REVIEW ARTICLE

Sensorimotor Incongruence in People with Musculoskeletal Pain: A Systematic Review

Sanneke Don, MSPT*,†; Lennard Voogt, PhD*,†,‡; Mira Meeus, PhD*,§,¶; Margot De Kooning, MSc*,†; Jo Nijs, PhD*,†

*Pain in Motion International Research Group; †Department of Rehabilitation Sciences and Physiotherapy, Human Physiology and Anatomy (KIMA), Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; ‡Department of Physiotherapy, Rotterdam University of Applied Sciences, Rotterdam, the Netherlands; §Department of Rehabilitation Sciences and Physiotherapy, Ghent University, Ghent; ¶Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

■ **Abstract**

Objectives: Musculoskeletal pain has major public health implications, but the theoretical framework remains unclear. It is hypothesized that sensorimotor incongruence (SMI) might be a cause of long-lasting pain sensations in people with chronic musculoskeletal pain. Research data about experimental SMI triggering pain has been equivocal, making the relation between SMI and pain elusive. The aim of this study was to systematically review the studies on experimental SMI in people with musculoskeletal pain and healthy individuals.

Methods: Preferred reporting items for systematic reviews and meta-analyses guidelines were followed. A systematic literature search was conducted using several databases until January 2015. To identify relevant articles, keywords regarding musculoskeletal pain or healthy subjects and the sensory or the motor system were combined. Study characteristics were extracted. Risk of bias was assessed using the Dutch Institute for Healthcare Improvement (CBO) checklist for randomized controlled trials, and level of evidence was judged.

Results: Eight cross-over studies met the inclusion criteria. The methodological quality of the studies varied, and populations were heterogeneous. In populations with musculoskeletal pain, outcomes of sensory disturbances and pain were higher during all experimental conditions compared to baseline conditions. In healthy subjects, pain reports during experimental SMI were very low or did not occur at all.

Discussion: Based on the current evidence and despite some methodological issues, there is no evidence that experimental SMI triggers pain in healthy individuals and in people with chronic musculoskeletal pain. However, people with chronic musculoskeletal pain report more sensory disturbances and pain during the experimental conditions, indicating that visual manipulation influences pain outcomes in this population. ■

Key Words: sensorimotor incongruence, chronic pain, musculoskeletal pain, visual feedback

INTRODUCTION

Chronic musculoskeletal pain is highly prevalent and a hard to treat disorder.[1–8] To resolve the complex puzzle of musculoskeletal pain, it seems important to explore the role of the central nervous system. When pain persists without any pathological cause, maladaptive

Address correspondence and reprint requests to: Sanneke Don, MSPT, Vrije Universiteit Brussel, Medical Campus Jette, Building F-Kine, Laarbeeklaan 103, BE-1090 Brussels, Belgium. E-mail: sanneke.don@vub.ac.be.

Submitted: July 24, 2015; Revised January 27, 2016; Revision accepted: February 8, 2016

DOI. 10.1111/papr.12456

neuronal plasticity may be accountable.[9–15] Based on cortical processes, Harris developed a theory that holds a mismatch between motor intention and sensory feedback accountable in contributing to long-lasting pain in individuals with unexplained chronic pain.[16] This cortical model of pain suggests that, possibly as a result of these maladaptive plastic changes, incongruence between motor output and proprioceptive and visual feedback results in pain and other sensory disturbances.[16,17] This discordance between motor output and peripheral feedback is called sensorimotor incongruence (SMI). It has been argued that restoring this discordance, targeting pain relief, might be therapeutically relevant for people with unexplained musculoskeletal pain.[16]

