. 2008; 136(1–2):44-52.
59. Abrahamsen R, Zachariae R, Svensson P. Effect of hypnosis on oral function and psychological factors in temporomandibular disorders patients. *Journal of Oral Rehabilitation*. 2009; 36 (8):556-570.
60. Castel A, Perez M, Sala J, Padrol A, Rull M. Effect of hypnotic suggestion on fibromyalgic pain: comparison between hypnosis and relaxation. *European Journal of Pain*. 2007; 11(4):463-468.
61. Elkins G, Cheung A, Marcus J, Palamara L, Rajab MH. Hypnosis to reduce pain in cancer survivors with advanced disease: a prospective study. *Journal of Cancer Integrative Medicine*. 2004; 2(4):167-172.
62. Grondahl JR, Rosvold EO. Hypnosis as a treatment of chronic widespread pain in general practice: a randomized controlled pilot trial. *BMC Musculoskelet Disord*. 2008; 9:124.
63. Haanen HC, Hoenderdos HT, van Romunde LK, et al. Controlled trial of hypnotherapy in the treatment of refractory fibromyalgia. *J Rheumatol*. 1991; 18(1):72-75.
64. Jones H, Cooper P, Miller V, Brooks N, Whorwell PJ. Treatment of non-cardiac chest pain: a controlled trial of hypnotherapy. *Gut*. 2006; 55(10):1403-1408.
65. Jensen MP, Barber J, Romano JM, et al. Effects of self-hypnosis training and EMG biofeedback relaxation training on chronic pain in persons with spinal-cord injury. *Int J Clin Exp Hypn*. 2009; 57 (3):239-268.
66. Dillworth T, Mendoza ME, Jensen MP, Capafons A. Mechanisms and outcomes of hypnosis for chronic pain. *Journal of the Spanish Association for the Medical Evaluation of Physical Injury*. 2010; 8(10):13-31.
67. Danziger N, Fournier E, Bouhassira D, et al. Different strategies of modulation can be operative during hypnotic analgesia: a neurophysiological study. *Pain*. 1998; 75(1):85-92.
68. Ginandes C, Brooks P, Sando W, Jones C, Aker J. Can medical hypnosis accelerate post-surgical wound healing? Results of a clinical trial. *Am J Clin Hypn*. 2003; 45(4):333-351.
69. Kiernan BD, Dane JR, Phillips LH, Price DD. Hypnotic analgesia reduces R-III nociceptive reflex: further evidence concerning the multifactorial nature of hypnotic analgesia. *Pain*. 1995; 60(1):39-47.
70. Derbyshire SW, Whalley MG, Stenger VA, Oakley DA. Cerebral activation during hypnotically induced and imagined pain. *NeuroImage*. 2004; 23(1):392-401.
71. Faymonville ME, Roediger L, Del Fiore G, et al. Increased cerebral functional connectivity underlying the antinociceptive effects of hypnosis. *Brain Research Cognitive Brain Research*. 2003; 17 (2):255-262.
72. Hofbauer RK, Rainville P, Duncan GH, Bushnell MC. Cortical representation of the sensory dimension of pain. *J Neurophysiol*. 2001; 86(1):402-411.
73. Nusbaum F, Redoute J, Le Bars D, et al. Chronic low-back pain modulation is enhanced by hypnotic analgesic suggestion by recruiting an emotional network: a PET imaging study. *Int J Clin Exp Hypn*. 2011; 59(1):27-44.
74. Faymonville ME, Laureys S, Degueldre C, et al. Neural mechanisms of antinociceptive effects of hypnosis. *Anesthesiology*. 2000; 92(5):1257-1267.
75. Wik G, Fischer H, Bragee B, Finer B, Fredrikson M. Functional anatomy of hypnotic analgesia: a PET study of patients with fibromyalgia. *European Journal of Pain*. 1999; 3(1):7-12.
76. McGeown WJ, Mazzoni G, Venneri A, Kirsch I. Hypnotic induction decreases anterior default mode activity. *Conscious Cogn*. 2009; 18(4):848-855.
77. Derbyshire SW, Whalley MG, Oakley DA. Fibromyalgia pain and its modulation by hypnotic and non-hypnotic suggestion: an fMRI analysis. *European Journal of Pain*. 2009; 13(5):542-550.
78. Raij TT, Numminen J, Narvanen S, Hiltunen J, Hari R. Strength of prefrontal activation predicts intensity of suggestion-induced pain. *Human Brain Mapping*. 2009; 30(9):2890-2897.
79. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci U S A*. 2001; 98(2):676-682.
80. Jensen MP, McArthur KD, Barber J, et al. Satisfaction with, and the beneficial side effects of, hypnotic analgesia. *Int J Clin Exp Hypn*. 2006; 54(4):432-447.
81. Lang EV, Benotsch EG, Fick LJ, et al. Adjunctive non-pharmacological analgesia for invasive medical procedures: a randomised trial. *Lancet*. 2000; 355(9214):1486-1490.
82. Jensen MP. A neuropsychological model of pain: research and clinical implications. *The Journal of Pain*. 2010; 11(1):2-12.
83. Jensen MP. *Hypnosis for chronic pain management: therapist guide*. New York: Oxford University Press; 2011.
84. Turk DC, Flor H. Chronic pain: a biobehavioral perspective. In: Turk RJGDC, ed. *Psychosocial factors in pain: critical perspectives*. New York: Guilford Press; 1999:18-34.
85. Turk DC, Okifuji A. Treatment of chronic pain patients: clinical outcomes, cost-effectiveness, and cost-benefits of multidisciplinary pain centers. *Critical Reviews in Physical and Rehabilitation Medicine*. 1998; 10:181-208.
86. Turk DC, Okifuji A. Interdisciplinary approach to pain management: philosophy, operations, and efficacy. In: Ashburn MA, Rice LJ, eds. *The management of pain*. Baltimore: Churchill-Livingstone; 1998: 235-248.
87. Kirsch I, Montgomery G, Sapirstein G. Hypnosis as an adjunct to cognitive-behavioral psychotherapy: a meta-analysis. *J Consult Clin Psychol*. 1995; 63(2):214-220.
88. Hammond DC, ed. *Handbook of hypnotic suggestions and metaphors*. New York: W. W. Norton & Company; 1990.
89. Erickson MH, Rossi EL. *The collected papers of Milton H. Erickson on hypnosis*. New York: Irvington Publishers; 1980. distributed by Halsted Press.
90. Erickson MH, Rossi EL. *The nature of hypnosis and suggestion*. New York: Irvington Publishers; 1980. distributed by Halsted Press.
91. Erickson MH, Rossi EL, Rossi SI. *Hypnotic realities: the induction of clinical hypnosis and forms of indirect suggestion*. New York: Irvington Publishers; 1976. distributed by Halsted Press.
92. Erickson MH, Rossi EL, Ryan MO. *Life reframing in hypnosis*. New York: Irvington Publishers; 1985.
93. Erickson MH, Rossi EL, Ryan MO, Sharp FA. *Healing in hypnosis*. New York: Irvington Publishers; 1983.
94. Keefe FJ, Rumble ME, Scipio CD, Giordano LA, Perri LM. Psychological aspects of persistent pain: current state of the science. *The Journal of Pain*. 2004; 5(4):195-211.
95. Jensen MP, Patterson DR. Control conditions in hypnotic-analgesia clinical trials: challenges and recommendations. *Int J Clin Exp Hypn*. 2005; 53(2):170-197.