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Hypnosis for Chronic Neuropathic Pain: A Scoping Review

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Abstract

Objective. Neuropathic pain is complex and often refractory. Clinical hypnosis has emerged as a viable treatment for pain. This scoping review is the first comprehensive review of hypnosis for chronic neuropathic pain. It critically assesses available evidence noting practice implications, literature gaps, and future research opportunities. **Subjects**. Individuals with chronic neuropathic pain treated with hypnosis. **Methods**. Following PRISMA guidelines, we searched PubMed, CINAHL, Embase, and PsycInfo for studies for which the intervention and primary outcome(s) were associated with hypnosis and neuropathic pain, respectively. Included studies were empirical, in English, and published from January 1996 to August 2021. **Results**. Nine articles with 301 total participants were reviewed. Neuropathic pain included, for example, complex regional pain syndrome (CRPS), brachial neuralgia, and spinal cord injury. Hypnosis dose varied with administration and format. Six studies used comparators. Every trial demonstrated pain and quality-of-life benefits, with several controlled trials indicating hypnosis as superior to active comparator or standard of care. CRPS-specific studies showed notable improvements but had significant study limitations. Methodological weaknesses involved trial design, endpoints, and recruitment strategies. **Conclusions**. The evidence is weak because of poor study design, yet encouraging both for analgesia and functional restoration in hard-to-treat chronic neuropathic pain conditions. We highlight and discuss key knowledge gaps and identify particular diagnoses with promising outcomes after hypnosis treatment. This review illustrates the need for further empirical controlled research regarding hypnosis for chronic neuropathic pain and provides suggestions for future studies.

Key Words: Chronic Pain; Complementary Medicine; Hypnosis; Neuropathic Pain; Pain Management; Quality of Life

Introduction

Chronic pain significantly affects quality of life and disability: it worsens overall health perception, interferes with everyday activities, and negatively impacts relationships and interpersonal interactions [1]. When compared with non-neuropathic pain, chronic *neuropathic* pain is estimated to have a prevalence between 3% to 17% in the general population [2] and is associated with sleep disturbances, mood disorders, morbidity, and poor quality of life [3, 4]. Moreover, chronic neuropathic pain tends to have a relatively poor prognosis and be refractory to common first-line pharmacotherapy [5].

There are several key challenges in the management of chronic neuropathic pain. First, fewer than half of patients are managed with a single treatment agent, and we lack a standardized management approach [6]. Similarly, current evidence does not address the long-term safety of combination therapy, nor does it support chronic opioid analgesics as first-line treatment [7, 8]. Unfortunately, practitioners often rely on third-line therapies, many patients take

chronic opioid analgesics, and much of neuropathic pain remains uncontrolled [4, 8–11].

Given these challenges, there is interest in nonpharmacological complementary and alternative medicine (CAM) for pain, including hypnosis. A recent meta-analysis found positive benefit of hypnosis for chronic pain [12], and another reported hypnosis as superior to standard care and other psychological interventions for non-headache chronic pain [13]. A review on neuromodulation for chronic pain concluded that training patients to use hypnosis could be feasible first-line therapy [14], and hypnosis also enhances the efficacy of other therapies such as cognitive behavioral therapy [15]. Given this, it is unsurprising that hypnosis and CAM therapies are becoming increasingly mainstream. To illustrate: the United States Department of Veterans Affairs (VA) authored a Provision of Complementary and Integrative Health document in 2017 [16], and the VA Health Care "Whole Person Pain Care" treatment recommendations incorporate a "range of conventional and complementary approaches" for pain management, including hypnosis [17].

Despite the significant challenges in managing neuropathic pain and data supporting hypnosis as a viable chronic pain treatment, the literature on hypnosis for chronic *neuropathic* pain is notably less robust. Persons with neuropathic chronic pain may be more likely than those with non-neuropathic pain to respond to hypnosis [18], highlighting the potential benefit and need for more research. To the authors' knowledge, this scoping review serves as the first formal review of hypnosis for chronic neuropathic pain. This review is necessary for several reasons: to identify and map available evidence, to report on evidence that may inform clinical practice, to examine how empirical research has been conducted thus-far, to analyze knowledge gaps, and to guide future research [19].

Methods

With guidance from an experienced librarian, MeSH terms (online Supplementary Data) were used to identify articles regarding chronic neuropathic pain and hypnosis in the following databases: PubMed, CINAHL, Embase, and PsycInfo. Inclusion criteria were that the study (1) involve empirical investigation, (2) be in the English language, (3) be published in the past 25 years (i.e., 1996 through August 2021), and (4) have intervention and primary outcome(s) associated with hypnosis and chronic neuropathic pain, respectively.

Studies identified by the search terms were screened for duplicates and underwent title and abstract review by two reviewers to assess for study criteria (M.M. and E.C.). Our reviewers noted that many articles could have been excluded for several reasons. To improve clarity and reproducibility, we decided to exclude articles sequentially by category: we excluded first all articles written prior to 1996, then those not written in English, then all nonempirical investigations (e.g., case reports, book chapters, letters to the editor, review articles), and finally those that did not study hypnosis for chronic neuropathic pain (Figure 1).

Following independent review, all three authors met to determine reviewer concordance. All authors then read the full-text articles identified for inclusion, with M.M. extracting information on study population, outcomes, metrics, design, and limitations (Table 1).