To ensure smoothness in motor action, a feedback loop exists between the predicted sensory consequences of movement and the actual sensory feedback.[18–20] SMI occurs when this predicted motor output is not coherent to the actual sensory feedback from the body, causing pain and other sensory disturbances. This is similar to motion sickness, when discordant information between the vestibular and visual systems results in nausea.[16] It is possible to induce SMI experimentally by distorting visual input during the execution of movements. A bimanual coordination experiment can create such a sensorimotor conflict. In a bimanual experiment, a mirror is placed between the limbs while participants move their limbs. Therefore, one limb is occluded from vision and is replaced by the mirror image of the other. During incongruent movements, both limbs are seen moving together in a congruent manner, while in fact they move incongruently and separately from each other. This artificial mismatch is called experimental SMI. Provided that SMI is a main driver for pain and sensory disturbances in an individual, it is expected that this experimental conflict between motor output and sensory feedback would cause an exacerbation of pain and sensory disturbances.[21] It is hypothesized that pain and sensory disturbances during experimental SMI might be warning signals produced by the central nervous system, to alert the individual of the discordance between motor output and sensory input.[21,22] Evidence has shown that experimental SMI causes pain and additional symptoms in participants with fibromyalgia and whiplash-associated disorders.[17,22–24] Contradictory evidence comes from studies investigating healthy individuals.[25–28] These studies show that experimental SMI does not cause pain, although most studies show that sensory disturbances are frequent. Evidence from brain imaging studies has demonstrated increased activity of the right dorsolateral prefrontal cortex in response to a sensorimotor conflict during the bimanual coordination experiment.[29] Despite these findings, the underlying mechanisms of SMI remain unclear, and no causal relation between SMI and pain can be made.

Despite the growing literature on experimental SMI, it remains unclear whether SMI causes pain or not and there seems a lack of studies reviewing the existing literature. Given the contradictory findings regarding the role of SMI in (chronic) pain and the lack of a systematic review, it seems important to summarize and critically evaluate the studies on SMI. Therefore, the aim of this study was to systematically review the studies on experimental SMI in people with musculoskeletal pain and healthy individuals to examine whether SMI triggers or changes pain in these populations.

METHODS

Search Strategy

A systematic literature search was conducted to review the available literature regarding sensorimotor (in)congruence in people with musculoskeletal pain and healthy individuals. Therefore, a search was conducted in Embase, Medline (OvidSP), Web of science, Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane, PubMed publisher, and Google Scholar up to January 2015. The search has been set up according to PICOS (participants: people with musculoskeletal pain and healthy individuals; interventions: experimental sensorimotor incongruence [incongruent visual feedback during active movement]; comparisons: moving without visual feedback or with normal visual feedback; outcomes: pain; study design: experimental studies). To identify relevant articles, three groups of keywords were combined: (1) musculoskeletal pain or healthy individuals and its synonyms; (2) the sensory and visual systems and all possible synonyms; and (3) the motor system and all possible synonyms, as well as sensory motor combinations including SMI or other synonyms and mechanisms involved. An overview of the search conducted in Embase (www.embase.com) is displayed in Table 1. Reference lists of relevant studies, books, and journals were hand searched and cross-referenced to identify additional studies that were not detected through the literature search. Several researchers in the field were contacted to make sure no important studies were missed.

Table 1. Search Strategy Used for Embase

('musculoskeletal pain'/exp OR myalgia/exp OR arthralgia/exp OR backache/exp OR 'neck pain'/exp OR 'shoulder pain'/exp OR 'limb pain'/exp OR 'arm pain'/exp OR 'leg pain'/exp OR (backache OR ((back OR musculoskelet* OR muscle* OR skelet* OR bone* OR joint* OR knee* OR shoulder* OR elbow* OR neck OR cervical OR limb* OR arm* OR leg* OR extremit* OR foot OR feet OR ankle*) NEAR/3 pain*) OR dorsalgi* OR arthralgi* OR myalgi* OR Cervicalgi*):ab,ti) AND ('normal human'/exp OR (((normal* OR healthy OR general) NEAR/3 (human* OR people* OR volunteer* OR subject* OR person* OR control* OR participant* OR populat* OR men OR male* OR women OR female* OR adult* OR group* OR individual* OR neck* OR back*)) OR (population NEAR/3 sample)):ab,ti) AND ('sensorimotor function'/exp OR 'sensorimotor cortex'/de OR 'sensory feedback'/de OR 'visual feedback'/de OR 'somatosensory stimulation'/de OR 'somatosensory cortex'/de OR 'somatosensory system'/de OR (('sensory system'/de OR 'visual system'/exp) AND ('motor system'/de OR 'motor cortex'/de OR 'primary motor cortex'/de OR kinesthesia/de)) OR 'cortical synchronization'/de OR 'body image'/de OR proprioception/de OR (sensorimotor* OR visuomotor* OR ((sensor* OR visu*) NEAR/3 (motor* OR feedback OR input OR kinesthe* OR locali* OR mislocali*)) OR somatosensor* OR ((cortical OR cortex) NEAR/3 (synchroni* OR pain OR reorgani* OR representat* OR organi*)) OR (body NEAR/3 (represent* OR image* OR schem* OR map)) OR mirror* OR propriocep* OR (kines* NEAR/3 (discriminat* OR percept*)) OR (motor* NEAR/3 imag*)):ab,ti)

