



Mental imagery training for treatment of central neuropathic pain: a narrative review

Jaskirat Kaur^{1,2} · Shampa Ghosh³ · Asish Kumar Sahani² · Jitendra Kumar Sinha¹

Received: 26 December 2018 / Accepted: 5 April 2019 / Published online: 15 April 2019
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Abstract

Mental imagery is a quasi-perceptual experience in the absence of external stimuli. This concept has intrigued psychologists, sportspersons, neurologists and other scientists for over a decade now. Imagery has been used in rehabilitation and the results have been promising. Researchers refer to this as healing the body through the mind. However, the challenge is lack of standardized protocols, homogeneity and consistency in application of mental imagery in different populations. The purpose of this review is to discuss and understand the role of mental imagery in the treatment of central neuropathic pain (CNP). Treatment options of CNP are inadequate and their benefits are short lived. We conducted an extensive search on various databases using combinations of different keywords and reviewed the available literature in this area. We were able to finalize twelve studies where mental imagery was used for treating CNP in spinal cord injury (SCI), stroke and multiple sclerosis. However, the methodology and techniques of mental imagery training used in these studies were non-homogeneous and inconsistent. This review provides a guiding framework to further explore the different techniques of mental imagery and their roles in treating CNP.

Keywords Spinal cord injury · Neuropathic pain · Hypnosis · Guided imagery · Graded motor imagery · Visual illusion

Abbreviations

CNS	Central nervous system
CPSP	Central post stroke pain
CRPS	Complex regional pain syndrome
DRG	Dorsal root ganglion
GMI	Graded motor imagery
IASP	International Association for the Study of Pain
NP	Neuropathic pain
CNP	Central neuropathic pain
PNP	Peripheral neuropathic pain
ROM	Range of motion
SCI	Spinal cord injury
tDCS	Transcranial direct current stimulation

TENS	transcutaneous electrical nerve stimulation
WHO	World Health Organization

Introduction

Pain is one of the most debilitating complications, among other neurological conditions. It may lead to fatigue, anxiety, depression, disturbances in sleep and deterioration in the overall quality of life [1]. Over the years, researchers have faced the challenge to define pain but have not been very successful due to its subjective nature. According to the International Association for the Study of Pain (IASP), pain can be defined as any unpleasant sensory and emotional occurrence associated with actual or prospective tissue injury, or described in terms of such damage [2].

Pain can be further classified into three types, namely nociceptive, inflammatory and neuropathic pain (NP). Each of these types is mediated by different mechanisms. The symptoms of NP may be localized or more generalized. Typically, the symptoms may be associated with painful or burning sensation (dysesthesia), hyperalgesia, or the perception of a non-nociceptive stimulus as painful (allodynia) [3]. NP can be subdivided into peripheral neuropathic pain

✉ Jitendra Kumar Sinha
jksinha@amity.edu; jitendrakumarsinha@gmail.com

¹ Amity Institute of Neuropsychology and Neurosciences (AINN), Amity University UP, Room No. 222A, J1 Block, Sector 125, Noida 201303, India

² Indian Spinal Injuries Centre (ISIC), Sector C, Vasant Kunj, New Delhi 110070, India

³ Indian Council of Medical Research-National Institute of Nutrition, Tarnaka, Hyderabad 500007, India

(PNP) that occurs due to involvement of the peripheral nervous system (e.g., painful diabetic neuropathy) and central neuropathic pain (CNP) which occurs after a central nervous system disorder (e.g., post-stroke, multiple sclerosis (MS) or spinal cord injury) [4]. The mechanisms of peripheral and central neuropathic pain are different. PNP occurs as a result of spontaneous firing of damaged nerve fibers and oversensitivity of pain pathways due to denervation [5]. On the other hand, CNP is associated with central sensitization and central re-organization at higher levels in the CNS [6]. Neuropathic pain is refractory and often difficult to treat. The available treatment options include medications (such as pregabalin, opioids), surgery and physical therapy interventions. However, there are side effects associated with the former two approaches and the physical therapy interventions are diverse and not well established [7, 8].