Results

Results of Search and Classification of Articles

Nine articles were selected for review out of 301 unique search results (Figure 1). Agreement on articles selected for review was 100%. Most abstracts ($n = 230$) were first excluded as they did not involve empirical investigation, with the reviewers noting that many of these nonempirical works *also* did not focus on hypnosis for chronic neuropathic pain. All included articles described empirical studies: 6 randomized control trials (RCTs) [18, 20–24], 2 pre-post studies [25, 26], and one retrospective investigation [27]. Two of the articles were conference abstracts describing RCTs not reported elsewhere [22, 23]. Given the limited available literature, a meta-analysis could not be performed. We have considered the primary findings of each study in Table 1, which we synthesize across study domains in detail below.

In deciding which studies to include, we used standard definitions for key concepts. The International Association for the Study of Pain's definition of neuropathic pain was used: "pain caused by a lesion or disease of the somatosensory nervous system." [28] We included two studies that investigated patients with both neuropathic and non-neuropathic pain, and when able separated out the data for these subgroups [18, 24]. We accepted each study's identification of a patient's pain as "chronic," but notably we considered and excluded two studies investigating the effect of hypnosis on an acutely painful experience in patients with other chronic pain, as the subject of investigation dealt with experimentally induced pain rather than chronic neuropathic pain [29, 30].

When considering hypnosis, we used the American Psychological Association's (APA) definition: "a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion" [31]. The APA defines hypnotic induction as "a procedure designed to induce hypnosis" [31]. Hypnosis can include the use of both hetero-hypnosis, which involves direct guidance by another person into trance, or self-hypnosis, a process that is self-induced [32]. Hypnosis strategies are described in Table 2 but included both hetero-hypnosis and self-hypnosis. One study used autogenic training [21], a self-induced state of focused relaxation with suggestion [33] that is considered by some to be a form of self-hypnosis and by others to not be hypnosis [32, 34]. Given the divergence in opinion, this study was included, but we clearly note the use of autogenic training throughout to avoid misrepresenting the literature.

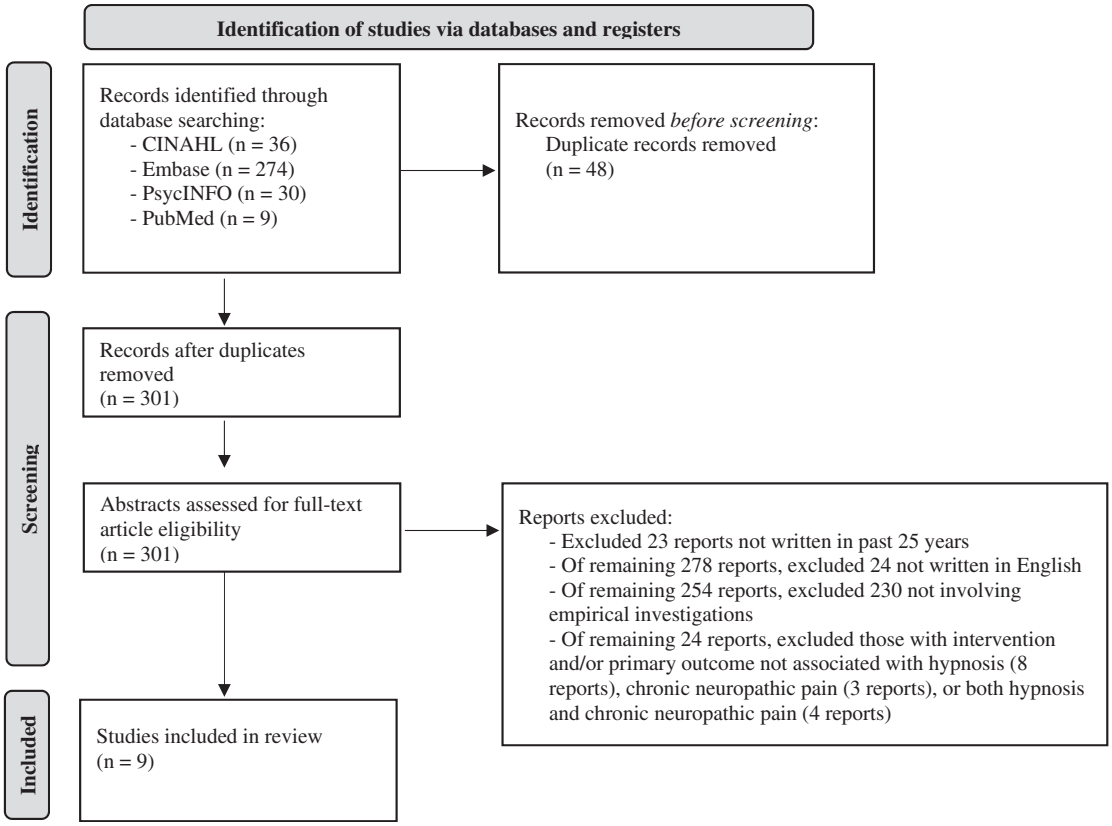

Figure 1. PRISMA study flow figure. This figure illustrates the methodology for conducting the abstract review and ultimately identifying the nine full-text articles included in this pragmatic review.

Participant Characteristics

Study sizes ranged from 12 to 70 with a mean of 34 participants. Two studies investigated persons with neuropathic and non-neuropathic pain: in one study 17 of 37 participants had neuropathic pain [18], and in another 59 of 70 participants did [24]. As such, the patients with neuropathic pain across all studies numbered 275. Five of the seven studies reporting gender of participants were predominately male [18, 21–23, 25]. More specifically, of the 253 gendered persons, 59.3% were male. None of the trials performed subgroup analyses to compare how males and females responded to hypnosis.