Selection Criteria

Studies were screened based on titles and abstracts and were selected based on inclusion and exclusion criteria. Studies were included if they were studies investigating people with musculoskeletal pain or healthy individuals, related to sensorimotor incongruence, concerning the effect of visual and proprioceptive information progressing on pain.

Studies were excluded if (1) they included participants with specific peripheral or neurological pathology, (2) they included animals, (3) they included participants younger than 18 years, (4) the article was not written in English full text, or (5) they were reviews, case reports, letters to the editor, or congress abstracts.

All included studies were obtained full text and screened for eligibility. In case of doubt, two other reviewers (J.N. and L.V.) judged the study for eligibility, and discussion took place until consensus was attained.

Risk of Bias Assessment

The methodological quality was independently assessed by two reviewers (L.V. and S.D.) using the Dutch Institute for Healthcare Improvement (CBO) checklist for randomized controlled trials (RCTs). The checklist was obtained via the website www.cbo.nl. The content of the questionnaire is displayed in Table 2. After the assessment, both reviewers analyzed the outcomes, and discussion took place until consensus was attained. In case of serious disagreement, the third reviewer (J.N.) judged the items of disagreement.

Based on study design and risk of bias assessment, levels of evidence were determined for each article based on the CBO levels of evidence from A1 to D. A level A1 study describes a systematic review based on at least 2 level A2 studies, and the result of each study must be consistent. A level A2 study is a double-blinded randomized clinical trial of good quality with a sufficient number of participants; a level B study is a randomized clinical trial of average quality with a nonsufficient number of participants or other types of study design (nonrandomized, comparing cohort study, patient-controlled research). Level C is a noncomparative study, and level D is an expert opinion. Levels of conclusion were determined based on the outcomes of the levels of evidence. Level of conclusion 1 is based on 1 A1 study or 2 independent A2 studies. Level of conclusion 2 is based on 1 A2 study or 2 independent B studies. Level of conclusion 3 is based on a level B or C study, and level of conclusion 4 is based on expert opinions.

Data Extraction and Analyses

The following data were extracted from included studies: (1) study design, (2) characteristics of study participants, (3) baseline measurement and outcome measures, (4) experimental characteristics (experimental stimulus, conditions, and apparatus), and (5) results. Authors of the included studies were contacted in case additional information or material was needed. Given the small number of eligible studies, the varying methods (including design and outcome measures) applied in the selected studies, and the varying study populations, statistical pooling of data was not feasible.

Table 2. The Dutch CBO Checklist for Randomized Controlled Trials

CBO questionnaire	
1	Random allocation?
2	Concealment of allocation?
3	Blinding participants from study hypothesis?
4	Blinding therapists?
5	Blinding outcome assessors?
6	Group comparability?
7	Sufficient follow-up?
8	Intention-to-treat analyses?
9	Equal approach?

CBO, Dutch Institute for Healthcare Improvement.