Mental imagery (MI) involves the cognitive processes of imagining something that is not actually present. MI techniques have been proven to reduce pain associated with phantom limb pain, complex regional pain syndrome and other types of pain with unknown pathology [6]. CNP results in maladaptive changes in the brain and existing evidence available regarding the use of MI for CNP in neurological conditions is limited. To the best of our knowledge, this is the first review that examines the different characteristics and techniques of MI used for treating CNP in neurological conditions.

Neuropathic pain

The NP Special Interest Group (NeuPSIG); a task force of the International Association for the Study of Pain (IASP) has redefined NP as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system [9]. In the current definition, the word *somatosensory system* replaced the word *nervous system* present in the old definition, so as to differentiate NP from other types of musculoskeletal pain arising indirectly from disorders of the motor system [10]. Examples of NP include peripheral neuropathy, post herpetic neuralgia, central post stroke pain, spinal cord injury (SCI) pain, and trigeminal neuralgia [11]. NP can be divided into two categories: (a) those that are consequences of a peripheral lesion or disease and (b) those that are consequences of a central lesion or disease [12].

Peripheral neuropathic pain

Peripheral neuropathic pain (PNP) results from damage to peripheral nerves. This may occur due to metabolic damage, toxins, medications, cytokines, and other inflammatory mediators, resulting in fiber density changes and neuronal hyper excitability [5]. Pain processing pathways constituting

unmyelinated C fibers and thinly myelinated A δ fibers may undergo fiber degeneration and alterations in voltage-gated sodium channels' expression resulting in ectopic firing and faulty signal transmission [13]. In addition, there is increased supply of (pro-) inflammatory mediators due to accumulation of infiltrating immune cells (neutrophils, macrophages and mast cells) resulting in nerve fiber sensitization and neuronal damage. The ultimate result of the maladaptive mechanisms is a state of inappropriate signaling from the peripheral neuron to its second-order targets, with multi-factorial errors in both transduction and transmission [14]. PNP may be seen in painful diabetic polyneuropathy, post herpetic neuralgia, HIV-associated NP, cancer pain and post-surgical pain [11].

Central neuropathic pain

Central neuropathic pain (CNP) is associated with central nervous system lesions. Another important term associated with CNP is central sensitization. IASP defines central sensitization as the increased responsiveness of nociceptive neurons in the CNS to their normal or sub-threshold afferent input [15]. Central sensitization occurs when the stimulation is sufficiently intense or repeated. This results in sensitization of spinal and supraspinal nociceptive pathways to subsequent stimuli. If the nociceptive input remains persistent, this central sensitization becomes maladaptive. In supraspinal regions, the resulting imbalance between descending facilitation and inhibition is another major contributor to ongoing pain. Maladaptive sub-cortical and cortical plasticity also contributes to the painful interpretation of incoming signals, resulting in the enhancement of the chronic pain state [16]. CNP can result from vascular (ischemic or hemorrhagic), infectious (abscess, encephalitis, myelitis), demyelinating, traumatic [brain or spinal cord), or neoplastic disorders. However, CNP occurs most commonly in stroke (central post stroke pain (CPSP)), MS and SCI [15]. Hence, the current review highlights the application and treatment effects of mental imagery training for CNP in these three conditions.

CNP in different neurological conditions

Pain in stroke

Stroke as defined by the World Health Organization (WHO) is a clinical syndrome consisting of rapidly developing clinical signs of focal (or global, in case of coma) disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than a vascular origin [17]. CPSP is a chronic syndrome, which may occur due to hemorrhagic or ischemic lesions particularly involving thalamus.

It may be spontaneous or in response to an external stimulus [18]. It has a prevalence of about 2–8% in stroke patients [19]. The pain may be continuous or intermittent and is associated with sensory abnormalities such as hyperalgesia or allodynia. The onset usually occurs between 1 and 3 months, and the majority of patients develop symptoms by 6 months [20]. Studies suggest that this type of pain occurs as a result of central inhibition, a decrease of GABAergic inhibition and central sensitization. However, the exact pathophysiology of CPSP remains unclear [21].