Type and Diagnosis of Neuropathic Pain

Varying neuropathic pain subtypes were investigated, including complex regional pain syndrome (CRPS), also known as reflex sympathetic dystrophy (RSD) [21, 24, 26, 27], chronic brachial neuralgia [20, 22, 24], chronic burn injury [23], and human immunodeficiency virus distal sensory polyneuropathy (HIV-DSP) [25]. One study including both neuropathic and non-neuropathic pain classified those with neuropathic pain as having spinal cord injury (SCI), transition zone pain, or radicular pain [18]. Another study containing neuropathic and non-neuropathic pain participants reported that the most common painful conditions were CRPS (35.7% of participants), lower back pain (22.9%), postoperative (10%) or post-traumatic (8.6%) peripheral neuropathic pain, limb osteoarthritis (5.7%), and cervicobrachial neuralgia (5.7%) [24]. When detailed, diagnostic approaches included expert examination [22, 25], imaging [21], specific diagnostic criteria [26, 27], and patients with a specific injury meeting predetermined criteria for chronic pain [18, 23].

Hypnosis Intervention

The studies varied in how investigators implemented hypnosis, with Table 2 providing more descriptive details. Eight of nine studies described regular individual hypnosis which, when specified, averaged 3–10 sessions [18, 20–25], most commonly occurred weekly [20–22, 25, 27], and had duration ranging 30–90 minutes [21, 24, 25, 27]. Other hypnosis interventions included self-hypnosis training [18, 24, 25], providing participants a pre-recorded self-hypnosis audio-recording for home practice [18], and physical therapy (PT) under hypnosis [27]. As described before, one study used autogenic training, which some consider a form of self-hypnosis [21]. Another study simply stated that "various hypnotherapeutic and other modalities were integrated into treatment" [26].

Control or Comparator Intervention

Six of nine studies were randomized and compared hypnosis to a control or comparator intervention. These included

Table 1. Data extraction

Author	Year	Article	Design	Number of Participants	Male (M) vs Female (F)	Pain	Intervention(s)	Timepoints	Primary Outcomes	Secondary Outcomes
Ahmad	2015	Hypnotherapy and Accupressure for Brachial Neuralgia	RCT	12		Chronic brachial neuralgia	(1) Hypnotherapy (four sessions, 1 week apart) or (2) Acupressure (two sessions fortnightly where given instructions + 2 week supply of accupressure patches)	Week 0, 2, and 4; month 4	VAS, BPI, SF36v2	
Dorfman	2013	Hypnosis for Treatment of HIV Neuropathic Pain	Pre-post	36 (41 ITT)	30M (73.2%), 11F (26.8%)	HIV-DSP	Three weekly training sessions in self-hypnosis (three one-on-one 70-minute sessions)	7 weeks pre- (3 sessions) + 7 weeks post-intervention (3 sessions)	SFMPQ (including total pain scale, VAS, PPI)	Affective state (CES-D; STAI), MOS-QOL
Fialka	1996	Autogenic Training for Reflex Sympathetic Dystrophy	RCT	18	12M (66.7%), 6F (33.3%)	CRPS	10 weeks either: (1) home therapy + weekly 90-minute autogenic training sessions or (2) home therapy alone (elevate limb, ice, therapeutic exercises (including three units supervised)	Pre- (week 0) and post-intervention (week 10)	VAS	ROM, skin temperature, limb volume difference, 4th phase of 4-phase bone scan
Flemming	1996	Reflex Sympathetic Dystrophy: Long-Term Remission with Hypnosis Suggests Different Paradigm for the Disease	Pre-post	41		RSD aka CRPS	"Various hypnotherapeutic and other modalities were integrated into therapy" + psych eval + myofascial therapy		Symptom severity, symptom frequency, ability to work	
Jensen	2009	Effects of Self-Hypnosis Training & EMG Biofeedback Relaxation Training on Chronic Pain in Persons with Spinal Cord Injury	RCT	28 (37 ITT) (17 with neuropathic pain)	28M (76%); 9F (24%)	Neuropathic pain subtypes: (1) spinal cord injury, (2) transitional zone, or (3) radicular pain	10 training sessions of variable frequency in (1) hypnosis or (2) biofeedback; each group given audio recording guiding either self-hypnosis or relaxation	Pre-treatment, post-treatment, 3-month follow-up	Average pain intensity and current pain intensity (NRS)	Average daily pain unpleasantness, pain interference (modified BPI), depressive symptoms (CES-D), perceived control over pain (SOPA); global satisfaction with treatment; and (if applicable) frequency and effects of self-hypnosis

(continued)