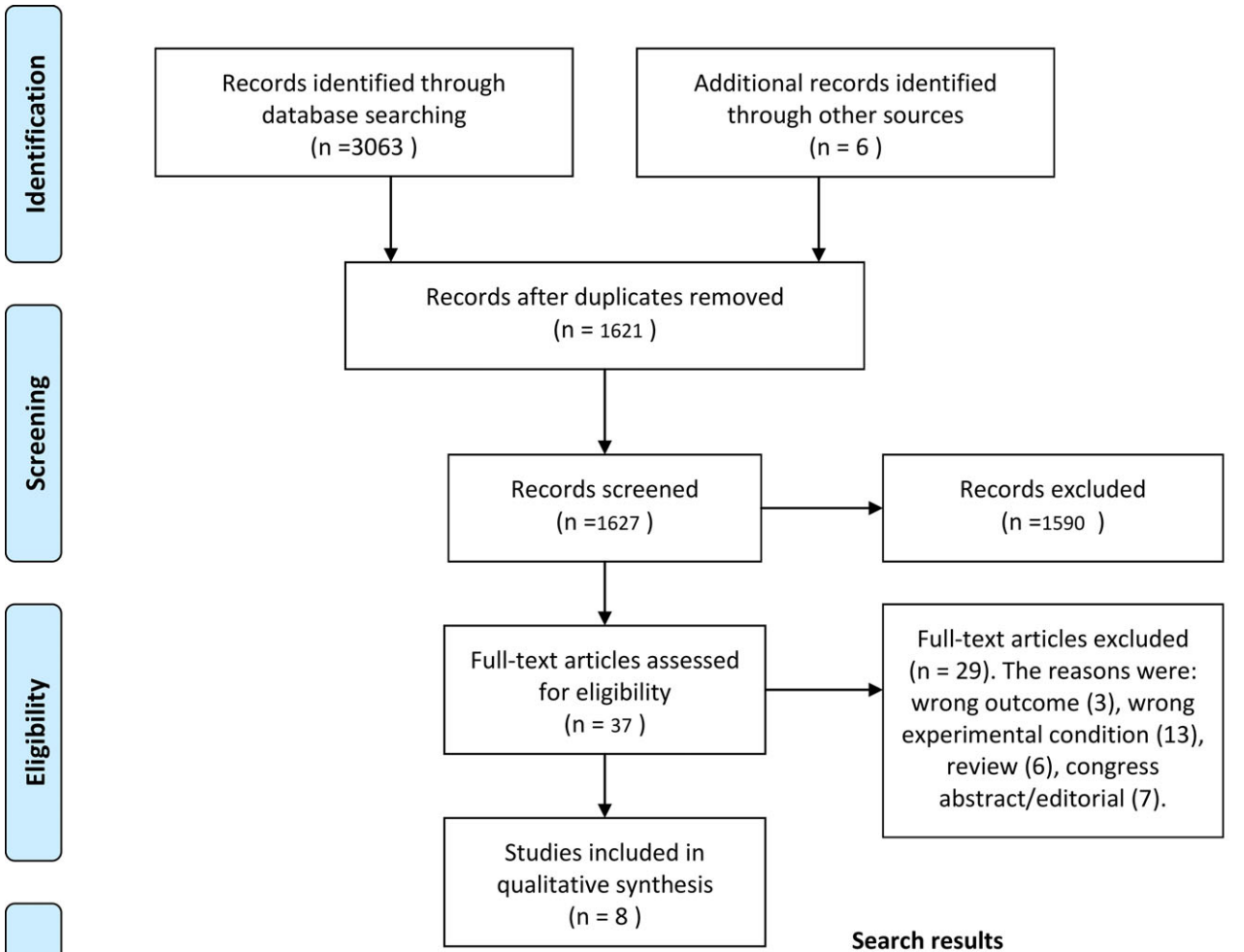
RESULTS

Study Selection

The flowchart for study selection and exclusion is presented in Figure 1. A total of 3,063 studies were identified, and after removing 1,442 duplicates, 1,621 studies remained. Subsequently, 6 additional studies were identified via hand searching, and 1,627 studies were screened. A total of 1,590 studies were removed after screening titles and abstracts. The remaining 37 studies were read full text and evaluated for eligibility. A total of 8 studies met the inclusion criteria.

Risk of Bias Assessment

Results of the risk of bias assessment are summarized in Table 3. The two reviewers (L.V. and S.D.) were unaware of each other's results. After individual



Search results

Embase.com	657	649
Medline (OvidSP)	367	39
Web-of-science	718	405
Scopus	887	301
Cinahl	130	16
Cochrane	45	2
PubMed publisher	59	54
Google Scholar	200	155
Total	**3063**	**1621**

Figure 1. This figure illustrates the selection process. The small table in the figure shows the number of studies found per database (in the first row) and the number of studies per database after removing the duplicates (in the second row).