Another type of pain common in stroke patients is complex regional pain syndrome (CRPS); commonly known as shoulder hand syndrome. It is a neuropathic pain syndrome characterized by spontaneous or stimulus evoked pain accompanied by autonomic and motor disturbances. CRPS is categorized into type I and type II pains. In type I CRPS, there is an absence of overt nerve damage, whereas type II pain follows peripheral nerve injury. In stroke patients type I is more common than type II. The incidence of CRPS post-stroke ranges from 1.5 to 70% [22]. The pain in CRPS is continuous and intense; sometimes inconsistent with the severity of the injury. It is associated with limited range of motion (ROM), edema, warmth, redness and tenderness to palpation in shoulder and wrist with elbow spared [23].

Pain in spinal cord injury

Pain in SCI can be classified into nociceptive (musculoskeletal or visceral) and neuropathic (above-level, at-level or below-level) pain types [24]. In a meta-analysis on NP in SCI, it was found that the overall pooled point prevalence of neuropathic pain post SCI was 53%. Moreover, pain below the level of the lesion was more common, particularly in older patients and those with tetraplegia and after 1 year of SCI [25]. The characteristics of CNP in SCI include burning (superficial) spontaneous pain, pressing (deep) spontaneous pain, paroxysmal pain, evoked pain and paresthesia/dysesthesia [26]. CNP following SCI is associated with significant changes in the neuroanatomy of multiple brain regions traditionally associated with nociceptive processing, including the ventral posterior region of the thalamus, prefrontal cortex, insular cortex, amygdala, and premotor cortex [27].

Pain in multiple sclerosis

MS is a chronic demyelinating disease of the CNS with a variable disease course. It is characterized by sensory impairments, lack of coordination, spasticity, motor weakness, fatigue and pain [28]. The prevalence of neuropathic pain in early stages of MS has been found to be 28% [29]. Neuropathic pain particularly comprises central neuropathic pain, trigeminal neuralgia and Lhermitte sign [30]. The

cause of pain is attributed to demyelinating lesions in areas involved in pain perception [31].

Mental imagery: concept

Humans can generate imagery, even in the absence of any triggering external stimulus. Mental imagery (MI) refers to the active process by which humans relive the sensations with or without external stimuli [32]. Richardson defined mental practice as the symbolic rehearsal of a physical activity in the absence of any gross muscular movements. Different terminologies such as visualization, imagery, and mental practice have been used to describe MI [33]. However, MI is not limited to only visualization, but it involves all senses. This cognitive operation utilizes different modalities such as visual, auditory, tactile, kinesthetic, olfactory, gustatory, or any combination of these senses [34]. Suinn maintained that the rich multimodal (utilizing all the senses) processes of imagery rehearsal are holistic, under conscious control, and can closely replicate the original experience, even arousing emotions similar to those associated with the experience [35].

MI and pain

The idea behind as how the brain imagines and how imagery works has intrigued neuroscientists over the decades. The effect of imagery on chronic pain has been explored and it has been suggested that there is shared representation of content and location between imagery and perception [36]. The presence of pain is associated with negative images [37]. The use of a mirror based on the concept of mirror neurons by Ramachandran et al. to train patients with phantom limb pain supports the role of MI in chronic pain [38]. MI modulates pain by altering the activity of the motor cortex, which is related to pain modulation [39]. In an experiment by Fardo et al., participants were required to imagine a glove or a wound on the forearm, and it was observed that pain perception increased during imagination of a lesion; whereas, it reduced while imagining a glove on the forearm [40]. Therefore, it is imperative to further understand the intricacies of imagery and its effect on pain, so that it can be used as interventions for treating CNP occurring in neurological conditions.

Techniques of MI used in CNP

Researchers have used various forms of MI for treating CNP in multiple neurological conditions. The commonly used techniques include guided imagery, graded motor imagery, visual illusion and hypnosis.

Guided imagery

Fitzgerald and Langevin [41] defined guided imagery (GI) as the interaction of mind and body using the power of imagination to bring about changes in physical, emotional, or spiritual dimensions [42]. It refers to the use of imagination to invoke one or more of the senses. It involves the ‘guiding’ of an individual through experiences in the mind, to access physical, emotional and spiritual dimensions to affect bodily change [43]. Patients listen to audio tapes that combine soothing music with quiet narrations of peaceful images [44]. GI involves the creation and controlled visualization of mental images. It has been successfully used for subsiding chronic pain due to cancer, musculoskeletal and post-operative conditions [45]. Researchers believe that the theoretical basis behind its efficacy is the pain gate theory. If the route of the painful stimuli can be blocked by a pleasant stimulus, perception of pain may be alleviated. Release of endorphins is also seen to be associated with positive cognition associated with GI [46].