Table 1. continued

Author	Year	Article	Design	Number of Participants	Male (M) vs Female (F)	Pain	Intervention(s)	Timepoints	Primary Outcomes	Secondary Outcomes
Lebon	2017	Physical Therapy (PT) Under Hypnosis for the Treatment of Patients with Type 1 CRPS of the Hand & Wrist: Retrospective Study of 20 cases	Retrospective study of 20 cases	20	7M (35%); 13F (65%)	RSD aka CRPS	PT under hypnotherapy for 45–60 minutes weekly to every-other-week with standard thrice weekly rehabilitation (PT) between sessions	"Until patient decided they had recovered"	Pain (VAS, analgesic use); stiffness (ROM); strength (pinch, grasp)	Functional scores (QuickDASH, PWRE); patient satisfaction; return to work; side effects
Razak	2019	A Comparative Study of Two Modalities in Pain Management of Patients Presenting with Chronic Brachial Neuralgia	RCT	40	40M (100%)	Chronic brachial neuralgia	(1) Hypnotherapy (four sessions, 1 week apart) or (2) Acupressure (two sessions fortnightly where given instructions + 2 week supply of accupressure patches)	1 month pre-treatment, pre-treatment, 4- and 16-weeks post-treatment	VAS, BPI, SF36v2	
Tonye	2021	Efficacy of a combination of hypnosis and transcutaneous electrical nerve stimulation (TENS) for chronic non-cancer pain: A randomized controlled trial	RCT	70 (72 ITT)	17M (24%); 53F (76%)	Peripheral neuropathic (31.4%), nociceptive (15.7%), and combined neuropathic and nociceptive 52.9%) pain	Eight visits over 6-month period with pain specialist and nurse explaining TENS and its use at first session, then telling patient to use TENS twice daily and either (1) separate pain and anesthesiology nurse inducing hypnosis while turning on TENS device for 30 minutes and instructing patient in home self-hypnosis or (2) no hypnotic induction or instruction	Days 0, 7, 21, 42, 56 in addition to Months 1, 3, 6	VAS	Analgesic consumption, SF36, compliance, PGIC
Wiechman	2019	A Randomized Controlled Trial of Hypnosis for Pain and Itch Following Burn Injury	RCT	27	16M (60%); 11F (40%)	Post-burn itch ("categorized as neuropathic pain")	(1) four sessions of hypnosis or (2) "treatment as usual"	48-hours post-intervention; 1, 3, 6, and 12-months post-intervention	NRS (pain, itch); 5-D Itch Scale	

This table includes the information from the 9 empirical studies included in this pragmatic review, as extracted and organized by author M.M. with verification from the other authors. Other data, such as detailed outcomes and further description of hypnotic interventions, were extracted elsewhere for the sake of space and organization.

BPI = brief pain inventory; CES-D = center for epidemiological studies depression scale; GPIC = global patient impression of change; HBP = high baseline pain; HIV-DSP = human immunodeficiency virus distal sensory polyneuropathy; IASP = international association for the study of pain; ITT = intention to treat; LBP = low baseline pain; MOS-QOL = medical outcomes study quality of life measures for HIV-infected patients; NRS = numerical rating scale 0–10; PCS = pain catastrophizing scale; PT = physical therapy; PPI = present pain intensity; ROM = range of motion; RDS = reflex sympathetic dystrophy; SCI = spinal cord injury; SF36v2 = SF36v2 health survey; SFMPQ = short form mcgill pain questionnaire; SOPA = survey of pain attitudes; STAI0 = state trait anxiety index; VAS = visual analogue scale.

Table 2. Hypnosis and hypnotic suggestion

	Description of Hypnosis	Hypnotic Suggestion Used (If Applicable)
Ahmad	"The hypnotherapist used a standardized pain analgesic protocol throughout the session and tailored induction with specific analgesia suggestions according to patient's need"	Not described in further detail
Dorfman	Three one-on-one 70 minute sessions: *Session 1*: Introduction to hypnosis, followed by sample hypnosis introduction, then introduction to concept of self-hypnosis. Hypnotist guides participant through self-hypnosis procedure, and participant given audio recording for self-hypnosis at home. *Session 2*: Participant performed self-hypnosis induction; any difficulties addressed. Participants instructed to use self-hypnosis over coming week to achieve target goals *Session 3*: Assume that participant could use self-hypnosis independently; participant performed self-hypnosis induction and addressed any difficulties.	Not described in further detail
Fialka	Patients seated comfortably in quiet room with dimmed lights, instructed to close their eyes. Rhythmic slow breathing prior to suggestion induction followed by physical therapy exercises. Patients encouraged to practice autogenic training at home.	"My arms and legs are heavy; my arms and legs are warm; my heartbeat is calm and regular; my body breathes itself—it breathes me; my abdomen is warm; my forehead is cool."
Flemming	Symptomatic relief using (1) general relaxation techniques, (2) direct suggestion under hypnosis, or (3) specific metaphor designed to alter perception of pain and other labile features of the disease. Reinforcement techniques (encouragement, myofascial therapy, ego-strengthening) to encourage a pain-free identity.	Not described in further detail
Jensen	Intervention script of about 40 minutes; induction followed by suggestion followed by return to fully alert state, repeated until all five analgesic suggestions administered. Participants received all five analgesia suggestions during first two sessions, and then the treating clinicians selected the suggestion to which they appeared the most responsive and provided that along with the decreased-suffering suggestion at each subsequent session. Third and fourth sessions recorded and given to patient to practice self-hypnosis at least daily.	Induction followed by 5 specific suggestions for analgesia or comfort/relaxation: (1) decreased pain, (2) deep relaxation, (3) hypnotic anesthesia, (4) decreased unpleasantness, (5) sensory substitution.
Lebon	Induction phase that allowed the patient to dissociate and protect themselves from the pain, prior to PT treatment.	Not described in further detail
Razak	Standardized pain analgesic protocol for all sessions with specific analgesia suggestions. Hypnotherapist also taught the patients self-hypnosis that could be used to reduce pain on a daily basis, outside the face-to-face sessions.	Not described in further detail
Tonye	Induction followed by suggestions for changing pain perception including the following steps: absorption, focused concentration, and dissociation.	Nurse asked the patient to represent pain, the alleviation of suffering, and relief by focusing on a quiet place or a quiet period of their lives. The nurse provided suggestions for analgesia and/or relaxation using metaphors constructed on the basis of the patient's words.
Wiechman	Four sessions of hypnosis	Not described in further detail

This table tabulates any information that articles provided about how hypnosis sessions were implemented in the protocol. Hypnotic suggestions, if described in the articles, are included.

standard of care [23, 24], acupressure [20, 22], weekly home therapy for CRPS (e.g., elevation of the affected limb, ice, therapeutic exercise, instruction booklet detailing home therapy programs, 3 sessions of supervised therapeutic exercise) [21], and biofeedback training [18].

