Comprehensive Review

PAIN®

The effect of bodily illusions on clinical pain: a systematic review and meta-analysis

Eva Boesch[a], Valeria Bellan[a,b,c], G. Lorimer Moseley[a,d], Tasha R. Stanton[a,d,*]

Abstract

This systematic review and meta-analysis critically examined the evidence for bodily illusions to modulate pain. Six databases were searched; 2 independent reviewers completed study inclusion, risk of bias assessment, and data extraction. Included studies evaluated the effect of a bodily illusion on pain, comparing results with a control group/condition. Of the 2213 studies identified, 20 studies (21 experiments) were included. Risk of bias was high due to selection bias and lack of blinding. Consistent evidence of pain decrease was found for illusions of the existence of a body part (myoelectric/Sauerbruch prosthesis vs cosmetic/no prosthesis; standardized mean differences = −1.84, 95% CI = −2.67 to −1.00) and 4 to 6 weeks of mirror therapy (standardized mean differences = −1.11, 95% CI = −1.66 to −0.56). Bodily resizing illusions had consistent evidence of pain modulation (in the direction hypothesized). Pooled data found no effect on pain for 1 session of mirror therapy or for incongruent movement illusions (except for comparisons with congruent mirrored movements: incongruent movement illusion significantly increased the odds of experiencing pain). Conflicting results were found for virtual walking illusions (both active and inactive control comparisons). Single studies suggest no effect of resizing illusions on pain evoked by noxious stimuli, no effect of embodiment illusions, but a significant pain decrease with synchronous mirrored stroking in nonresponders to traditional mirror therapy. There is limited evidence to suggest that bodily illusions can alter pain, but some illusions, namely mirror therapy, bodily resizing, and use of functional prostheses show therapeutic promise.

Keywords: Bodily illusions, Mirror therapy, Perception, Systematic review, Meta-analysis

1. Introduction

A growing body of evidence points to a complex relationship between pain and disruptions of other bodily perceptions of the painful part. First, structural and functional differences between people with and without pain, both cortically and subcortically, include areas clearly involved in bodily awareness and perception.[20,26,50] Second, distortions of bodily perception most often involve the body part feeling larger than it really is,[41,30] with behavioral hand size estimation tasks confirming this altered perception.[41] Similar distortions can be evoked experimentally by anaesthetizing the area, a procedure known to alter response profiles of primary somatosensory cortex neurones,[4] or by cutaneous stimulation,[23] which suggests that cortical and perceptual dysfunction might simply reflect peripheral disturbances. However, inducing the illusion that a body part is enlarged increases movement-evoked swelling in people with complex regional pain syndrome (CRPS),[48] and treatments that target these functional brain changes, such as graded motor imagery and sensorimotor retraining, reduce pain,[40,43,51] which suggests the link may be bidirectional. Importantly, reductions in pain appear to be coincident with restoration of functional cortical representation.[50]

One way to manipulate perception, and thus experimentally evaluate the relationship between pain and perception, is through illusions. Recent studies have found that illusions can alter pain levels in conditions such as osteoarthritis (OA), CRPS, and neuropathic pain.[44,48,52] Furthermore, some illusions have been used to interrogate the idea that pathological pain results from a mismatch between motor intention and motor output.[34,46] Over a decade of investigations into the potential utility of using illusions to modulate pain have yielded sometimes sophisticated and costly treatments,[7] but, with the exception of mirror therapy,[18,6] there appears to have been no attempt to take stock, synthesize, and critically evaluate what is now a substantial literature evaluating illusions and pain. As with any treatment that may be provided to patients, it is imperative to understand the current evidence supporting its use. Thus this systematic review and meta-analysis aimed to determine the current evidence concerning the effects of bodily illusions on both acute and chronic pain.

2. Methods

2.1. Data sources

A systematic search strategy in MEDLINE, EMBASE, PsycINFO, CINAHL, Amed and PubMed was used to identify studies evaluating the effect of bodily illusions on pain (from relative date of inception to February 28, 2014). Search strategies were modified

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

[a] *Sansom Institute for Health Research and PainAdelaide Consortium, University of South Australia, Adelaide, Australia,* [b] *Department of Psychology, University of Milano-Bicocca, Milan, Italy,* [c] *NeuroMI—Milan Center for Neuroscience, Milan, Italy,* [d] *Neuroscience Research Australia, Randwick, Australia*

**Corresponding author. Address: School of Health Sciences, University of South Australia, GPO Box 2471, Adelaide, SA 5001, Australia. Tel.: +618 8302 2090; fax: +618 8302 2853. E-mail address: tasha.stanton@unisa.edu.au (T. R. Stanton).*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painjournalonline.com).

PAIN 157 (2016) 516–529

http://dx.doi.org/10.1097/j.pain.0000000000000423

to meet the specific requirements of each database (See **Table 1** for Medline search strategy). Reference lists of potentially eligible studies and relevant systematic reviews were hand searched. Last, 4 experts in the field (Dr Alberto Gallace, Dr Roger Newport, Dr Diana Torta, Dr Martin Diers) were contacted to identify any additional eligible studies that may have been missed by the search. This systematic review was guided by principles from the Cochrane Collaboration of Systematic reviews and the Preferred Methods of Reporting of Systematic Review and Meta-Analyses (PRISMA) statement.[39] We conducted this review using an a priori protocol (available from T.R.S. upon request).

2.2. Study selection

Studies were eligible for inclusion if they recruited participants with an acute or chronic painful condition, if they evaluated the effect of a bodily illusion on pain, and if they compared illusion results with control condition or to a healthy (pain-free) control group, and if they provided results for a quantitative measure of pain. Specifically, studies had to use illusions that altered the perception of the painful body part. No restriction was placed on language.

Studies were excluded if they recruited only healthy pain-free controls or if the illusion did not alter the perception of the body (eg, the illusion only altered perception of the environment or the illusion was a used merely as a distraction). Studies that evaluated combination treatment (ie, illusions and another nonillusory active treatment in one person) were not included, unless the control group also received the nonillusory active treatment (such that the sole effect of illusion could be determined). All types of study designs, except case studies, were considered eligible for inclusion.

2.2.1. Definition of a bodily illusion

A bodily illusion was defined as a phenomenon in which an external stimulus is interpreted by the neural system in such a way that the resultant perception of the body is significantly different from reality. This may include alterations to the size/shape, location, movement, or ownership (eg, the rubber hand illusion [RHI][5]) of the painful body part. Additionally, this includes illusions of pain-free, normal function of the body part and/or illusory existence of an amputated body part (ie, mirror therapy). This definition of a bodily illusion was determined by consultation with 3 experts in the field (Dr Alberto Gallace, Dr Martin Diers, Dr Roger Newport).

2.3. Study inclusion

The titles and abstracts of all studies retrieved by the search were initially screened by 2 independent assessors (E.B., V.B.) and any discrepancies were discussed. If consensus was unable to be reached, a third independent assessor (T.R.S.) was consulted. Following this initial screen, the full text of potentially eligible studies were formally evaluated for inclusion using an identical process and using a custom-designed, piloted inclusion form.

Table 1

Medline search strategy.

Medline search:
exp illusion/ OR illusion*.mp OR rubber hand illusion*.mp OR mirror therap*.mp OR perceptual distortion/ OR size perception/ OR tendon vibration.mp OR virtual reality.mp OR visual illusion.mp OR body schema.mp OR Body Image/ OR sensation/ OR multisensory integration.mp OR sensory motor.mp OR sensorimotor.mp OR integration.mp OR incongruence.mp
AND
pain/ OR chronic pain/ OR acute pain/ OR experimental pain.mp OR neuropathic pain.mp OR Pain Threshold/ OR complex regional pain syndrome.mp OR Reflex Sympathetic Dystrophy/ OR Complex Regional Pain Syndrome/ OR phantom limb pain.mp OR Phantom Limb/ OR phantom pain.mp

2.4. Risk of bias assessment

The risk of bias was assessed by 2 independent reviewers using custom-designed piloted forms that included assessment of selection bias, detection bias, blinding, statistical methods, reporting bias, performance bias, and other forms of relevant bias (eg, the presence of concomitant treatment). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[61] were used to inform risk of bias assessment for cross-sectional repeated measures and observational studies. Randomized controlled trials (RCT) were assessed with additional questions on allocation concealment and adequate sequence generation on the basis of the Cochrane risk of bias guidelines.[29] Assessment of bias related to crossover effects and randomization of test condition was completed for repeated measures studies.

2.5. Data extraction

Two independent reviewers used a customized piloted data extraction form to retrieve the following information from included studies: study design (ie, case–control, repeated within-subject measures, RCT), sample size, demographics of participants (eg, age, gender) and control groups (if applicable), type and nature of control (ie, control condition vs separate control group; placebo or inactive control vs active intervention), inclusion and exclusion criteria for participants, source of participants, type and duration of illusion, credibility of illusion, other clinical information (eg, concomitant conditions, time since amputation). Quantitative pain measures (ie, intensity of pain, duration of pain relief, number of participants with pain) were extracted including the baseline scores (where reported), postintervention scores, and pain scores from all follow-up time points. If applicable, change scores for pain measures were also extracted. For pain outcomes, measures of central tendency (mean or median) and measures of dispersion (SD, interquartile range, 95% confidence intervals [95% CI]) were extracted for each group/testing condition. If included studies provided insufficient information, study authors were contacted up to 3 times. If no response was received after 3 attempts, the data were considered unobtainable.

2.6. Data synthesis and analysis

Included studies were grouped according to the type of illusion and the similarity of the illusion they used: (1) Bodily resizing illusions (ie, technology was used to alter the visual size of the body part); (2) mirror therapy; (3) illusions of virtual walking (use of a mirror and video projector set-up to induce an illusion of walking); (4) illusions of a new limb (functional prostheses used in amputees to cause a feeling of possessing the limb); (5) illusions of ownership (rubber hand illusion); and (6) illusions of incongruent movement (use of a mirror and bilateral limb movement; arms move in opposite directions and this induces an incongruence between vision and the actual movement [eg, reflected image of nonpainful arm moving upwards, but hidden painful arm actually moving downwards]).