Graded motor imagery

Another form of motor imagery used to treat chronic pain is graded motor imagery (GMI). It was described by Butler and Moseley and is based on the principle of “train the brain”. Studies suggest that application of GMI helps in cortical re-organization that eventually results in reduction of pain [47]. It has been used effectively in treating chronic pain arising from CRPS, phantom limb pain, stroke, carpal tunnel syndrome, neck and back pain among others [48, 49]. GMI is graded, i.e., it involves three sequential phases: laterality training, imagined motor imagery (explicit) and mirror therapy. Mirror therapy provides visual feedback that is useful in modulating somatic pain by providing powerful feedback into the cortex. The patients place their affected limb inside a mirror box and watch movements of their non-affected limb in the mirror. This tricks the brain as it visualizes the affected side to be moving in a pain-free normal movement pattern [48]. Mirror therapy has been used in the past to improve motor control and pain in patients with CRPS post stroke [50].

Visual illusion

Studies in SCI patients have utilized visual illusion for treating chronic NP [51, 52]. An illusion is created of normal movement instead of non-functional or painful limb in a manner that the patients get the impression that affected part has the ability to function [53]. Sakamoto et al. [54] have shown that combining observation and imagery of an action enhances corticospinal excitability in comparison to observation or imagery alone. Visual illusion is hypothesized to

cause neuroplastic changes that may affect pain. Another proposed mechanism by which they may act is by restoring the body schema that is distorted as a result of disease or trauma [53].

Hypnosis

Hypnosis has been used for treating chronic pain in fibromyalgia, low back pain, disability-related pain, cancer-related pain, irritable bowel syndrome and headache [55–57]. Hypnosis is an altered state of consciousness—a transition from a normal, ordinary state of consciousness [58]. It results in an increased focused attention and lack of attention to external stimuli. The patient is always in control and can stop the process of hypnosis whenever he desires to do so [59].

Search strategy

A comprehensive review of the literature was performed covering the period from 2000 to 2018. The electronic search was performed using the following databases: MEDLINE (via OvidSP), EMBASE (via OvidSP), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, Academic Search Premier, Web of Science, Allied and Complementary Medicine, PubMed, the Cochrane Collaboration, and the Physiotherapy Evidence Database (Pedro). Search terms included combinations of the keywords mental imagery, guided imagery, relaxation, hypnosis, neuropathic pain, pain management, pain relief, visual illusion, mental imagery techniques, stroke, spinal cord injury, multiple sclerosis, central neuropathic pain, peripheral neuropathic pain, mental imagery techniques, visual imagery, kinesthetic imagery and neurological diseases. The references of the articles found were reviewed to identify other relevant research studies. The articles found were also forward-searched to identify related articles. No new articles were retrieved using these procedures. Searches were limited to English language and human studies only. Search results have been elaborated in Table 1.

Discussion

Imagery is not just a visualization technique, but it involves all the senses [42]. This review appraises the evidence related to MI training for CNP in neurological conditions. Although the results were encouraging still this remains as one of the least explored areas. Studies conducted on MI training show a promising future, but the available evidence is heterogeneous. Twelve studies that were identified after reviewing the literature are discussed in Table 1.

Table 1 Summary of studies on the application of mental imagery techniques for treatment of central neuropathic pain