Timepoints

Seven of nine studies provided specific timepoint data. The initial data points were immediately pre-treatment [18, 20, 21, 23, 24], 4 weeks pre-treatment [22], or 7 weeks pre-treatment [25]. Post-intervention follow-up ranged from 7 weeks [25] to 1 year post-treatment [23], with the average last data point collected 19.9 weeks post-intervention.

Outcomes and Findings: Pain

Pain-focused primary outcomes included visual analog scale (VAS) [20–22, 24, 25, 27, 29], brief pain inventory

(BPI) [18, 20, 22], pain intensity numerical rating scale (NRS) [18, 23], present pain intensity (PPI) [25], short-form McGill pain questionnaire (SFMPQ) [25], symptom severity and frequency [26], analgesic use [24, 27], itching intensity [23], and the 5-D itch scale [23].

Current Pain: The most common pain outcome used was the VAS to assess current pain, which was used in six studies. All studies reporting VAS found a significant decrease in pain with hypnosis, with the pre- to post-treatment difference (i.e., the change in pain, Δ_{pain}) ranging from 1.04 [25] to 4.0 [27] points on the 10-point VAS scale. Of the 4 studies reporting VAS with comparator interventions, the evidence for hypnosis versus comparator is mixed. Hypnosis was superior to acupressure in decreasing 4-month post-treatment mean pain scores (from 8.67 ± 1.75 pre-treatment to 5.83 ± 1.83 post-treatment in hypnosis group (Δ_{pain} 2.84), compared with from 8.50 ± 1.38 pre-treatment to 7.16 ± 2.32 post-treatment in acupressure group (Δ_{pain} 1.34)) [20]. While acupressure reduced pain intensity faster than hypnosis in the first 2 weeks of treatment [22], the benefits from hypnosis were more durable [20, 22]. Burn patients had no significant difference in pain scores when they underwent autogenic training compared with "treatment as usual;" [21] Similarly, there was no significant difference in the pain reduction achieved by use of transcutaneous electrical nerve stimulation (TENS) with or without hypnosis [24].

Pain Intensity: Pain intensity was measured by the BPI, NRS, and PPI in five studies. Of the three studies reporting BPI, there were mixed results with respect to the benefit of hypnosis. When compared to acupressure, hypnosis produced no significant difference in pain interference between groups in one study [22] but produced a greater reduction in pain intensity in a second study [20]. In the first study using acupressure, both groups saw significant reductions in pain interference and intensity post-treatment, but the hypnosis group maintained gains at 4-month follow-up compared with the acupressure group [22]. There was no significant difference between hypnosis and biofeedback [18] or standard of care [23] with respect to pain intensity as measured by the NRS [18, 23]. Likewise, there was no significant difference in 3-month average daily pain intensity between biofeedback and hypnosis groups [18], and both hypnosis and "treatment as usual" for burn patients led to decreased pain intensity over time [23]. In one study, PPI improved from 3.40 pre-hypnosis to 2.90 post-treatment after three hypnosis sessions [25].

Other pain experiencing: Other pain-centered outcomes include symptom-specific outcomes, medication use, and overall assessment of the quality and intensity of subjective pain. Mean total pain scores in patients with HIV-DSP decreased with hypnosis and were maintained at 7 weeks post-intervention; at study exit, 26 patients (72%) had improved pain scores with mean pain reduction of 44% [25]. CRPS symptom severity and frequency also improved: whereas most (83%) patients described their symptoms as constant and uncontrolled pre-hypnosis, the most common descriptions for post-hypnosis symptoms were occasional and easily-controlled (40%) or symptom-free (34%) [26]. The evidence for effect of hypnosis on analgesic use is mixed. In one retrospective study of 20 patients with CRPS who underwent PT under hypnosis, all patients were on analgesic medication before intervention and only 40% used analgesics afterwards [27]. In contrast, an RCT comparing TENS use and hypnosis with TENS alone found no difference in analgesic use between groups [24]. Furthermore, hypnosis provided no significant benefit in post-burn itching [23].

Outcomes and Findings: Quality-of-Life, Psychological Measures, and Functional Improvement

Most studies included outcomes focused on quality of life, psychological measures, and functional improvement: SF36v2 Health Survey (SF36v2) [20, 22, 24, 25], Center for Epidemiological Studies Depression Scale (CES-D) [18, 25], ability to work [26], joint stiffness [27], hand strength [27], simple hand value (SHV) [27], State Trait Anxiety Inventory (STAI) [25], Survey of Pain Attitudes (SOPA) [18], Patient Global Impression of Change (PGIC) [24], and several CRPS-focused metrics [21].