When 2 or more studies evaluated 1 type of illusion and used a comparable illusion and control condition, pooling of data using

Revman 5.0 software[11] was considered. When similar control conditions were used within 1 study (ie, Ref. 48) the most conservative effect estimate was used for pooling. Furthermore, when numerous pain outcomes were provided within 1 study, the most commonly recognized pain outcome measure (decided a priori) was used for pooling.

For nominal level pain outcome measures, odds ratios (OR) were calculated. For pooling of between-subject study designs, the Manzel–Haetzel random effects analysis was used. For within-subject study designs (ie, repeated measures, cross-over), the natural logarithm of the ORs (lnOR) and its standard error (SE [lnOR]) were inputted into Revman using the generic inverse-variance (GIV) function, so as to allow pooling (as per Cochrane Collaboration's recommendations for crossover study designs[29]). Calculation of SE (lnOR) was completed using the marginal probabilities of success method.[2,17] When adequate data were not available to calculate SE (lnOR), correlation coefficients from similar studies (with similar comparisons) were imputed; in these cases, sensitivity analyses were performed using correlations ± 0.1.[29]

For continuous measures of pain outcomes, all pooling used a GIV random effects model to calculate standardized mean differences (SMD; used due to differences between studies in pain measurement scales). SMDs were calculated by dividing the mean difference in posttreatment pain scores between illusory condition and nonillusory control condition by the pooled SD. When studies used change scores, the mean difference of the pre-/postchange scores between illusory and nonillusory conditions was divided by the pooled SD of the difference scores. For within-subject study designs, we used the postcondition correlation coefficients, calculated from individual patient data, to calculate the standard error of the SMD (SE [SMD]).[29] When adequate information was not provided/available, a correlation coefficient, taken from a similar study for which individual patient data were present, was imputed. The robustness of this imputation was evaluated by reanalyzing these data with the correlation coefficient increased and decreased by 0.1.[29] For all comparisons involving within-subject study designs, the SMD (and its SE) were entered into Revman using the GIV method.[29] When necessary, SMD and SE (SMD) for between-group study designs were calculated using Revman. Last, in meta-analyses with significant pooled effect estimates, we calculated the absolute treatment effect by multiplying the SMD by a representative between-subject SD for an appropriate pain scale as per established recommendations.[29]

Interpretation of effect estimates (SMD) was according to Cohen (small ≤ 0.2; moderate $= 0.5$; large ≥ 0.8).[12] Heterogeneity of pooled studies was assessed using the χ^2 test and I^2 statistic. When the χ^2 had $P < 0.10$, statistically significant heterogeneity was considered present; when $I^2 > 60\%$, substantial heterogeneity was considered present.[29] Where appropriate, data were presented as effect estimates (SMD/OR and the 95% CI). For ease of clinical interpretation, significant effect estimate data were also presented as absolute change in pain (note: the scales differ for each study, therefore we present the results as percentage change). For each stage of the review process, kappa values (κ) were calculated to evaluate chance-corrected agreement between raters.

3. Results

The search strategy resulted in a total of 2213 citations, of which 20 studies (21 experiments; Ref 58 reported 2 experiments) met the eligibility criteria and were included in the present review.[7–10,13,15,19,31,33–35,37,44,48,52,54,57–59,63] See **Figure 1** for a flow chart of this process and **Table 2** for details of these included studies. Authors of 12 studies were contacted to retrieve necessary pain outcomes or within-subject correlations (for pooling): some/all of the missing information was provided for 8 studies,[13,15,19,44,48,52,54,63] necessary data were unable to be provided in 3 studies[33–35] and 1 author was unable to be contacted.[7] Agreement between raters was $\kappa = 0.794$ at the screening stage and $\kappa = 0.096$ at the inclusion stage. The latter low agreement score reflected rater differences in the perceived eligibility of virtual reality studies; these differences were resolved upon clarification of inclusion criteria.

3.1. Study design

Included studies utilized a variety of study designs. Six studies used an RCT study design[7–10,37,59]; 2 studies were non–randomized control studies[63,19]; 1 study used a cross-sectional study design[31]; 1 study a 3×3 mixed design.[54] The remaining 10 studies (11 experiments) used repeated-measure study designs,[13,15,33–35,44,48,52,57,58] involving within-subject comparisons.

3.2. Type of health condition

Eligible studies evaluated a variety of chronic pain conditions (ie, pain persisting for at least 3 months[36]) including neuropathic pain in paraplegic patients[44,59]; phantom limb pain (PLP) [7,10,19,31,57,58,63]; fibromyalgia only (FMS[33]); whiplash associated disorder (WAD[13]); FMS and CRPS[34]; CRPS only[35,48,54]; CRPS poststroke[8,9]; upper extremity pain poststroke[37]; OA of the hand[52]; upper back pain.[15] No studies assessed the effect of bodily illusions in acute/subacute pain conditions (ie, pain for less than 3 months).

3.3. Type of illusion and control conditions

Three studies evaluated the effect on pain of bodily resizing illusions, (ie, altering the perceived size of the painful body part[15,48,52]); 8 studies evaluated the effect of mirror therapy,[7–10,19,35,37,57] 2 studies evaluated virtual walking (using mirror set-up[44,59]); 2 studies creating the illusion of an existing body part (using functional prostheses in amputees[31,63]); 2 studies (3 experiments) evaluated the effect of embodiment (via synchronous stroking of a rubber hand or body[57,58]); 3 studies evaluated incongruent movement illusions (ie, incongruence between vision and proprioception using a mirror set-up[33,34]). All studies compared the effect of bodily illusions on pain with a nonillusory control condition, illusory control condition, or both. Three studies additionally compared the pain group's results with those from a healthy pain-free control group[13,15,33] and 1 study compared the pain group's results with those from a separate clinical pain control group.[54]

3.4. Risk of bias

All studies had a high risk of bias (**Table 3**). Sample size was small in most and only 3 studies performed an a priori power calculation.[8,13,37] Participants were blinded in 25% of experiments (5 studies[8,13,33,59,63]) and assessors in only 20% of experiments (4 studies[8,31,37,59]). In 33% of experiments, credibility of the illusion was evaluated and deemed credible[15,44,54,57–59]; and only 33% of experiments with a repeated-measures study design adequately controlled for crossover effects.[13,44,48,57] None of the 6 RCTs

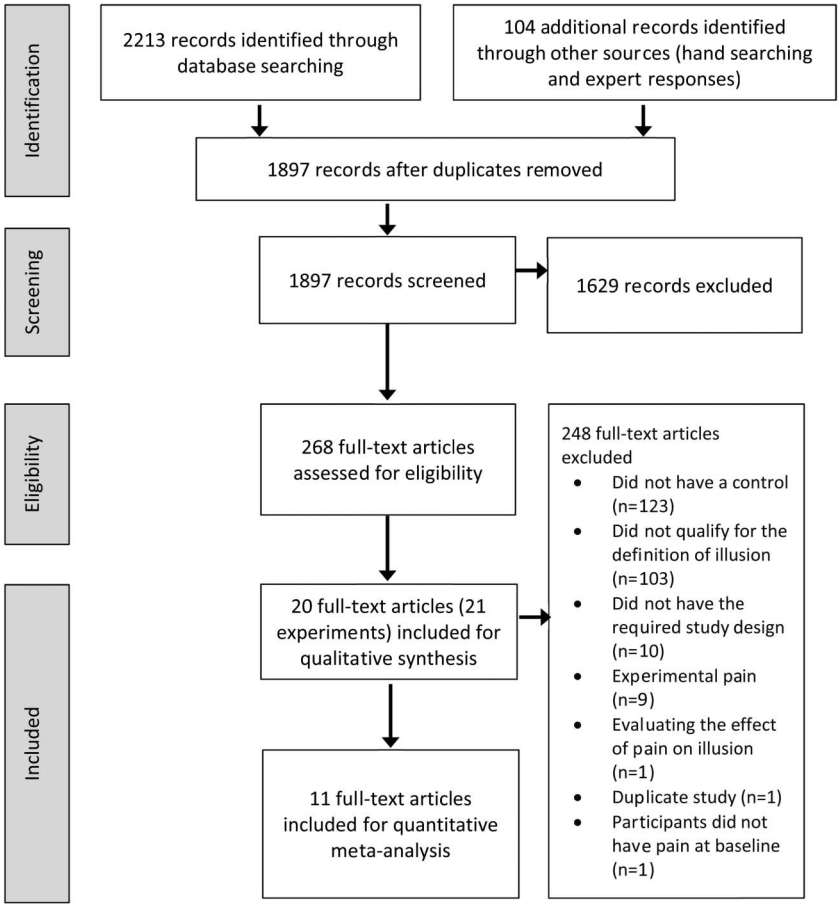

Figure 1. Flow chart detailing the screening and inclusion process (www.prisma-statement.org).

included in the review had a low risk of bias—blinding of participants was not possible in most studies. Agreement between raters ranged between $\kappa = 0.151$ and $\kappa = 1.0$. Only 2 categories, "standardized diagnosis" and "incomplete outcome reporting," were below $\kappa = 0.6$. Of all bias ratings, 4.5% required consultation with the third assessor.

3.5. Outcomes: effect of illusions on pain

For all studies using continuous outcomes, the individual effect sizes are shown in **Figure 2A**.