First author and year	Type of study/study design	Sample/condition	Intervention/type of MI	Outcomes measures	Duration	Main results
Stroke						
Polli et al. (2017) [62]	Non-randomized controlled trial	28 with first-ever stroke Mean (SD) age: EXPTT group-56.6 (12.5) years CONT group-58.8 (13.3) years Gender: EXPTT group: 10 males and 4 females and CONT group: 11 males and 3 females	EXPTT (<i>n</i> = 14): GMI CONT (<i>n</i> = 14): conventional rehabilitation	VAS Pain section of FMA WMFT TRS FIM SQ	20 sessions for 1 h for 4 weeks	Significant improvements were seen in GMI group over control group for both motor functions at WMFT ($p=0.002$) and pain section of FMA ($p=0.006$) Pre and post intervention VAS scores did not show any change Scores of pain FMA showed improvement in GMI group post intervention ($p=0.04$) Significant reduction in VAS scores in MT group compared to CONT group ($p<0.001$) Significant decrease in VAS scores post intervention (median 3 (range 1–6) scores from pre intervention scores (median 6) (range 2–6) were seen in MT group ($p<0.001$))
Vural et al. (2015) [61]	RCT	30 patients with first-ever stroke with CPRSI Mean age: EXPTT group-68.9 (10.5) years CONT group-61.4 (11.9) Gender: EXPTT group: 8 males and 7 females and CONT group: 9 males and 6 females	EXPTT: MT along with conventional rehabilitation CONT: conventional rehabilitation	VAS BRS FMA FIM MAS	2–4 h/day; 5 days/week for 4 weeks	Significant reduction in VAS scores in MT group compared to CONT group ($p<0.001$) Significant decrease in VAS scores post intervention (median 3 (range 1–6) scores from pre intervention scores (median 6) (range 2–6) were seen in MT group ($p<0.001$))
Cacchio et al. (2009) [50]	RCT	24 patients with stroke with diagnosis of CRPS1 Median age: 62 years (range: 53–71) Gender: 11 males and 13 females	3 groups (i) Active-mirror group: viewed a reflected image of their unaffected arm in a mirror (ii) Covered-mirror group: viewed a covered mirror (iii) MI group	Primary outcome measure 100-mm VAS Secondary outcome measures: WMFT Brush induced allodynia Edema	30 min daily for 4 weeks	Active-mirror group: 88% reported reduced pain Covered-mirror group: 12% reported reduced pain, 25% reported no change in the pain level, and 62% reported increased pain MI group: 25% reported reduced pain 75% reported increased pain VAS scores after 4 weeks for active mirrored group differed significantly from covered mirror group ($p=0.002$) and MI group ($p<0.001$)

Table 1 (continued)

First author and year	Type of study/ study design	Sample/condition	Intervention/type of MI	Outcomes measures	Duration	Main results
Cacchio et al. (2009) [60]	RCT	48 with first-ever stroke with CPRS1 Mean (SD) age: EXPPTT group-57.9 (9.9) years CONT group-58.8 (9.4) for Gender: EXPPTT group-11 males and 13 females and CONT group: 11 males and 13 females	EXPPTT: MT along with conventional rehabilitation CONT: conventional rehabilitation	VAS Tactile allodynia WMFT MAL	30 min., 5 times/week for 2 weeks followed by 1 h of MT 5 times/week for next 2 weeks; 6-month follow-up	EXPPTT group: Reduction in VAS scores (at rest and movement) ($p < 0.001$) and tactile allodynia pre-intervention and post intervention Reduction in VAS scores (at rest and movement) ($p < 0.001$) and tactile allodynia pre-intervention and at 6-month follow-up Significant improvements in scores of WMFT and MAL pre intervention and post intervention ($p < 0.001$) and at 6-month follow-up ($p < 0.001$) CONT group: There were no significant improvements seen in pre intervention and post intervention pain scores Improvements were seen in EXPPTT group over CONT group in VAS scores ($p < 0.001$) and tactile allodynia pre-intervention and post intervention and tactile allodynia pre-intervention and at 6-month follow-up ($p < 0.001$)
SCI Lovas et al. (2016) [67]	RCT	40 SCI patients Mean age (SD): Massage group-48.9 (12.2) years GI group-43 (10.7) years Gender: Massage group-16 males, 4 females GI group-18 males, 2 females	2 groups Group 1-Massage therapy Group 2-GI	SF-MPQ CFS	30 min once a week for 5 weeks	Significant reduction of pain scores were seen in both MT ($p = 0.049$) and GI ($p = 0.032$) groups There was no significant difference between the scores of SF-MPQ between MT and GI groups Similarly, CFS scores also showed a reduction in both MT ($p = 0.004$) and GI groups ($p = 0.037$)
Ozkul et al. (2015) [66]	RCT (cross over trial)	24 SCI Mean age: 32.3 (13) years Gender: 18 males, 6 females	2 groups Group A: VI application followed by TENS Group B: TENS application followed by VI	MPQ VAS NPS BPI	VI Session: 10 sessions 15 min/day; 5 days/week for 2 weeks	Decrease pre post session VAS scores ($p < 0.05$) Improvement of sharpness, hotness, unpleasurateness and depth parameters of NPS post treatment ($p < 0.05$) Improved "ability to get around" on BPI post treatment