Overall quality of life and function: The most common quality-of-life outcome measure was the SF-36v2, applied in 4 studies. All studies showed improved SF-36v2 metrics with hypnosis, but they varied as to whether this improvement was significantly different from the improvement with comparator (if used). In two trials improvement with hypnosis was not significantly different from improvement with acupressure [20] or TENS unit monotherapy [24], and the third utilizing SF-36v2 lacked comparator [25]. The fourth study utilizing SF-36v2 also compared hypnosis to acupressure, finding that both groups had improved physical and mental component scores 16-weeks post-treatment compared with pre-treatment [22]. However, while the acupressure group's general health peaked 4 weeks into treatment, the hypnosis group showed improved mental health up to 4 months post-treatment and was superior in the durability of improved scores across dimensions of physical and emotional roles, social functioning, and emotional distress. A noncontrolled pre-post trial on self-hypnosis training also showed improvement in physical and role function, pain-related well-being, and perceived change in health status [25]. In a CRPS trial, integration of hypnosis and other modalities into standard therapy improved patients' ability to return to work [26]. Pre-treatment, most (70%) patients were not working at all and only 16% were working full-time. Post-treatment, most (57%) were working full-time and only 27%

remained out of the workforce [26]. A study comparing the use of TENS with and without hypnosis found no difference in serial SF-36v2 results between the groups [24].

Psychological measures: Outcomes suggest that hypnosis may benefit some patients with depression. Hypnosis combined with PT decreased depression-related symptoms in patients who scored high for depression before treatment [25]. When compared with biofeedback, hypnosis was associated with a slight but significant decrease in pre- to post-treatment depressive symptoms; there was a marked *increase* in these symptoms in the biofeedback group. Neither group had ongoing significant changes in depressive symptoms at 3-month follow-up [18]. Only one study investigated anxiety, reporting no measurable change in STAI following hypnosis [25].

The evidence regarding coping with and control of pain is mixed. When evaluating attitudes toward pain, SCI patients significantly increased their perceived ability to control pain (i.e., self-efficacy) with hypnosis, but this was not maintained at 3-month follow-up [18]. When assessing satisfaction through the PGIC, there was no difference in impression of change between groups using TENS units with or without hypnosis [24].

Syndrome-specific measures: The remaining quality-of-life outcomes were restricted to the 3 available CRPS-focused studies, which support potential improvement with hypnosis in some CRPS-focused metrics. CRPS patients who underwent regular PT under hypnosis with standard thrice-weekly PT between sessions had significantly increased range of motion (ROM), strength (pinch and grasp), and simple hand value (SHV) [27]. Another CRPS trial showed that integration of hypnosis and other modalities into standard therapy helped patients return to work [26]. A third CRPS trial found a statistically significant difference between home therapy alone ("control") and autogenic training with respect to skin temperature, which decreased in autogenic training group from $34.5^{\circ}C \pm 0.7$ before treatment to $32.2^{\circ}C \pm 0.9$ after, but increased in control from $32.7^{\circ}C \pm 0.6$ before treatment to $33.5^{\circ}C \pm 0.6$ after, with no difference in inter-limb volume. Both groups improved flexion and extension [21].

Outcomes and Findings: Mediators

Several trials investigated potential mediators for success. One study's attempts to predict response to treatment by assessing for participants' general hypnotizability (i.e., measured responsiveness to suggestion) and treatment outcome expectations found weak, non-significant associations [18]. Another study also tested for hypnotizability, only offering hypnosis to patients with "high capacity" for suggestion [26].

Outcomes and Findings: Unique or Notable Results

The studies described several unique and notable results outside of the described outcome metrics, including sustained value in the intervention despite enduring pain and lack of benefit to non-neuropathic pain patients.

Several studies suggested patients may find benefit from hypnosis regardless of pain reduction. One reported that both hypnosis and acupressure decreased pain intensity at 4- and 16-weeks post-treatment but that hypnosis was clearly superior in maintaining improved scores of "role physical," "social functioning," "role emotion," and mental health aspects [22]. Despite lacking a "clinically meaningful" decrease in daily pain, many patients who were trained in self-hypnosis in another trial reported treatment satisfaction and continued to practice self-hypnosis (80% of participants) or listen to audio recordings (60%) at 3-month follow-up [18]. Interestingly, another study found no systematic relationship between the amount of self-hypnosis practice and decrease in total pain scores [25].

Additionally, and especially pertinent, are findings regarding which patient subgroups responded to hypnosis in a study that included individuals with and without neuropathic pain. *All* patients who responded to hypnosis had neuropathic pain, and *none* of the patients with non-neuropathic pain responded to hypnosis. This finding was statistically significant for time, treatment condition, and pain type interaction [18].

Limitations and Weaknesses

Broadly across studies, methodological limitations surround uncontrolled design, follow-up period, recruitment, and inclusion criteria, potentially biasing results. One-third of the trials reviewed lack a control or comparator group [25–27], and of the seven that specify data timepoints only four report follow-up beyond 3 months [20, 22–24] and only two beyond 4 months [23, 24]. The two studies with the longest follow-up found no significantly different outcomes between control and intervention groups [23, 24]. Several studies reported difficulties with recruitment, one noting that 25% of eligible persons did not consent as they "did not believe in hypnosis" [23] and another only offering hypnosis to interested, highly-hypnotizable patients [26]. Two trials without comparator interventions used non-hypnosis modalities in addition to hypnosis including thrice-weekly PT [27], psychiatric evaluation and therapy [26], and myofascial therapy [26]. While the practical integration of modalities may maximize treatment benefit for participants, these designs make isolating treatment effects impossible. Very few protocols explicitly described the hypnotic inductions and suggestions used (Table 2), hindering reproducibility and standardization. Finally, with the average study size of 34 participants, some of the studies reviewed may be inadequately powered to detect differences between hypnosis and control groups.