Table 3. Results of Risk of Bias Assessment

Study	Random allocation?	Concealment of allocation?	Blinding participants from study hypothesis?	Blinding therapists?	Blinding outcome assessors?	Group comparabillity?	Sufficient follow-up?	Intention-to-treat analyses?	Equal approach?
Daenen et al.[25]	+	?	+	/	+	/	/	/	+
Daenen et al.[24]	+	?	+	/	?	/	/	/	+
Daenen et al.[23]	+	?	+	/	?	/	/	/	+
Foell et al.[28]	+	?	+	/	?	/	/	/	+
McCabe et al.[22]	+	?	+	/	?	/	/	/	+
McCabe et al.[17]	+	?	+	/	?	/	/	/	+
Roussel et al.[26]	?	?	+	/	?	/	/	/	+
Wand et al.[27]	+	+	+	/	+	/	/	/	+

+, yes; ?, not described; /, not applicable.

assessment, results were compared, and the reviewers agreed on most items (92.5%) of methodological quality. Discrepancies between authors were discussed until agreement was reached. The methodological quality was judged according to the levels of evidence of the CBO and was judged as level B for all studies. The level of conclusion was judged as level 2. In most studies (87.5%), experimental conditions were randomized.[17,22–25,27,28] Few studies (12.5%) reported allocation concealment[27] and blinding of assessors.[25,27] All studies held participants naive to the purpose of the study,[17,22–28] and 3 studies thereof (37.5%) described exactly how participants were given a different rationale of the study to prevent expectancy bias.[17,22,26] Conditions were standardized in all studies. A washout period was part of the protocol in all studies to avoid bias from carry-over effects. In 4 studies, the washout period was described as a rest period that lasted until sensations disappeared or returned to their baseline status.[23–26] The study of Wand et al.[27] had the longest washout period (15 minutes). The study of Foell et al.[28] had the shortest washout period (1 second). A total of 4 studies (50%) reported a sample size calculation.[23,24,26,27] In most studies, a baseline movement condition was implemented to correct for biases due to muscle fatigue or other possible effects of movement.[17,22–27]

Study Characteristics

Study characteristics are summarized in Table 4. All studies were cross-over experiments. A sensorimotor conflict, triggered via incongruent visual feedback during movement, was part of the protocol in all included studies. All studies investigated SMI via a bimanual coordination experiment in which a mirror or whiteboard was placed between the participants' moving limbs. In the bimanual experiments, participants moved their limbs in a congruent and incongruent manner while they were viewing the whiteboard or the mirror. The whiteboard obscures any view of the limb behind the board, and the mirror reflects only the limb adjacent to the mirror. In the mirror congruence condition, the visual input from the limb in the mirror is coherent with the movement of the limb that is obscured by the mirror. Conversely, in the mirror incongruence condition (which represents experimental SMI), both limbs are moving incongruent from each other, and therefore, the visual input is incoherent with the movement of the limb behind the mirror.

Different types of participants were included in the studies: Wand et al., Foell et al., and McCabe et al. included healthy individuals,[22,27,28] Daenen et al.[24] included participants with chronic whiplash-associated disorder, Daenen et al.[23] included participants with acute whiplash-associated disorder, McCabe et al.[17] included participants with fibromyalgia, Roussel et al.[26] included dancers with and without musculoskeletal complaints, and Daenen et al.[25] included violinists with and without musculoskeletal complaints. All studies included pain as an outcome measure using a modified Likert scale (all ranging from 0 to 10).

Experimental conditions varied among the studies. Foell et al.[28] implemented a movement task of the arms and a movement task of the hands. Daenen et al., Roussel et al., and Wand et al. implemented a movement task of the arms.[23–27] McCabe et al.[17,22] implemented a movement task of the arms and a movement task of the legs. Most studies defined the control condition as moving the limbs without looking in the mirror or whiteboard,[17,23–27] while 2 studies defined the control condition as the whiteboard condition.[22,28]