Table 1 (continued)

First author and year	Type of study/ study design	Sample/condition	Intervention/type of MI	Outcomes measures	Duration	Main results
Soler et al. (2010) [52]	Double-blind, placebo-controlled trial, RCT	39 SCI Mean age: 45 (15.5) years; Gender: 30 males and 9 females	Four groups (i) tDCS + VI (ii) tDCS + CI (iii) tDCS sham + VI (iv) tDCS sham + CI (placebo)	NRS NPSI BPI NRS for anxiety ranging from 0 (no anxiety) to 10 (worst anxiety) PGIC	10 sessions, 20 min each for 2 weeks	Pain intensity scores reduced by 29.7% with respect to baseline in the tDCS + VI group in comparison with VI ($p=0.008$) and placebo groups ($p=0.004$) Decreased overall pain NRS for VI post-treatment baseline pain: 7.2 (1.6) to post-treatment pain: 6.4 (1.6) Decreased pain NRS for tDCS + VI group post-treatment baseline pain: 7.5 (1.2) to post-treatment pain: 5.2 (1.5) There were no changes in the NPSI symptoms between groups tDCS + VI group showed highest improvement for BPI interference scores Anxiety decreased significantly in the tDCS + VI group, tDCS + CI and tDCS sham stimulation + VI groups ($p < 0.019$)
Gustin et al. (2008) [65]	Pre post study design	15 SCI patients (7 with below-level NP and 8 without pain) Age range: 26–67 years; Gender: all males	MI task Imagine right ankle plantar flexion and dorsiflexion for 8 min	VAS for neuropathic and non-neuropathic symptoms	3 times daily for 7 days	SCI with NP: increase in pain during imagined movements from 2.9 (0.7) to 5.0 (1.0) during MI ($p < 0.01$). 6 out of 7 subjects reported an increase in pain during MI SCI subjects without NP: MI evoked an increase in non-painful sensation intensity from a baseline of 1.9 (0.7) to 4.8 (1.3) ($p < 0.01$) Two subjects without a history of pain or non-painful phantom sensations had onset of dysesthesia while performing imagined movements

Table 1 (continued)

First author and year	Type of study/ study design	Sample/condition	Intervention/type of MI	Outcomes measures	Duration	Main results
Moseley (2007) [51]	Case series	5 paraplegics Mean age: 32.2 (8.3) years	Part 1: Patients undertook three conditions (i) virtual walking: with mirror placed in front of a screen (ii) GI (iii) Watching a film Part 2: Trial was followed by four patients virtual walking	MPQ VAS pain (100 mm)	Part 1: 10 min once Part 2: Virtual walking 10 min; 15 sessions for 3 weeks	Part 1: Reduction in VAS scores for virtual walking was 42 mm (11–73 mm), 18 mm (4–31 mm) for guided imagery and 4 mm (–3–11 mm) while watching the film Part 2: The mean (95% CI) time to return to pre-task pain VAS was 34.9 min (20.1–49.8 min) after virtual walking; 13.9 min (–0.9 to 28.8 min) after the guided imagery and 16.3 min (1.5–31.2 min) after the film McGill Pain Questionnaire were stabbing, cutting, burning, stinging and intense Part 2 Mean (95% CI) decrease in pain VAS was 53 mm (45–61 mm) at post training and 43 mm (27–53 mm) at 3-month follow-up
MS Hossein-zadegan et al. (2016) [70]	RCT	60 MS patients Mean (SD) age: EXPTT group-34 (8.2) years CONT group-33.4 (7.8) Gender: only females in both groups	EXPTT (<i>n</i> = 30): S-HYP CONT (<i>n</i> = 30): conventional rehabilitation	NRS MPQ WSGC GHQ-28	10 times a day	Lower levels of pain in S-HYP group ($p < 0.005$) Scores of quality of pain decreased from 1.5 (0.5) to 0.9 (0.3) in S-HYP group ($p < 0.005$)
Jensen et al. (2011) [69]	Repeated measure design	15 MS patients Mean (SD) age: 52.6 years (range 41–65 years) Gender: 80% females	Each participant received four treatment conditions (a) an education control condition (CONT) (b) S-HYP (c) CR (d) CR + S-HYP	Primary outcome measures NRS PCS Secondary outcome measures Intensity of worst pain in past 24 h Modified version of Pain Interference Scale of BPI	16 sessions that included 4 sessions each of 4 different treatment modules	Significant pre- to post-session decrease in NRS scores for HYP ($p = 0.001$) and CR-HYP ($p = 0.001$) treatment conditions Average daily pain intensity was significantly lower after CR-HYP Levels of pain interference after HYP were lower than before treatment