Several studies noted limitations with respect to comparator design. With acupressure, investigators were unable to determine a standard acupressure point given

inter-patient meridian variability [20]. When comparing home therapy and weekly autogenic training with the control of home therapy alone, there was a difference in patient-therapist contact time between groups and investigators suggested that concomitant home therapy in both groups overshadowed true autogenic training benefits [21]. Investigators who used biofeedback noted that this comparator intervention may have included some components of hypnosis-like focused attention and suggestions [18].

There are several notable study-specific weaknesses and limitations. One trial used an open-ended patient-determined endpoint, stopping hypnosis "when patients decided they had recovered enough…to do activities of daily living with no or minimal pain" [27]. Another integrated non-hypnotherapeutic approaches into the treatment plan without comparator intervention and also had patients categorize their pain vaguely without more granular data (e.g., "controlled" versus "uncontrolled") [26]. Finally, in one study, participants randomized to hypnosis had significantly higher average pain intensity, less perceived control over pain, more depression, and more pain interference at baseline then those assigned to the control [18].

Discussion

While we note some promising trends in the emerging literature, which justifies further research into hypnosis for chronic neuropathic pain, no single trial definitively supports the use of hypnosis for all patients with neuropathic pain. Furthermore, a comprehensive review of the limited available empirical research does not support this use. There are not enough quality studies on the subject to draw definitive clinical or scientific conclusions, and the studies done thus-far are widely disparate, making finding cohorts of well-designed trends difficult. Thus, with regard to informing practice, the evidence is weak due to poor study design, but at the same time is also highly encouraging both for analgesia and functional restoration. Any trends are based on combining a very small number of studies.

Notwithstanding these limitations and others discussed later, we do suggest preliminary indication for consideration of hypnosis for *some* patients with chronic neuropathic pain. Two-thirds of trials included comparators, and hypnosis was significantly superior on improving pain and/or quality-of-life metrics when compared with acupressure for brachial neuralgia [20, 22] and biofeedback for SCI pain [18]. Hypnosis was superior in decreased 4-month pain intensity [20], decreased daily average pain (maintained at 3-month follow-up) [18], and more durable pain reduction at 4-month follow-up [22]. In addition to suggesting that hypnosis may improve chronic neuropathic pain metrics, the data include some support for it improving quality-of-life metrics. Hypnosis was superior to comparator in improving some depression metrics [18] and preserving improved mental health aspects including physical and emotional roles, social functioning, and mental health [22]. While not without substantial limitations, the trials lacking comparator intervention reported significant, impressive improvement in quality-of-life metrics including return to work [26]; CRPS-related metrics [27]; depression in high-risk patients (when hypnosis was combined with PT) [25]; and SF36v2 outcomes including physical and role function, pain-related well-being, and perceived change in health status [25]. The benefits suggested in this review support future studies to further elucidate if and when hypnosis may benefit patients with neuropathic pain.

With respect to examining how research has been conducted to date, we highlight the limitations of current studies on hypnosis for chronic neuropathic pain. First, one-third of the trials lacked comparator intervention, and in the half of the trials with comparator intervention there was improvement in both groups with no significant difference between the two. This is especially important as some of the "strongest" support for hypnosis came from trials lacking comparator intervention and including non-hypnosis treatments alongside hypnosis. For example, one study reported that 60% of patients achieved long-term remission characterized by either the absence of pain or intermittent mild pain that could be relieved with self-hypnosis [26]. However, the trial lacked both a comparator and representative sample while supplementing non-hypnosis modalities (i.e., psychiatric evaluation, psychotherapy, and myofascial therapy) into the treatment, making it impossible to isolate the effect of hypnosis. Other specific examples where systematic error was likely introduced include the use of open-ended patient-determined endpoints [27] and selection bias where a majority of patients were identified as having a high capacity for hypnosis [26]. The open-ended patient-determined endpoint resulted in a 3–12 week range in treatment length; it is difficult to generalize results when the success of treatment depends on the patients' subjective interpretation, and this range also begs the question: what inter-individual differences determined effective response in 3 weeks versus 12? With respect to hypnotic capacity, it is widely acknowledged that individual differences in hypnotizability play a role in hypnosis efficacy, with preliminary evidence that high hypnotizability is an advantage in the context of pain modulation [12, 35]. Differences in baseline pain between control and intervention groups risk regression to the mean making the change in pain appear more significant in the group with more extreme pain at [18]. In addition to the aforementioned issues, only 4 trials collected data beyond the 3-month mark [20, 22–24]. Given that the usual definition of "chronic" pain includes persistence for 3–6 months [36], it is difficult to identify any modality as a viable solution if it is not studied beyond this timepoint. As previously mentioned, 2 articles described patients with both neuropathic and non-

neuropathic pain components. Studies reporting on pure neuropathic pain more closely aligned with our review's aims and facilitated interpretation of the existing data, but the studies reporting on mixed neuropathic and non-neuropathic pain are likely more representative of an actual patient population. It is our experience that "real life" patients with pure neuropathic pain are rare in pain treatment centers, where many patients also have myopathic components to their pain experience. It is possible that the other 7 studies did not completely characterize the participants' pain experience, and the literature would benefit from future studies that characterized the other aspects of pain that coexist with chronic neuropathy. Small sample size is also a weakness with a mean of 34 participants per study. The final and perhaps most obvious weakness in the current evidence is that it is limited, with just 9 empirical studies to review and two of these being conference abstracts [20, 23]. As such, we devote the rest of our discussion to how an understanding of both promising evidence and known gaps can guide future research.