3.5.1. Resizing illusions

Various methods were used to induce resizing illusions: binoculars were used to magnify/minify hand size[48]; specialized video equipment was used to stretch/shrink hand size (congruent vision and touch used to induce the illusion)[52]; altered video was used to enlarge/downscale back size.[15] All 3 studies assessed pain intensity (preillusion to postillusion) and 2 reported on the change of "clinical" (ie, preexisting) pain intensity.[48,52] However, because of differences in the type of illusion (magnify whole body part vs stretch one area of the body part), population studied and hypothesized direction of effect, these studies were unable to be pooled.

In studies that evaluated change in preexisting clinical pain intensity, illusions that reduced the size of the affected body part consistently reduced pain compared with controls (**Fig. 2**). In people with CRPS, a visual illusion that decreased the overall size of the affected hand significantly reduced pain compared with no-resizing of the painful body part (SMD = −0.87, 95% CI = −1.43 to −0.32). This corresponds to a pain increase of 9.5% above the pain induced by hand movements alone (95% CI = 7% to 18.5%). Similarly, in people with hand OA, a multisensory illusion (combining touch and vision) that "shrunk" the affected painful joint, significantly reduced pain compared with a resizing illusion on a nonpainful area of the hand (SMD = −0.59, 95% CI = −0.95 to −0.23). This is an equivalent pain decrease of 24.1%, (95% CI = 9.0% to 37.3%). On the contrary, illusions that increased the size of the affected body part had differential effects in CRPS and OA, but findings were in the directions hypothesized. Compared with no-resizing of the painful body part, visual illusions that increased the apparent size of the CPRS-affected hand significantly increased pain above that induced by hand movements alone (SMD = 0.54, 95% CI = 0.04-1.05; equivalent pain increase of 14.0%, 95% CI of 5.2% to 23.0%). In OA, multisensory illusions that "stretched" the size of the painful joint, significantly decreased pain compared with resizing illusions of a nonpainful part of the hand (SMD = −1.12, 95% CI = −1.55 to −0.70; equivalent pain decrease of 34.7%, 95% CI of 21.8% to 48.3%).

One study investigated pain intensity and unpleasantness of externally applied nociceptive stimuli (pressure and electrical) during illusory resizing of the back in people with chronic back pain.[15] Neither illusions of an enlarged back nor a downscaled back had an effect on pain intensity or unpleasantness for either nociceptive stimulus (vs watching a normal-sized back;

Table 2

Characteristics of included studies.

Study and design	Participants	Illusion(s) evaluated	Control condition(s)	Pain outcome(s)	Time points of pain assessment
Resizing illusions					
Diers et al.[15]; within-subject repeated measures; between-subject comparison	Chronic upper back pain (n = 18, 13 f); aged 54.74 (9.14) y	Viewed video of: (1) enlarged back; (2) downscaled back	(1) Viewed video of the normal-sized back; (2) compared all conditions with 18 age-matched healthy controls	Pain intensity (0-10 NRS) during pressure and electrical stimulation	Baseline and postintervention
Moseley et al.[48]; within-subject repeated measures	Upper limb CRPS (n = 10 m); aged 35.1 (11.7) y	(1) Magnifying size; (2) minimizing size of affected hand during standardized hand movements (10 min)	(1) Watching the hand; (2) watching the hand through binoculars (no size change)	(1) Peak intensity of pain (0-100 VAS); (2) Recovery time (return to pretask pain)	Baseline and during illusion; f/u until return to pretask pain (up to 20 min)
Preston and Newport[52]; within-subject repeated measures	Hand OA (n = 20, 18 f); aged 70.5 (6.5) y	(1) Shrinking; 2. Stretching of the painful joint (10 s)	(1) Shrinking nonpainful joint; (2) stretching nonpainful joint; (3) resizing entire hand	Pain intensity (0-21 NRS)	Immediately before and during the illusion
Mirror therapy—1 session					
Brodie et al.[7]; RCT	LL amputees (n = 80, 35 m); aged 54 (range 20-83) y	Mirror therapy—symmetrical movements with intact hand and imagined movement with PL (n = 41)	Identical procedure but mirror obscured (n = 39)	Pain intensity (0-100 VAS)	Baseline and postintervention
Flinn and Hotle[19]; unrandomized control trial	Amputees (n = 10, 7 m); aged 36 (range 21-50) y	Mirror therapy with movement while wearing a hand prosthesis (n = 4)	No intervention (n = 6)	Pain intensity (0-10 VAS)	Baseline and postintervention
McCabe et al.[35]; within-subject repeated measures	Upper and lower limb CRPS (n = 7, 4 f, 5 lower limb); aged 33 (range 24-40) y	Mirror therapy—symmetrical movements with both limbs if possible	(1) Identical procedure, viewing both limbs (no mirror/nonreflective surface); (2) identical procedure, nonreflective surface	Pain intensity (0-10 VAS)	Baseline and postintervention
Schmalzl et al.[57]; repeated measures case–control; unrandomized	UL amputees (n = 6, 4 f) with no/limited success with mirror therapy; aged 55 (39-80) y	Mirror plus simultaneous stroking of stump and corresponding area on hand (8 min)	(1) Mirror therapy—symmetrical movements with intact hand and imagined movement with PL (8 min); (2) 1 trial of stroking with the mirror covered (1 min)	Pain intensity (0-10 VAS): (1) average: average of "pre" pain ratings to average of "post" pain ratings; (2) cumulative: average of baseline pain ratings (first "pre") to average of final (last "post") pain ratings	Baseline and postintervention
Mirror therapy—prolonged treatment					
Cacchio et al.[9]; RCT	CRPS poststroke (n = 48, 13 f); aged 57.9 (9.9) y	Mirror therapy (2 wk × 30 min, 2 wk ×1 h) + stroke rehab program	Stroke rehab program	Pain intensity (0-10 VAS): (1) at rest; (2) on movement	Baseline, 1 wk postintervention, 6 mo postintervention
Cacchio et al.[8]; RCT; crossover	CRPS poststroke (n = 24); median age 62 (range: 53-71) y	Mirror therapy (4 wk × 30 min/d; n = 8)	(1) Covered mirror therapy (4 wk × 30 min/d; n = 8); (2) motor imagery (4 wk × 30 min/d; n = 8)	Pain intensity (0-100 VAS): (1) at rest; (2) on movement	Baseline, 4 wk, 8 wk (weekly ratings also taken)
Chan et al.[10]; randomized sham-controlled trial; crossover	LL amputees with PLP (n = 22 m); aged 29 (8.8) y	Mirror therapy (4 wk × 15 min/d; n = 6)	(1) Covered mirror therapy (4 wk × 15 min/d; n = 6); (2) mental visualization (4 wk × 15 min/d; n = 6)	Current pain intensity (0-100 VAS)	Baseline, 4 wk, 8 wk (weekly ratings)
Michielsen et al.[37]; RCT	Chronic pain poststroke (n = 40, 20 f); aged 57 (12.8) y	Mirror therapy (bilateral hand movements; 6 wk: 1×/wk with therapist and 5×/wk [1 h] home sessions; n = 20)	Bilateral hand movements (6 wk: 1×/wk with therapist and 5×/wk [1 h] home sessions; n = 20)	Pain intensity (0-100 VAS)	Baseline, posttreatment and 6 mo follow-up
Virtual reality					
Moseley[44]; within-subject repeated measures	Neuropathic pain following paraplegia (n = 5 m); aged 32 (8) y	Virtual walking illusion (10 min)	(1) Watching an animated comedy film (10 min); (2) guided imagery (10 min)	(1) Pain intensity (0-100 VAS); (2) duration of pain relief (time to return to pretask pain levels)	(1) Every 30 s from 3 min before, to 1 h after each condition; (2) up to 1 h after each condition

(*continued on next page*)

Table 2 (*continued*)

Study and design	Participants	Illusion(s) evaluated	Control condition(s)	Pain outcome(s)	Time points of pain assessment
Soler et al.[59]; RCT	Neuropathic pain following paraplegia (n = 39, 20 m); aged 45 (15.5) y	Virtual walking illusion + sham tDCS (n = 9; 2 wk: 10 sessions × 10 min)	(1) Active: tDCS + illusory control (n = 10); (2) placebo: illusory control (landscapes/shapes/faces movie) + sham tDCS (n = 10); (3) virtual walking illusion with tDCS (n = 10)*	Pain intensity (0-10 NRS): (1) overall pain; (2) continuous pain; (3) paroxysmal pain	Baseline, immediately postintervention (day 14), and 2, 4 and 12 wk postintervention
Functional prosthesis					
Lotze et al.[31]; cross-sectional study; between group comparison	14 Amputees with PLP (n = 14; gender not reported)	Myoelectric prosthesis with extended use and wear (n = 5; aged 49.1 [19.1] y; 5.4 [3.3] y postamputation)	No prosthesis, cosmetic prosthesis, myoelectric prosthesis with minimal use and wear (n = 9; aged 43.8 [17.9] y; 22.3 [18.7] y postamputation)	West Haven Yale Multidimensional Pain Inventory (MPI) Pain Intensity scale (0-6)	Current phantom limb pain levels and retrospective pain levels, preprosthesis (pain recall)
Weiss et al.[63]; non-RCT	21 Amputees with PLP (n = 21; gender not reported)	Sauerbruch prosthesis (n = 9, only 7 had PLP; median age 34 [range 25-78 y])	Cosmetic prosthesis (n = 12, only 7 had PLP; median age 63 [range 20-75 y])	Phantom limb pain intensity (VAS 0-10 cm)	Baseline (postamputation/ preprosthesis) and postprosthesis. Follow-up time period unclear
Embodiment illusions					
Reinersmann et al.[54]; 3 × 3 mixed model	(1) CRPS 1 (n = 24, 12 m) aged 53.4 y (range: 34-78); (2) UL pain (n = 21); aged 51.8 y (range: 32-71)	Rubber hand on affected side, synchronous stroking and continuous stabbing of rubber hand with syringe (20 s)	(1) Rubber hand on unaffected side, synchronous stroking + continuous stabbing (20 s); (2) asynchronous stroking	Pain intensity: NRS 0-10 for baseline; VAS (0-100) for post condition	Baseline and postcondition
Schmalzl et al.[58] (experiment 1); within-subject repeated measures	Amputees with PL sensations + presence of telescoping (n = 8, 1 m); aged 50 y (range 23-65)	Synchronous stroking of stump and referred finger of intact mannequin (VR full-body illusion)	Asynchronous stroking of stump and referred finger	Pain intensity (0-10 VAS)	Baseline and postintervention
Schmalzl et al.[58] (experiment 2); within-subject repeated measures	As above	Synchronous stroking of stump and empty space below wrist of mannequin with amputated hand (VR)	Synchronous stroking of stump of participant and stump of mannequin	Pain intensity (0-10 VAS)	Baseline and postintervention
Incongruent movement					
Daenen et al. 2012[13]; within-subject repeated measures; between group comparison	Chronic WAD (n = 35; 26 f); aged 43.8 (9.6) y	Incongruent movements with mirror (M IC)	(1) M C; (2) WB IC; (3) WB C; (4) congruent movement (no whiteboard/ mirror; CC); (5) incongruent movement (no whiteboard/mirror; IC); (6) compared to 31 matched healthy controls (24 f; aged 43.2 [16.1] y)	Proportion of subject reporting pain	Postcondition
McCabe et al.[33]; within-subject repeated measures; between group comparison	FMS (n = 29; 28 f); aged 47.9 (11.1) y	Incongruent movements with mirror (M IC; 20 s)	(1) M C (20 s); (2) WB IC (20 s); (3) WB C (20 s); (4) compared to 29 matched pain-free, healthy participants	(1) Proportion of subject reporting pain; (2) peak pain intensity on Likert Scale (0-10)	Baseline and post condition
McCabe et al.[34]; within-subject repeated measures	CRPS or FMS (n = 23; 20 f); age not reported	Incongruent movements with mirror (M IC; 20 s)	(1) M C (20 s); (2) WB IC (20 s); (3) WB C (20 s)	Proportion of subjects reporting pain: (1) mild (aching); (2) moderate (crampy, sharp); (3) severe (extremely painful)	Post condition