Table 1 (continued)

First author and year	Type of study/ study design	Sample/condition	Intervention/type of MI	Outcomes measures	Duration	Main results
Jensen et al. (2009) [68]	Quasi-experimental study	22 MS patients Mean age: 51.7 years	8 subjects received S-HYP and the remaining 14 were randomly assigned to either S-HYP ($n=15$) or PMR ($n=7$) group	Primary outcome measures NRS Average daily pain intensity Secondary outcome measures Pain Interference Scale from BPI	10 sessions of either S-HYP or PMR	Significant decrease in pain intensity in S-HYP group ($p<0.001$) but non-significant for PMR group Change in average daily pain intensity was 47% for S-HYP group and 14% of PMR from pre- to posttreatment There was a decrease in pain interference for S-HYP participants ($p<0.001$) but not for PMR group

RCT randomized controlled trial, SCI spinal cord injury, EXPTT Experimental Group, CONT Control Group, MT massage therapy, GI guided imagery, MPQ McGill Pain Questionnaire, SF-MPQ Short-form McGill Pain Questionnaire, CR cognitive restructuring, CFS Chalder's Fatigue Scale, tDCS Transcranial Direct Current Stimulation, VI Visual Illusion, CI control illusion, NRS Numeric Rating Scale, BPI Brief Pain Inventory, PGIC Patient Global Impression of Change, VAS Visual Analog Scale, NP neuropathic pain, NPSI Neuropathic Pain Symptom Inventory, MI mental imagery, GMI graded motor imagery, WMFT Wolf Motor Function Test, FMA Fugl-Meyer Assessment, TRS Tardieu Rating Scale, FIM Functional Independence Measure, SQ Satisfaction Questionnaire, CRPS Chronic Regional Pain Syndrome, MS Multiple Sclerosis, PCS Pain Catastrophizing Scale, S-HYP self-hypnosis, MT mirror therapy, BRS Brunnstrom Recovery Stages, MAS Modified Ashworth Scale, MAL Motor Activity Log

Effect of MI post stroke

Pain in stroke is often neglected. We selected four studies where imagery was used for treating post stroke pain. Out of these, three studies reported patients with pain resulting from CRPS type I [50, 60, 61]; while in the fourth study, the cause of pain after stroke was not stated [62]. GMI, which integrates both explicit and implicit forms of imagery in a systematic manner, has shown promising results in the past. Mirror therapy, a simple yet effective treatment can be used alone or as a part of GMI regimen. Evidence shows that mirror therapy enhances proprioceptive inputs leading to sensory–motor reorganization [60]. Significant improvement in pain scores was reported in all the three studies after mirror therapy training. Visual analog scale (VAS) was used as an outcome measure in all the 4 studies; however, in 2 studies, signs of neuropathic pain, namely allodynia, were also assessed [50, 60]. The findings of these studies were based on pain scales only and none of these studies used neuroimaging techniques to corroborate their findings. As the interventional strategies for post stroke pain are limited; more robust studies are needed in this area [50].