Although generally positive in their nature regarding interesting individual findings with patients, case reports ($N = 16$) were not formally reviewed as they did not contain empirical information. Qualitatively, these reports note meaningful changes in pain and function with hypnosis for refractory chronic neuropathic pain. Case studies described 21 patients treated successfully with hypnosis for trigeminal neuralgia (11 patients) [37–44], postherpetic neuralgia (four patients) [45, 46], CRPS (two patients) [47, 48], diabetic neuropathy [49], Hansen's disease with resistant neuralgia [50], post-traumatic brain injury pain [51], and post-SCI neuropathic pain [52]. These cases may be of interest to guide further research in specific populations.

With respect to guiding future research: Reviewed studies investigated different subsets of chronic neuropathic pain, and a look at which groups benefited from hypnosis may help guide both patient selection and areas for future study. Especially notable in the context of this review's focus on hypnosis for chronic *neuropathic* pain are one trial's findings that hypnosis proved effective for neuropathic pain patients, but that those with non-neuropathic chronic pain did not respond to hypnotic intervention [18]. This contextualizes the study reporting no meaningful difference in outcomes when TENS units were used with or without hypnosis as, unfortunately, this study on both neuropathic and non-neuropathic pain noted that 84.3% of participants had a component of neuropathic pain but did not perform subgroup analyses to see if there was a difference between non-neuropathic and neuropathic pain response to hypnosis. The three studies without comparators described pain and quality-of-life benefits for patients with HIV-DSP [25] and CRPS [26, 27]. Of the studies with comparators, hypnosis was superior for patients with chronic brachial neuralgia [20, 22] and SCI [18]. The trials found no meaningful difference for patients with chronic burn pain undergoing hypnosis [23] compared with treatment-as-usual. The literature would benefit from more controlled trials involving patients with CRPS, as studies without comparator intervention reported impressive significant improvements [26, 27] but the one 18-person RCT on autogenic training did not [21], making it impossible to draw conclusions within this population. Finally, most successful case reports on the subject describe patients with trigeminal neuralgia, but no empirical investigations have yet studied this. Given the small sample sizes and hypnosis implementation variation, among other factors, it is still unclear what specific conditions receive the most benefit from hypnosis. However, we suggest that investigations focusing on chronic brachial neuralgia, SCI, CRPS, and trigeminal neuralgia may be particularly fruitful.

Viewing the subtypes of neuropathic pain included in empirical trials alongside the "last resort" use of hypnosis in case reports brings up another interesting point of discussion: It is important to consider the clinical severity that both patients and providers face when confronted with neuropathic pain. The conditions included in these studies are notoriously some of the most difficult to treat, and we imagine that many of the patients feel desperate. Flemming and colleagues highlight this, reporting that at baseline 83% of participants described their pain as "severe" and "constant" and that only 16% of participants worked full-time pre-intervention [26]. The high baseline severity and refractory nature of chronic neuropathic pain in these study populations must be emphasized, as it both contextualizes the results and restricts the available sample in a way that does not match the general patient population. We ask the reader to consider the minimal side effect profile of hypnosis, especially when compared with conventional chronic pain medications (with side effects) and procedures (with risks). Given the minimal side effects and possible benefits, we purport that hypnosis may be integrated into management of neuropathic pain sooner than it currently is, especially if future studies provide additional information regarding benefits suggested in some of the empirical data reviewed.

To help the field reach more definitive conclusions on if, when, and how hypnosis may benefit patients with neuropathic pain, we emphasize several key recommendations for future trials.

- For the importance of replication, investigators should precisely describe how hypnosis was implemented, including delineating the series of suggestions used and details such as intervention number, duration, and frequency.
- Randomization and comparator intervention(s) should be included and carefully designed. There are several active

comparator interventions suggested for hypnosis, including one recently designed by Kendrick and colleagues [53].
- As hypnosis is a complex intervention involving the use of a dissociated state, multiple suggestions, metaphors, and so forth, it is important that investigators design trials to isolate what they aim to investigate. The Medical Research Council and National Institute for Health Research published guidelines in 2019 for developing and evaluating complex interventions [54].
- Clear timepoints and longer follow-up are warranted.

We look to future studies to reach more definitive conclusions on the benefit of hypnosis for chronic neuropathic pain. In addition to improving the current data by following the above suggestions, another possible direction is to determine if the goals of hypnosis could be accomplished in less time. A recent study suggested that meaningful change could be found after 4 sessions of hypnosis, which can also be implemented via telemedicine formats [55]. If further data support this, we anticipate this would greatly improve accessibility for patients. As described above, special attention should be paid to the following neuropathic pain subtypes: chronic brachial neuralgia, SCI, CRPS, HIV-DSP, and those not yet empirically studied (e.g., painful diabetic neuropathy and trigeminal neuralgia).

Conclusion

This scoping review maps the available evidence on hypnosis for chronic neuropathic pain, analyzing the nine empirical investigations on the subject. We discuss preliminary trends regarding the use of hypnosis for some patients with chronic neuropathic pain, especially those with chronic brachial neuralgia, SCI, and possibly CRPS and HIV-DSP. We conclude that the evidence is weak, because of poor study design, yet highly encouraging both for analgesia and functional restoration. We discuss key knowledge gaps and concerns with how some experiments have been conducted. This scoping review illustrates the need for further empirical controlled research regarding hypnosis for chronic neuropathic pain and provides suggestions for future studies.

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Supplementary Data

Supplementary data are available at *Pain Medicine* online.

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