* Data for the virtual walking illusion + tDCS group not included in the present review.

C, congruent; CRPS, Complex Regional Pain Syndrome; f, female; fMRI, functional Magnetic Resonance Imaging; FMS, fibromyalgia; HC, healthy controls; IC, incongruent; LL, lower limb; m, male; M, mirror; MPI, West Haven Yale Multidimensional Pain Inventory; MPQ, McGill Pain Questionnaire; n, number of participants; NRS, Numeric Rating Scale; OA, osteoarthritis; PL, phantom limb; PLP, phantom limb pain; PRI, McGill Pain Questionnaire Pain Intensity Scale; SCI, spinal cord injury; UL, upper limb; VAS, Visual Analogue Scale; WB, whiteboard.

Table 3

Risk of bias of included studies.

Studies	Selection	Detection bias		Blinding		Statistical			Missing data		
	Consecutive or random sampling	*Standardized diagnosis of test group*	*Standardized diagnosis of controls*	*Blinding of tester*	*Blinding of participants*	*Sample size appropriate*	*Baseline characteristics similar*	*Confounding variables controlled*	*Missing data (<20%)*	*Incomplete outcome data adequately addressed*	*Drop-out rate (<20%)*
Resizing illusions											
Moseley et al.[48]	●	●	●	●	●	●	●	●	●	N/A	N/A
Preston and Newport[52]	●	●	N/A	●	●	●	●	●	●	N/A	N/A
Diers et al.[15]	●	●	●	●	●	●	●	●	●	N/A	N/A
Mirror therapy—one session											
Brodie et al.[7]	●	●	N/A	●	●	●	●	●	●	N/A	●
Flynn and Hotle[19]	●	●	N/A	●	●	●	●	●	●	●	N/A
McCabe et al.[35]	●	●	N/A	●	●	●	●	●	●	N/A	N/A
Schmalzl et al.[57]	●	●	N/A	●	●	●	●	●	●	N/A	N/A
Mirror therapy—prolonged treatment (4-8 wk)											
Cacchio et al.[9]	●	●	N/A	●	●	●	●	●	●	●	●
Cacchio et al.[8]	●	●	N/A	●	●	●	●	●	●	●	●
Chan et al.[10]	●	●	N/A	●	●	●	●	●	●	●	●
Michielsen et al.[37]	●	●	N/A	●	●	●	●	●	●	●	●
Virtual walking											
Moseley[44]	●	●	N/A	●	●	●	●	●	●	●	N/A
Soler et al.[59]	●	●	N/A	●	●	●	●	●	●	●	●
Functional prosthesis (illusion of a real limb)											
Lotze et al.[31]	●	●	N/A	●	●	●	●	●	●	N/A	N/A
Weiss et al.[63]	●	●	●	●	●	●	●	●	●	N/A	N/A
Embodiment illusions											
Reinersmann et al.[54]	●	●	●	●	●	●	●	●	●	N/A	N/A
Schmalzl et al. (exp 1)[58]	●	●	N/A	●	●	●	●	●	●	●	N/A
Schmalzl et al. (exp 2)[58]	●	●	N/A	●	●	●	●	●	●	●	N/A
Incongruent movement illusions											
Daenen et al.[13]	●	●	●	●	●	●	●	●	●	N/A	N/A
McCabe et al.[34]	●	●	N/A	●	●	●	●	●	●	●	N/A
McCabe et al.[33]	●	●	●	●	●	●	●	●	●	N/A	N/A

(*continued on next page*)

Table 3 (*continued*)

Studies	Reporting		Performance bias			Concomitant treatments	RM—specific		RCT—specific	
	Reporting bias (all outcomes/groups reported)	*Other bias*	*Credibility of illusion determined*	*Illusion well described*	*Illusion piloted, preestablished results presented*		*Test conditions randomized*	*Crossover effect*	*Method of randomization adequate*	*Treatment allocation concealed*
Resizing illusions										
Moseley et al.[48]	●	●	●	●	●	●	●	●	N/A	N/A
Preston and Newport[52]	●	●	●	●	●	●	●	●	N/A	N/A
Diers et al.[15]	●	●	●	●	●	●	●	●	N/A	N/A
Mirror therapy—one session										
Brodie et al.[7]	●	●	●	●	●	●	N/A	N/A	●	●
Flynn and Hotle[19]	●	●	●	●	●	●	N/A	N/A	N/A	N/A
McCabe et al.[35]	●	●	●	●	●	●	●	●	N/A	N/A
Schmalzl et al.[57]	●	●	●	●	●	●	●	●	N/A	N/A
Mirror therapy—prolonged treatment (4-8 wk)										
Cacchio et al.[9]	●	●	●	●	●	●	N/A	N/A	●	●
Cacchio et al.[8]	●	●	●	●	●	●	N/A	N/A	●	●
Chan et al.[10]	●	●	●	●	●	●	N/A	N/A	●	●
Michielsen et al.[37]	●	●	●	●	●	●	N/A	N/A	●	●
Virtual walking										
Moseley[44]	●	●	●	●	●	●	●	●	N/A	N/A
Soler et al.[59]	●	●	●	●	●	●	N/A	N/A	●	●
Functional prosthesis (illusion of a real limb)										
Lotze et al.[31]	●	●	●	●	N/A	●	N/A	N/A	N/A	N/A
Weiss et al.[63]	●	●	●	●	N/A	●	N/A	N/A	N/A	N/A
Embodiment illusions										
Reinersmann et al.[54]	●	●	●	●	●	●	●	●	N/A	N/A
Schmalzl et al. (exp 1)[58]	●	●	●	●	●	●	●	●	N/A	N/A
Schmalzl et al. (exp 2)[58]	●	●	●	●	●	●	●	●	N/A	N/A
Incongruent movement illusions										
Daenen et al.[13]	●	●	●	●	●	●	●	●	N/A	N/A
McCabe et al.[34]	●	●	●	●	●	●	●	●	N/A	N/A
McCabe et al.[33]	●	●	●	●	●	●	●	●	N/A	N/A

Exp, experiment; N/A, not applicable; RM, repeated measures.