Effect of MI in SCI pain

Post SCI, there is a mismatch between sensory feedback and motor commands sent to the affected limb. Evidence shows that after injury, there is a reorganization of primary somatosensory cortex (S1) leading to chronic pain [63]. Reduction in pain scores after mental imagery intervention suggests that it has a potential in producing analgesic-like effects for patients having neuropathic pain after SCI. In most of these studies, visual illusion was created with a mirror. It is believed to modify the disconnect between stimulus and response and aids in the reversal of maladaptive changes due to cortical re-organization [64]. Contrary to the above findings, in a study by Gustin et al. [65], 6 out of 7 patients showed an increase in pain after they were asked to focus on imagined movements of the foot. The authors of this study suggested that SCI leads to enhanced excitability of the neurons in brain areas such as the thalamus and cortex, and movement imagery in the presence of enhanced cortical excitability may have resulted in increased pain and an allodynia-like effect. The conflicting results could be due to low sample size, differences in variables such as the level of injury, time lapse since the injury and the absence of standardized protocol adapted in these studies.

The effect of visual illusion was compared with other modalities used for electrical stimulation in these studies. Visual illusion when combined with transcranial direct current stimulation (tDCS) showed more effective pain reduction than any of the modalities used alone [52]. It has been suggested that both imagery and tDCS enhance corticospinal

excitability, hence reversing the effect of intracortical inhibition. Additionally, it was found that activation of mirror neuron system may contribute to reduced pain in visual illusion group. In another study, transcutaneous electrical nerve stimulation (TENS) was compared with visual illusion in a crossover study and it was found that both techniques were effective in reducing neuropathic pain symptoms [66]. In this review, we did not include articles related to virtual reality where computer-based technology was used to connect users to an artificial virtual environment. Another technique of mental imagery used in SCI for pain relief was GI. When compared with massage, it was effective in reducing pain in SCI by enhancing the parasympathetic responses in the patients [67].

Effect of MI in MS

The prevalence rate of pain in MS ranges between 29 and 83% of the population [30]. Studies related to the use of MI as treatment of MS pain were limited and the most common technique recognized was self-hypnosis. The use of self-hypnosis was identified in three studies [68–70] but the methodology adopted in all the studies was not similar. In one study, Jensen et al. [68] compared hypnosis with progressive muscle relaxation and found that pain scores improved with hypnotic treatment. However, since progressive muscle relaxation has similar mechanism of pain relief as hypnosis, it behaved like an active condition rather than a control for comparison. In another study, each patient underwent 4 sessions of 4 different treatment modules; hence, isolated effects of each intervention could not be ascertained [69]. Although most available studies indicate the beneficial effects of self-hypnosis in MS pain, there was a wide range of hypnotic suggestions used in these studies.

Limitations, relevance and conclusions

Although the findings of studies in this area are intriguing, but there are certain limitations. The most important limitation is that MI protocol was not standardized. The studies reviewed in the present article have used various techniques of imagery training, henceforth making it difficult to reach a conclusion regarding which technique will be more effective for the patients. Nonetheless, there were significant improvements in most of the studies with MI training in one form or the other. Secondly, the number of subjects was less in most of the studies, which directly affected the power of the study and limited its reliability and generalizability. Thirdly, even though the basic pathology of NP was same but depending on the condition, there were variations among different clinical conditions with respect to the nature and characteristics of CNP.

In spite of these limitations, the present review highlights some interesting findings. This is the first review to focus on MI techniques for CNP in neurological conditions. It helps to bring about the similarity and differences in the nature and treatment of MI techniques for treating CNP. The available techniques presently used for MI and outcomes are so varied that they could not be confined to a single inclusion criterion. The studies are limited in this area; hence, this narrative review can form a basis of further systematic reviews. In future, systematic reviews and meta-analysis can be conducted for an in-depth understanding of the various aspects of imagery in management of pain in these conditions. In conclusion, MI techniques have tremendous potential in treating chronic, painful NP conditions. They are innovative, effective, easy to use and cost effective, and should be used as an adjunct or independently as a treatment modality for CNP.

Compliance with ethical standards

Conflict of interest There is no conflict of interest to declare. None of the authors received any financial support to conduct this study or to prepare the manuscript. The people who have made substantial contributions towards the work reported in this manuscript are included in the list of authors.

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