Table 4. Study Characteristics

Authors	Study design	Sample	Outcome measures	Stimulus	Experimental conditions	Results
Daenen et al.[25]	Randomized crossover experiment	11 violinists with and 9 violinists without baseline musculoskeletal complaints	Frequency (%) of reported sensations	Bimanual coordination test	(1) WC, (2) WI, (3) MC, (4) MI, (5) CC, (6) CI	Frequency of pain during test protocol: 0% Frequency of sensations during MI (55%) and CC/CI: (15%) Difference in frequency of sensations between test conditions ($P \geq 0.05$) and between groups during MI ($P = 0.025$) and MC ($P = 0.012$) Differences between test and control conditions ($P = 0.063$ to $P = 0.001$)
Daenen et al.[24]	Randomized crossover experiment	35 chronic WAD, 31 healthy controls	Frequency (%) and intensity (NRS) of sensations	Bimanual coordination test	(1) WC, (2) WI, (3) MC, (4) MI, (5) CC, (6) CI	Chronic WAD • Frequency of pain during test protocol: 60% • Mean intensity of sensations (NRS): WC (4.69), WI (4.71), MC (4.86), MI (5.11), CC/CI (2.71) • Differences between test conditions ($P \geq 0.05$)* and between test and control conditions in intensity of sensations ($P \leq 0.05$) Healthy controls • Frequency of pain during test protocol: 0% • Mean intensity of sensations (NRS): WC (0.35), WI (0.58), MC (0.19), MI (1.61), CC/CI (0) • Difference between MI and WI in frequency ($P = 0.003$) and intensity of sensations ($P = 0.002$) • Difference between MI and CI in intensity of sensations ($P \leq 0.05$)
Daenen et al.[23]	Randomized crossover experiment	30 acute WAD	Frequency (%) and intensity (NRS) of sensations	Bimanual coordination test	(1) WC, (2) WI, (3) MC, (4) MI, (5) CC, (6) CI	Frequency of pain during test protocol: 43% Mean intensity of sensations (NRS): WC (4.03), WI (3.87), MC (4.33), MI (4.20), CC (2.80), CI (2.43) Differences between test conditions ($P \geq 0.05$)*, MI compared to CI in frequency ($P \leq 0.05$) and between test and control conditions in intensity of sensations ($P \leq 0.05$)
Foell et al.[28]	Randomized crossover experiment	113 healthy volunteers	Frequency (%) and intensity (NRS) of sensations	Bimanual coordination test	Arm: (1) MC, (2) MI, (3) WC, (4) WI Hand: (5) MC, (6) MI, (7) WC, (8) WI	Mean intensity of pain (NRS) during all conditions: arm (< 0.5), hand (< 0.5) Frequency of pain during MI (%): arm (1.8%), hand (0.9%) No significant difference in pain intensity and frequency between conditions
McCabe et al.[22]	Randomized crossover experiment	41 healthy volunteers	Frequency (%) of reported sensations	Bimanual coordination test	Upper limbs: (1) WC, (2) WI, (3) MC, (4) MI Lower limbs: (5) WC, (6) WI, (7) MC, (8) MI	Intensity of pain during test protocol (NRS): < 2 Frequency of pain of in arms and legs (%): MI (15%), MC (12%), WI/WC (2%)

Table 4. (Continued)

Authors	Study design	Sample	Outcome measures	Stimulus	Experimental conditions	Results
McCabe et al.[17]	Randomized crossover experiment	29 patients with FM and 29 healthy controls	Frequency (%) of reported sensations	Bimanual coordination test	CC and CI first. Upper limbs: (1) WC, (2) WI, (3) MC, (4) MI Lower limbs: (5) WC, (6) WI, (7) MC, (8) MI	Patients with FM • Intensity of pain during test protocol (NRS): 5 • Frequency of pain in arms and legs (%): MI (31%), MC (24%), WI (31%), WC (28%) Healthy controls • Intensity of pain during test protocol (NRS): < 2 • Frequency of pain in arms and legs (%): MI (10%), MC (14%), WI/WC (3%)
Roussel et al. [26]	Randomized crossover experiment	18 dancers with baseline musculoskeletal pain and 26 dancers without baseline symptoms	Frequency (%) and intensity (NRS) of sensations	Bimanual coordination test	(1) WC, (2) WI, (3) MC, (4) MI, (5) CC, (6) CI	Dancers with pain • Mean intensity of sensations (NRS): WC (0.67), WI (1.11), MC (0.39), MI (1.61), CC/CI (0) • Frequency of sensations during MI: 56% Pain-free dancers • Mean intensity of sensations (NRS): WC (0.81), WI (1.08), MC (0.96), MI (1.88), CC/CI (0) • Frequency of sensations during MI: 50% Both groups • Frequency of pain during test protocol: 5% • Frequency of sensations during MI: 52% • Differences between test conditions ($P \geq 0.05$) and groups ($P \geq 0.05$)* in intensity of sensations • Differences between test and control conditions ($P \leq 0.001$) and MI compared to WI ($P \leq 0.001$) in frequency of sensations
Wand et al.[27]	Randomized crossover experiment	35 healthy volunteers	PPT and pain intensity (NRS)	Bimanual coordination test	(1) MC, (2) MI, (3) CC, (4) CI	Mean pain intensity scores (NRS): MC (1.2), MI (1.4), CC (1.3), CI (1.5) PPT between conditions ($P = 0.887$) Intensity of pain between conditions ($P = 0.771$)