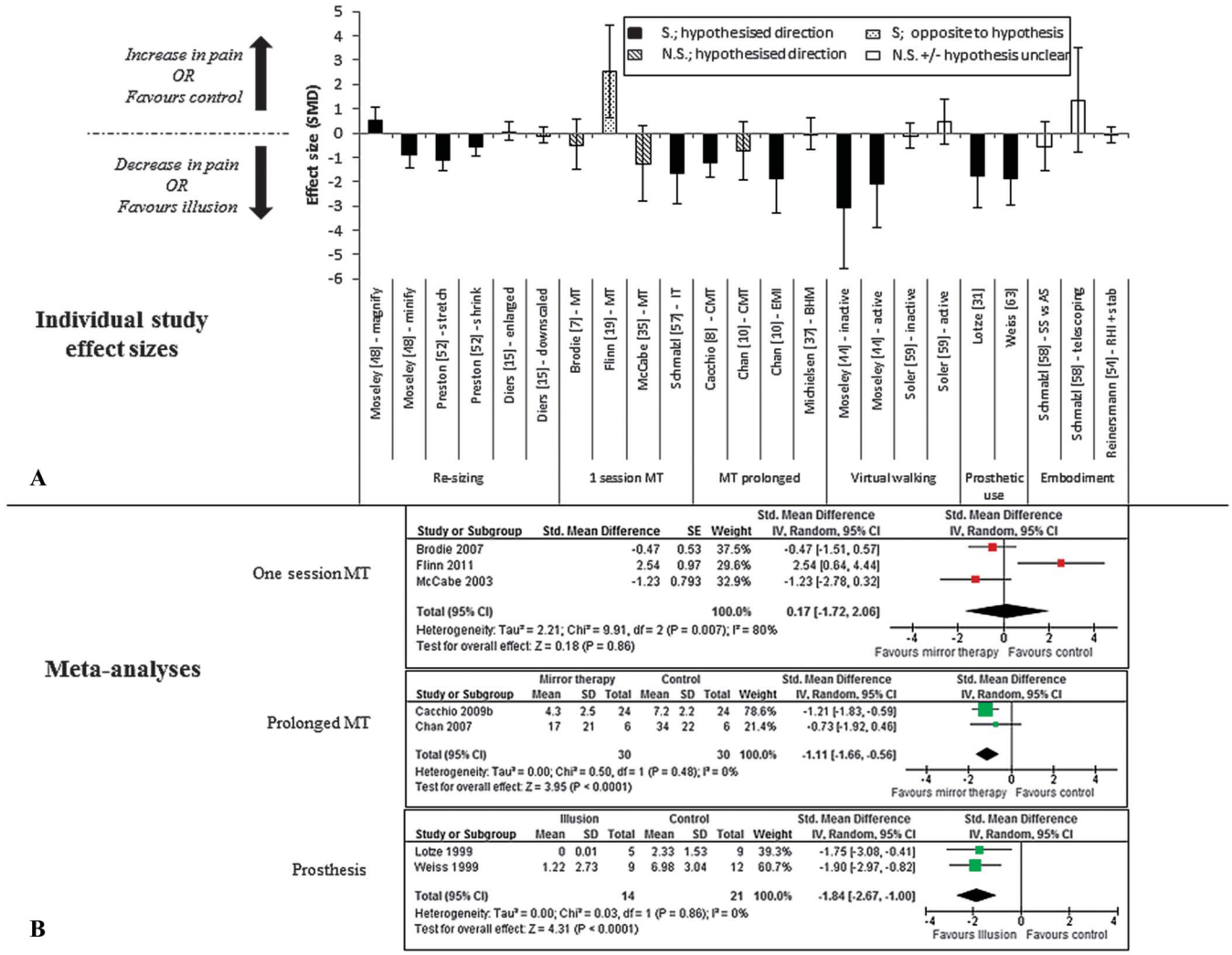

Figure 2. (A) Effect estimates for studies evaluating continuous outcomes of pain (standardized mean differences and 95% confidence intervals). (B) Pooled effects on pain of 1 session of mirror therapy (compared with covered mirror therapy or no intervention), prolonged mirror therapy (compared with covered mirror therapy), and functional prostheses (compared with no/cosmetic prosthesis). For 1 session of the mirror therapy, the SD of the difference scores[29] was imputed for Brodie et al.[7] using a correlation of 0.70 for pre-/posttreatment pain results. This correlation was taken from studies with similar pre-post data.

Active, active control condition; AS, Asynchronous stroking; BHM, bilateral hand movements; CMT, covered mirror therapy; EMI, explicit motor imagery; inactive, inactive control condition; IT, illusory touch (using traditional mirror box set-up); MT, mirror therapy; NS, nonsignificant; RHI, rubber hand illusion; S, significant; SS, synchronous stroking; stab, threatening stimuli (stabbing).

nonsignificant SMDs ranging from −0.08 to 0.12 and −0.05 to −0.10, respectively; Supplementary Table 1, available online at http://links.lww.com/PAIN/A181). Comparisons between those with back pain and a healthy control sample found conflicting results for pain intensity/unpleasantness over the 3 conditions and 2 types of nociceptive stimuli (Supplementary Table 1, available online at http://links.lww.com/PAIN/A181).

One study also evaluated the time to return to pretask pain levels.[43] During illusory hand magnification in CRPS, the time to return to pretask pain levels was significantly longer ($P = 0.03$) than it was for both illusory reduction of the hand and no-illusion control conditions. During illusory reduction of hand size, time to pretask pain return was significantly shorter than no-illusion control conditions ($P = 0.03$).

3.5.2. Mirror therapy—1 session

Four studies evaluated the effect of 1 session of mirror therapy on pain, of which 3 could be pooled. These 3 studies compared mirror therapy (movement of intact limb) with covered mirror therapy (mirror obscured by cloth; in CRPS[35] and in PLP[7]) or with no treatment in PLP[19] and found a nonsignificant pooled effect estimate (SMD = 0.17, 95% CI = −1.72 to 2.06; **Fig. 2B**), suggesting no effect of 1 session of mirror therapy. The individual and pooled results were unchanged based on sensitivity analyses (See Supplementary Figure 1, available online at http://links.lww.com/PAIN/A181).

The fourth study explored illusory touch (using a mirror therapy set-up) in upper limb amputees with PLP that were previously unresponsive to traditional movement-based mirror therapy. Illusory touch was induced through synchronous stroking of the stump with mirrored stroking of the referred sensation location on the intact hand and was compared with mirrored movements and with covered mirror intact-hand stroking.[57] In both comparisons, illusory stroking reduced pain levels (SMD = −1.65, 95% CI = −2.89 to −0.42 and SMD = −5.13, 95% CI = −8.99 to −1.28, respectively). This is an equivalent pain decrease of 17.0% (95% CI = 4.0% to 29%) compared with mirror movements and 14.0%

(95% CI = 4.0% to 25.0%) compared with covered mirror intact-hand stroking.

3.5.3. Mirror therapy—prolonged treatment

Four RCTs evaluated the effect of a course of mirror therapy (4–6 weeks treatment) on pain compared with covered mirror therapy,[8–10] motor imagery,[9,10] or bilateral hand movements.[37] Of these, only 1 study was additional to those reported in a recent systematic review on graded motor imagery in pain (see Ref. 6 for full details), but this inclusion allowed for pooling of 2 studies.[10,8] Pooled results found that 4 weeks of mirror therapy (compared with covered mirror therapy) resulted in a large, significant reduction in pain (SMD = −1.11, 95% CI = −1.66 to −0.56; **Fig. 2B**). This effect is equivalent to a pain decrease of 33.0% (95% CI = 12.0% to 37.0%). A third study (for which insufficient data were present to allow pooling)[9] corroborated this result: those receiving mirror therapy had a significantly increased odds of experiencing pain reduction, as compared with those receiving covered mirror therapy (OR = 49.0, 95% CI = 2.53 to 948.62). Results comparing mirror therapy to another active treatment, motor imagery,[9,10] were unchanged from the past review[6] finding that mirror therapy reduced pain to a larger extent than motor imagery.

The evidence suggests that this effect on pain is maintained over time. At the 6-month follow-up, Cacchio et al.[8] found a large, significant decrease in pain in people with CRPS after stroke, who were in the mirror therapy group (SMD = −1.44, 95% CI = −2.08 to −0.80), as compared with those in the covered mirror group. Furthermore, 2 studies in which the control groups (covered mirror and mental imagery and stroke rehabilitation) crossed over to mirror therapy after 4 weeks, found similar pain reductions as those experienced by the initial mirror therapy group.[9,10] They also found sustained reductions in pain at 8 weeks in the initial group that received mirror therapy. In contrast, the previous review[6] reported results of only 1 study that found a small nonsignificant effect size of mirror therapy compared with bilateral hand movements (SMD = −0.34, 95% CI = −0.96 to 0.29) at the 6-month follow-up.

3.5.4. Virtual reality—virtual walking

The 2 studies that assessed the effect of virtual walking on neuropathic pain in people with paraplegia did so by projection of a video of "walking legs" onto a screen that was aligned with the reflected image of the participant's upper body and trunk (mirror positioned in front of the wheelchair).[44,59] These studies compared virtual walking with both inactive and active control conditions; data were unable to be pooled because of differences in duration of the treatment (1 session[44] vs 10 sessions[59]) and the use of different control conditions. Results varied for both inactive and active control comparisons (**Fig. 2A**). When compared with watching a comedy film,[44] virtual walking reduced pain to a greater extent (SMD = −3.07, 95% CI = −5.56 to −0.58; equivalent pain decrease of 38.0% [95% CI = 7.2% to 68.8%]) but in the second study,[59] where virtual walking was compared with viewing landscapes/faces (plus receiving sham tDCS), the effect estimate was nonsignificant (SMD = −0.11, 95% CI = −0.62 to 0.40). Similarly, when compared with guided imagery,[44] virtual walking demonstrated a large significant reduction of pain (SMD = −2.10, 95% CI = −3.91 to −0.30; equivalent pain decrease of 24.0% [95% CI = 3.4% to 44.7%]); however, when virtual walking (plus sham tDCS) was compared with tDCS (plus viewing pictures of faces/landscapes),[59] the effect estimate was nonsignificant (SMD = 0.48, 95% CI = −0.44 to 1.40).

Moseley[44] also evaluated the duration of pain relief: the virtual walking task resulted in a longer duration of pain relief (34.9 minutes [range: 20.1-49.8]), as compared with the guided imagery task (13.9 minutes [range: 0.9-28.8]) and with the control condition of watching a comedy film (16.3 [range: 1.5-31.2]). Soler et al.[59] performed follow-ups at the end of treatment and at 2 and 4 weeks posttreatment, measuring overall, continuous and paroxysmal pain scores. There were no significant differences in overall pain or continuous pain scores between the virtual walking group and the placebo group or the tDCS group at any time point (nonsignificant SMDs ranging from −0.11 to 0.98; Supplementary Table 2, available online at http://links.lww.com/PAIN/A181). Paroxysmal pain scores were significantly reduced at all time-points in the virtual walking group but only when compared with the placebo group (Supplementary Table 2).

3.5.5. Illusion of existence of body part

The 2 studies that used functional prostheses in amputees with PLP to create an illusion of an "existing" body part used either a myoelectric prosthesis (uses electric potentials from voluntarily contracting muscles in the stump to operate)[31] or the Sauerbruch prosthesis, (mechanical insertion of prosthesis into the muscle belly and movement is driven via physical muscle contraction).[63] Pooled results (**Fig. 2B**) found that use of functional prosthesis in amputees with PLP had a large significant pain reduction (SMD = −1.84, 95% CI = −2.67 to −1.00) compared with cosmetic prosthesis use,[63] and no/rare myolectric prosthesis use.[31] This effect is equivalent to a pain reduction of 50.0% (95% CI = 27.0% to 73.0%).

3.5.6. Embodiment illusions

Two studies (3 experiments) evaluated the effect of embodiment illusions on pain.[58,54] Due to the variation in methods, data were unable to be pooled (**Fig. 2A**). One study evaluated the effect of a full-body illusion in upper limb amputees (4/7 had PLP) when the mannequin was intact (compared synchronous vs asynchronous stroking; experiment 1) and when the mannequin was missing a hand (compared telescoping vs nontelescoping illusion; experiment 2).[58] That is, synchronously stroking the area of the stump that referred sensation to the phantom limb and the corresponding "referral" area on the rubber hand (intact mannequin) or corresponding area of space (mannequin missing a hand). Synchronous stroking of an intact mannequin had a nonsignificant pain reduction compared with asynchronous stroking (SMD = −0.55, 95% CI = −1.56 to 0.47) and telescoping had a nonsignificant increase in pain compared with nontelescoping (SMD = 1.36, 95% CI = −0.79 to 3.50).

The second study evaluated the RHI, followed by stabbing of the rubber hand with a syringe both in people with CRPS and in a clinical pain control group: synchronous stroking of the affected hand (+stabbing) was compared with asynchronous stroking of the affected hand and with synchronous stroking of the unaffected hand (+stabbing).[54] No differences in pain were found between groups or between experimental conditions in either group (nonsignificant SMDs ranging from −0.19 to 0.12; Supplementary Table 3, available online at http://links.lww.com/PAIN/A181).

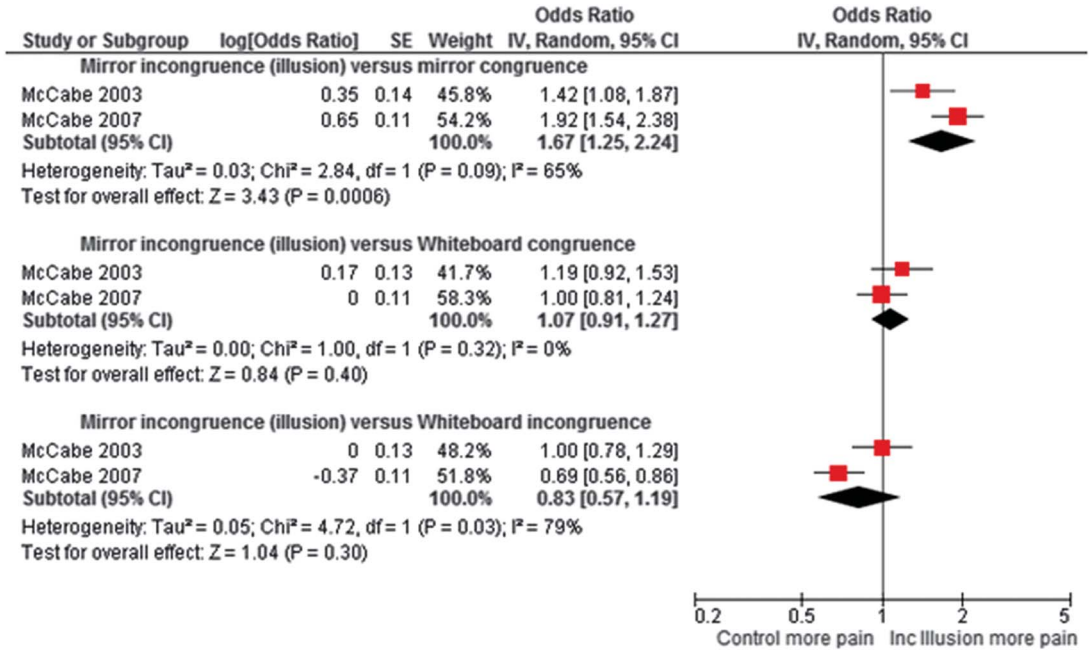

Figure 3. Pooled effects for incongruent movement illusions (compared with nonillusory control conditions) on pain. Imputed correlations were calculated from Daenen et al. 2012[13] due to use of identical comparisons (0.716 for mirror incongruence vs mirror congruence comparison, 0.657 for mirror incongruence vs whiteboard incongruence comparison, and 0.716 for mirror incongruence vs whiteboard congruence comparison).

3.5.7. Incongruent movement illusions

3.5.7.1. Within-subject comparisons

Three studies evaluated the effect of incongruent movement illusions, which were hypothesized to induce and/or increase pain.[13,33,34] In these studies, the mirror provided a reflected image of the nonpainful body part; the painful body part was hidden from view behind the mirror. Participants moved the painful and the nonpainful body part in opposite directions creating incongruence between vision (reflected image of arm in the mirror) and proprioceptive feedback. The results were varied.

Only 2 studies[33,34] evaluated exacerbation of preexisting symptoms and performed similar within-subject comparisons and thus were pooled (**Fig. 3**). In people with pain (CRPS or FMS[34] or FMS[33]), there was a significant increase in the odds of experiencing pain during incongruent movement illusions, as compared with congruent movements using a mirror (OR = 1.67; 95% CI = 1.25-2.24), but no differences when compared with incongruent movements without visual cue (whiteboard; OR = 0.83; 95% CI = 0.57-1.19), or congruent movements with whiteboard (OR = 1.07; 95% CI = 0.91-1.27). Sensitivity analyses imputing correlations ±0.1 did not alter these results. In people with CRPS or FMS, incongruent movement illusions resulted in higher reports of severe pain (17%) than congruent mirror movements (4%) and incongruent/congruent movements without visual cue (both 0%).[34]

In the third study,[13] however, participants with WAD (and without arm pain) were *not* more likely to develop pain in the arm during the incongruent movement illusion than during control conditions (congruent mirror, Incongruent whiteboard, congruent whiteboard; nonsignificant ORs ranging from 1.00 to 1.12; Supplementary Table 4, available online at http://links.lww.com/PAIN/A181). People with WAD only had increased odds of developing arm pain during the incongruent movement illusion compared with general movement alone, ie, in which no mirror or whiteboard was used.

3.5.7.2. Comparison with healthy controls

Two studies also compared the pain population to healthy controls[33,13]; neither study found that incongruent movement illusions selectively increased pain to a greater extent in a painful population than in healthy controls (ie, pain increase also occurred during control conditions). In the first study, people with FMS did not have increased odds of experiencing pain compared with healthy controls during an incongruent movement illusion (OR = 3.90; 95% CI = 0.93 to 16.31) or with a congruent mirror control condition (OR = 1.99, 95% CI = 0.51 to 7.71)[33] but had increased odds of experiencing pain during both whiteboard control conditions (incongruent: OR = 12.60, 95% CI = 1.48 to 107.54; congruent: OR = 10.67, 95% CI = 1.24 to 91.98). In the second study,[13] people with WAD had increased odds of experiencing arm pain compared with healthy controls, but this occurred for all conditions (congruent mirror/whiteboard: OR = 66.60, 95% CI = 3.78 to 1173.63; incongruent mirror/whiteboard: OR = 59.59, 95% CI = 3.38 to 1050.18), including 2 movement conditions without view of the whiteboard or mirror, suggesting that it was merely movement in people with WAD that was pain provoking.

4. Discussion

We evaluated the current evidence for the effect of bodily illusions on pain. With the caveat that all studies had a high risk of bias, consistent evidence emerged: a decrease in pain was imparted by functional prosthetic use (illusory limb presence); illusory reduction in the apparent size of the body part; synchronous touch; and prolonged mirror therapy treatment. Illusory increase in the apparent size of the body part consistently modulated pain in the hypothesized direction (direction varied between conditions). Inconsistent effects on pain were found for virtual walking. No effects on pain were found for 1 session of mirror therapy, for embodiment illusions and for most incongruence illusions, although incongruent movement illusions had greater odds of increasing pain

than congruent mirrored movements did. Our findings are limited to chronic pain—no studies evaluated acute pain.

4.1. Resizing illusions

The coexistence of cortical misrepresentation of the body and perceptual size dysfunction in chronic painful conditions[37,43] underpins the investigation of resizing illusions. Changing how the painful body part looks may induce changes in cortical representation[56] and thus affect pain. We found limited evidence for bodily resizing illusions (3 studies, n = 48), but the evidence suggests that the type of condition, perceptual dysfunction and illusion (general vs targeted) may be important. For example, people with CRPS often report that their affected arm feels *bigger* than the healthy arm[30,41,49]; illusions that magnified the entire CRPS-affected hand increased pain and illusions that "minimized" the hand decreased pain.[48] Conversely, people with OA perceive their hand to be *smaller* than healthy controls do[24] and stretching illusions centered on the painful joint had a larger effect on pain than shrinking illusions did.[52] Perhaps pain relief depends on normalizing the perceptual dysfunction. Moreover, it is interesting that visual resizing of the whole hand did not affect OA pain, but multisensory illusions did.[52] Clearly more work is needed to elucidate these findings. Last, resizing illusions in chronic back pain did not alter intensity or unpleasantness of pain evoked by experimental nociceptive stimuli,[15] raising the possibility of differential effects on chronic pain vs acute nociceptive processing.

4.2. Mirror therapy

Mirror therapy is thought to reduce pain by providing pain-free visual feedback of normal limb movement. The effect has been attributed to removing incongruence between motor intention and sensory feedback for the painful (or phantom) limb,[27,32] but cognitive mechanisms associated with threat appraisal have also been proposed.[45] There is limited evidence that 1 session of mirror therapy does *not* reduce pain,[7,19,35] but limited-to-moderate evidence that prolonged mirror therapy does, at least when compared with inactive control conditions[8–10] or explicit motor imagery.[9,10] Nonsignificant effects for 1 session of mirror therapy may reflect reduced power (n = 18 vs n = 30 for prolonged therapy), or alternatively, a cumulative effect of prolonged mirror therapy.

Interestingly, nonresponders to traditional mirror therapy had significant pain reduction with congruent tactile and visual information (synchronous stroking), applied using the traditional mirror box set-up.[57] Perhaps the presence of multisensory congruent information is most important to the effects on pain, rather than the modality of the multisensory components. Indeed, that tactile input could be as effective as traditional mirror therapy has been proposed previously.[45] It is interesting to speculate that tactile multisensory information might avoid the associative pairing of movement with pain[14,60] and thus be less likely to trigger nociception, the latter also being a premise to graded motor imagery.[43]

4.3. Virtual walking illusions

Virtual walking aims to create the illusion of normal leg function. Again, evidence is limited (2 studies, n = 44): 1 small randomized repeated-measures study[44] found significant pain reductions but a larger RCT[59] found no effect. Although the studies differed on inactive control conditions—Soler et al.[59] used a double-sham (sham tDCS and sham illusion), whereas Moseley[44] compared with a comedy film to control for distraction—that virtual walking group of Soler et al. also received sham tDCS suggests that these differences are not likely relevant. It may be that the samples differed in other ways or that virtual walking does not add an effect above and beyond nonspecific effects of treatment. However, that virtual walking illusions were more effective at relieving pain than guided imagery,[44] which has known efficacy compared with placebo,[22] but not tDCS with the motor cortex,[59] suggests that comparison with common treatments for chronic pain is necessary before clinical implementation.

4.4. Functional prosthesis—illusory existence of a missing body part

Although the creation of illusory existence of a missing body part was not the primary aim of these studies,[31,63] they clearly induce such an experience. Limited evidence (2 studies, n = 35) suggests that use of functional prostheses reduces PLP. The large between-group difference in the time wearing the prosthesis (22 vs 5 years)[31] and the significant between-group age difference,[63] suggests caution in interpreting these studies' findings.

4.5. Embodiment illusions

Embodiment illusions are hypothesized to influence pain through "replacing" the real, painful body part with an artificial counterpart.[25] It is certainly intuitively attractive: we might be able to reduce pain by "projecting it" away from our body. That the RHI induces limb-specific changes in temperature regulation[47] and histamine reactivity[1] raises the possibility of modulation of nociception at a tissue or spinal level as well. Evidence exists that embodiment modulates physiological responses to painful stimuli: decreased arousal responses occur with high levels of self-identification with an avatar.[55] However, in healthy volunteers, the evidence is conflicting as to whether the RHI does[28] or does not[38] decrease experimentally induced thermal pain. Perhaps the experimental methodology used for embodiment is essential to the modulatory effects on pain. Alternatively, perhaps the pain is not decreased in intensity or unpleasantness but simply felt elsewhere: indeed, participants report that the evoked pain is felt in the rubber hand, not the stimulated hand.[38] Our review found that embodiment does not modulate pain—full-body embodiment illusion[58] did not decrease pain and RHI combined with threat (stabbing)[54] did not increase pain, suggesting that embodiment and pain modulation may be separate processes.

4.6. Incongruent movement illusions

Incongruent movement illusions have been used to test the hypothesis that incongruence between motor intention and motor action causes or exacerbates pain.[27,32] We found limited evidence (3 studies, n = 87) against this idea—incongruence illusions did not selectively cause or exacerbate pain in patients when compared with control conditions or healthy controls. The sole exception was that incongruence illusions were more likely to result in pain exacerbation than mirrored, congruent movements,[33,34] although it is interesting to speculate that the latter may constitute a dosage of traditional mirror therapy. That performing opposing movements with the arms, but without visual feedback, aggravated pain in FMS patients (more so than in healthy controls)[33] might simply reflect motor or biomechanical demands of the task.

4.7. Dosage of illusion application

The evidence is primarily limited to short-duration bodily illusions (eg, 20 seconds-15 minutes). Repeated/prolonged interventions might be required to decrease pain[53]: studies evaluating at least 4 weeks of mirror therapy[8–10,37] all reported significant pain reduction. Moreover, evidence suggests a positive effect of graded motor imagery,[40,42,43] which incorporates 2 weeks of intensive mirror therapy training, in people with CRPS or PLP.

4.8. Strengths and limitations

We emphasized rigor by conforming to the gold-standard approach to meta-analytical reviews.[39,29] We used a sensitive search strategy, hand searching references and consulting experts; yet, it remains possible that we missed eligible studies. We developed, in collaboration with field experts, clear constraints around what bodily illusions entailed, but we recognize that the results may have varied if our definition did. The wide variety of methodologies, types of illusions, and patient groups limited pooling and thus meta-analytical power. Although we required all studies to have a control condition/group to minimize the risk of significant results because of nonspecific effects of treatment, the high risk of bias of included studies (lack of blinding) raises the possibility that pain relief may have been mediated, at least in part, by expectation.[3,16] Included RCTs generally blinded the assessors, which strengthens our confidence in these findings.

4.9. Future research

Robust and suitably powered RCTs are needed. Furthermore, understanding the underlying mechanisms of the illusions would facilitate refinement of those that show promise. For example, a common feature of bodily illusions is that they are multisensory in nature, raising the possibility that the conditions in which these illusions are effective may have deficits in multisensory integration. Indeed, the lack of therapeutic success of traditional mirror therapy in amputees with telescoped limbs (ie, when vision does not match what they perceive),[21] but the efficacy of synchronous touch (ie, vision of touch matches referred sensation areas)[57] suggests that this is a relevant consideration. Preliminary evidence that illusory touch improves sensation in peripheral neuropathy[62] further supports this idea. Clearly more work is needed to clarify these relationships.

4.10. Conclusion

This review found promising effects on pain for resizing illusions, functional prosthetic use for PLP, and mirror therapy, suggesting that evaluation of repeated treatment is warranted. Due to the limited evidence base, caution must be employed in prematurely dismissing other illusion methodologies. Further studies with larger samples and varying dosages are essential before solid conclusions can be drawn.

Conflict of interest statement

T. R. Stanton received travel and accommodation support from Eli Lilly Ltd for a Western Canada speaker's tour (September 2014); this was unrelated to the present topic. G. L. Moseley consults for Pfizer, Kaiser Permanente, Providence Health, NOIgroup Australasia and Workers' Compensation Boards in Australia and North America. G. L. Moseley receives royalties from his published books (Explain Pain, Explain Pain handbook, Graded Motor Imagery handbook, Painful Yarns). E. Boesch and V. Bellan have no conflict of interests to declare.

E. Boesch was supported by a University of South Australia (UniSA) Division of Health Sciences Honours Scholarship and a UniSA School of Health Sciences Conference Scholarship. V. Bellan was supported by a postgraduate scholarship from the University of Milano-Bicocca. G. L. Moseley was supported by a National Health and Medical Research Council Research Fellowship (ID1061279). T. R. Stanton was supported by a Canadian Institute for Health Research Postdoctoral Training Fellowship (ID223354) and National Health & Medical Research Council Early Career Fellowship (ID 1054041).

Acknowledgements

The authors thank Carolyn Berryman for her valuable help selecting and including studies; Neil O'Connell for his statistical assistance with the meta-analytical techniques; Dr Alberto Gallace, Dr Roger Newport, Dr Diana Torta, Dr Martin Diers for their valuable help in identifying missed studies and Dr Alberto Gallace, Dr Roger Newport, Dr Martin Diers for establishing a consensus about the definition of bodily illusion.

Appendix A. Supplemental Digital Content

Supplemental Digital Content associated with this article can be found online at http://links.lww.com/PAIN/A181.

Article history:
Received 3 June 2015
Received in revised form 15 October 2015
Accepted 5 November 2015
Available online 14 November 2015

References

[1] Barnsley N, McAuley JH, Mohan R, Dey A, Thomas P, Moseley GL. The rubber hand illusion increases histamine reactivity in the real arm. Curr Biol 2001;21:R945–946.
[2] Becker MP, Balagtas CC. Marginal modelling of binary cross-over data. Biometrics 1993;49:997–1009.
[3] Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. J Neurosci 2005; 25:10390–402.
[4] Bjorkman A, Weibull A, Rosen B, Svensson J, Lundborg G. Rapid cortical reorganisation and improved sensitivity of the hand following cutaneous anaesthesia of the forearm. Eur J Neurosci 2009;29:837–44.
[5] Botvinik M, Cohen J. Rubber hands "feel" touch that eyes see. Nature 1998;391:756.
[6] Bowering KJ, O'Connell NE, Tabor A, Catley MJ, Leake HB, Moseley GL, Stanton TR. The effects of graded motor imagery and its components on chronic pain: a systematic review and meta-analysis. J Pain 2013;14:3–13.
[7] Brodie EE, Whyte A, Niven CA. Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a "virtual" limb upon phantom limb pain, sensation and movement. Eur J Pain 2007; 11:428–36.
[8] Cacchio A, De Blasis E, De Blasis V, Santilli V, Spacca G. Mirror therapy in complex regional pain syndrome type 1 of the upper limb in stroke patients. Neurorehabil Neural Repair 2009;23:792–9.
[9] Cacchio A, De Blasis E, Necozione S, di Orio F, Santilli V. Mirror therapy for chronic complex regional pain syndrome type 1 and stroke. N Engl J Med 2009;361:634–6.
[10] Chan BL, Witt R, Charrow AP, Magee A, Howard R, Pasquina PF, Heilman KM, Tsao JW. Mirror therapy for phantom limb pain. N Engl J Med 2007;357:2206–7.
[11] Cochrane Collaboration. Review Manager (Revman). Book Review Manager (Revman). City: Nordic Cochrane Centre, 2011.
[12] Cohen J. Statistical power analysis for the behavioural science. Hillsdale, MJ: Lawrence Erlbaum Associates, 1998.
[13] Daenen L, Nijs J, Roussel N, Wouters K, Van Loo M, Cras P. Sensorimotor incongruence exacerbates symptoms in patients with

chronic whiplash associated disorders: an experimental study. Rheumatology 2012;51:1492–9.
[14] De Jong JR, Vlaeyen JW, Onghena P, Cuypers C, Den Hollander M, Ruijgrok J. Reduction of pain-related fear in complex regional pain syndrome type I: the application of graded exposure in vivo. PAIN 2005; 116:264–75.
[15] Diers M, Zieglgansberger W, Trojan J, Drevensek AM, Erhardt-Raum G, Flor H. Site-specific visual feedback reduces pain perception. PAIN 2013; 154:890–6.
[16] Eippert F, Bingel U, Schoell ED, Yacubian J, Klinger R, Lorenz J, Buchel C. Activation of the opioidergic descending pain control system underlies placebo analgesia. Neuron 2009;63:533–43.
[17] Elbourne DR, Altman DG, Higgins JPT, Curtin F, Worthington HV, Vail A. Meta-analysis involving cross-over trials: methodological issues. Int J Epidemiol 2002;31:140–9.
[18] Ezendam D, Bongers RM, Jannink MJ. Systematic review of the effectiveness of mirror therapy in upper extremity function. Disabil Rehabil 2009;31:2135–49.
[19] Flinn SR, Hotle AC. A case series report on amputees with pro digit hand prostheses receiving mirror therapy. J Hand Ther 2011;24:390–1.
[20] Flor H, Braun C, Elbert T, Brinbaumer N. Extensive reorganization of primary somatosensory cortex in chronic back pain patients. Neurosci Lett 1997;224:5–8.
[21] Foell J, Bekrater-Bodmann R, Diers M, Flor H. Mirror therapy for phantom limb pain: brain changes and the role of body representation. Eur J Pain 2014;18:729–39.
[22] Fors EA, Sexton H, Gotestam KG. The effect of guided imagery and amitriptyline on daily fibromyalgia pain: a prospective, randomized, controlled trial. J Psychiatr Res 2002;36:179–87.
[23] Gandevia SC, Phegan CML. Perceptual distortions of the human body image produced by local anaesthesia, pain and cutaneous stimulation. J Physiol 1999;514:609–16.
[24] Gilpin HR, Moseley GL, Stanton TR, Newport R. Evidence for distorted mental representation of the hand in osteoarthritis. Book Evidence for distorted mental representation of the hand in osteoarthritis. City, 2014. p. 258–63.
[25] Giummarra MJ, Georgiou-Karistianis N, Nicholls ME, Gibson SJ, Bradshaw JL. The phantom in the mirror: a modified rubber-hand illusion in amputees and normals. Perception 2010;39:103–18.
[26] Gwilym SE, Filippini N, Douaud G, Carr AJ, Tracey I. Thalamic atrophy associated with painful osteoarthritis of the hip is reversible after arthroplasty. Arthritis Rheum 2010;62:2930–40.
[27] Harris AJ. Cortical origin of pathological pain. Lancet 1999;354:1464–6.
[28] Hegedüs G, Darnai G, Szolcsány T, Feldmann Á, Janszky J, Kállai J. The rubber hand illusion increases heat pain threshold. Eur J Pain 2014;18: 1173–81.
[29] Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. In: Higgins JPT, Altman DG, Sterne JAC, editors. Book cochrane handbook for systematic reviews of interventions. City: The Cochrane Collaboration, 2011.
[30] Lewis JS, Kersten P, McCabe CS, McPherson KM, Blake DR. Body perception distrubance: a contribution to pain in complex regional pain syndrome (CRPS). PAIN 2007;133:111–19.
[31] Lotze M, Grodd W, Birbaumer N, Erb M, Huse E, Flor H. Does use of myoelectric prosthesis prevent cortical reorganization and phantom limb pain? Nat Neurosci 1999;2:501–2.
[32] McCabe CS. Simulating sensory disturbances in healthy controls-implications for pathology. Rheumatology 2005;42:63.
[33] McCabe CS, Cohen H, Blake DR. Somaesthetic disturbances in fibromyalgia are exaggerated by sensory-motor conflict: implications for chronicity of the disease? Rheumatology 2007;46:1587–92.
[34] McCabe CS, Haigh RC, Halligan PW, Blake DR. Distorting proprioception in chronic pain patients exacerbates sensory disturbances—implications for pathology. Rheumatology 2003;42:145.
[35] McCabe CS, Haigh RC, Ring EFJ, Halligan PW, Wall PD, Blake DR. A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1). Rheumatology 2003;42: 97–101.
[36] Merskey H, Bogduk N. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. Seattle, WA: IASP Press, 1994.
[37] Michielsen ME, Selles RW, Van Der Geest JN, Eckhardt M, Yavuzer G, Stam HJ, Smits M, Ribbers GM, Bussmann JB. Motor recovery and cortical reorganization after mirror therapy in chronic stroke patients: a phase II randomized controlled trial. Neurorehabil Neural Repair 2011; 25:223–33.
[38] Mohan R, Jensen KB, Petkova VI, Dey A, Barnsley N, Ingvar M, McAuley JH, Moseley GL, Ehrsson HH. No pain relief with the rubber hand illusion. PLoS One 2012;7:1–7.
[39] Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:1–28.
[40] Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. PAIN 2004;108:192–8.
[41] Moseley GL. Distorted body image in complex regional pain syndrome. Neurology 2005;65:773.
[42] Moseley GL. Is successful rehabilitation of complex regional pain syndrome due to sustained attention to the affected limb? A randomised clinical trial. PAIN 2005;114:54–61.
[43] Moseley GL. Graded motor imagery for pathologic pain: a randomised controlled trial. Neurology 2006;67:2129–34.
[44] Moseley GL. Using visual illusion to reduce at-level neuropathic pain in paraplegia. PAIN 2007;130:294–8.
[45] Moseley GL, Gallace A, Spence C. Is mirror therapy all it is cracked up to be? Current evidence and future directions. PAIN 2008;138:7–10.
[46] Moseley GL, McCormick K, Hudson M, Zalucki N. Disrupted cortical proprioceptive representation evokes symptoms of peculiarity, foreignness and swelling, but not pain. Rheumatology 2006;45:196–200.
[47] Moseley GL, Olthof N, Venema A, Don S, Wijers M, Gallace A, Spence C. Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. Proc Natl Acad Sci U S A 2008;105:13169–73.
[48] Moseley GL, Parsons TJ, Spence C. Visual distortion of a limb modulates the pain and swelling evoked by movement. Curr Biol 2008;18:R1047–8.
[49] Peltz E, Seifert F, Lanz S, Mueller R, Mayhoefner C. Impaired hand size estimation in CRPS. J Pain 2011;12:1095–101.
[50] Pleger B, Ragert P, Schwenkreis P, Forster A, Wilimzig C, Dinse H, Volkmar N, Maier C, Tegenthoff M. Patterns of cortical reorganization parallel impaired tactile discrimination and pain intensity in complex regional pain syndrome. NeuroImage 2006;32:503–10.
[51] Pleger B, Tegenthoff M, Ragert P, Forster A, Dinse HR, Maier C. Sensorimotor returning in complex regional pain syndrome parallels pain reduction. Ann Neurol 2005;57:425–9.
[52] Preston C, Newport R. Analgesic effects of multisensory illusions in osteoarthritis. Rheumatology 2011;50:2314–15.
[53] Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. Proc Biol Sci 1996;263:377–86.
[54] Reinersmann A, Landwehrt J, Krumova EK, Petersburs J, Ocklenburg S, Gunturkun O, Maier C. The rubber hand illusion in complex regional pain syndrome: preserved ability to integrate a rubber hand indicates intact multisensory integration. PAIN 2013;154:1519–27.
[55] Romano D, Pfeiffer C, Maravita A, Blanke O. Illusory self-identification with an avatar reduces arousal responses to painful stimuli. Behav Brain Res 2014;261:275–81.
[56] Schaefer M, Flor H, Heinze HJ, Rotte M. Morphing the body: illusory feeling of an elongated arm affects somatosensory homunculus. Neuroimage 2007;36:700–5.
[57] Schmalzl L, Ragno C, Ehrsson HH. An alternative to traditional mirror therapy. Illusory touch can reduce phantom limb pain when illusory movement does not. Clin J Pain 2013;29:e10–18.
[58] Schmalzl L, Thomke E, Ragno C, Nilseryd M, Stockselius A, Ehrsson HH. "Pulling telescoped phantoms out of the stump": manipulating the perceived position of phantom limbs using a full-body illusion. Front Hum Neurosci 2011;5:1–12.
[59] Soler D, Kumru H, Pelayo R, Vidal J, Tormos JM, Fregni F, Navarro X, Pascual-Leone A. Effectiveness of transcranial direct current stimulation and visual illusion on neuropathic pain in spinal cord injury. Brain 2010; 133:2565–77.
[60] Vlaeyen JW, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. PAIN 2012;153:1144–7.
[61] von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Br Med J 2007;335:806–8.
[62] Wand BM, Stephens SE, Manqharam EI, George PJ, Bulsara MK, O'Connell NE, Moseley GL. Illusory touch temporarily improves sensation in areas of chronic numbness: a brief communication. Neurorehabil Neural Repair 2014;28:797–9.
[63] Weiss T, Miltner WH, Adler T, Bruckner L, Taub E. Decrease in phantom limb pain associated with prosthesis-induced increased use of an amputation stump in humans. Neurosci Lett 1999;272:131–4.