*For both intensity and frequency of sensations.
WC, whiteboard congruent; WI, whiteboard incongruent; MC, mirror congruent; MI, mirror incongruent; CC, control congruent; CI, control incongruent; WAD, whiplash-associated disorder; NRS, numeric rating scale; FM, fibromyalgia; PPT, pressure pain threshold; VNRS, verbal numeric rating scale.

Study Findings Regarding Sensorimotor Incongruence

Participants with Chronic Pain. McCabe et al.[17] showed that 31% of the participants with fibromyalgia experienced pain and 69% experienced pain and/or additional sensations (eg, discomfort, changes in temperature, changes in the perception of limb weight, perceived additional or lost limbs, disorientation, stiffness, or tiredness) during the mirror incongruence condition. The frequency of reported sensations was not different across the experimental conditions (ie, the mirror congruence and mirror incongruence conditions and whiteboard congruence and whiteboard incongruence conditions) in participants with fibromyalgia, although frequencies were higher than baseline reports. Pain intensity measurements were not compared between conditions, although it was reported that the mean intensity of pain during the protocol for all participants was scored as 5 on a verbal numeric rating scale (ranging from 0 to 10).[17] In the study by Daenen et al.[25], none of the studied professional violinists, of which 45% suffered from musculoskeletal complaints, experienced pain during the mirror incongruence condition. However, 55% reported sensations (eg, discomfort, a feeling of peculiarity, changes in the perception of limb weight, a perceived loss of an arm or an additional arm, or temperature changes) compared to 15% in the control conditions. There were no significant differences between the mirror congruence and whiteboard congruence conditions and between the mirror incongruence and whiteboard incongruence conditions, although there were significant differences between these test and control conditions. Intensity of pain was not an outcome measure. Violinists with musculoskeletal complaints reported significantly more sensations during the mirror incongruence and mirror congruence conditions than did violinists without baseline symptoms.[25]

In the study by Daenen et al.[23], 60% of the participants with chronic whiplash-associated disorder experienced pain during the whole test protocol. This study investigated the effect of experimental SMI on all sensations combined. Therefore, the study did not report on perceived pain, and the percentage of pain reports during the mirror incongruence condition was not described. The mean intensity score of reported sensations was highest for the mirror incongruence condition: 5.11 on a numeric rating scale (ranging from 0 to 10). There were no differences in intensity of sensations between the mirror congruence and whiteboard congruence conditions and between the mirror incongruence and whiteboard incongruence conditions, although there were significant differences between the test and control conditions.[24] In addition, the same research group, using the same experimental setup, showed that 43% of the participants with acute whiplash-associated disorder experienced pain during the test protocol.[23] Again, pain reports during the mirror incongruence condition were not described. The mean intensity score of reported sensations was highest during the mirror congruence condition: 4.33 on a numeric rating scale. There were no significant differences in intensity or frequency of sensations between the mirror congruence and whiteboard congruence conditions and between the mirror incongruence and whiteboard incongruence conditions. However, there were significant differences between the test and control conditions. The pattern of sensations between the acute and chronic whiplash-associated disorder groups was not significantly different. However, the pattern of sensations was significantly different between both whiplash-associated disorder groups (acute and chronic) and the healthy controls.[23]

In the study of Roussel et al., 56% of the dancers with musculoskeletal pain experienced sensations during the mirror incongruence condition. The mean intensity score of reported sensations was highest for the mirror incongruence condition: 1.61 on a numeric rating scale. For the two groups combined (dancers with and without musculoskeletal complaints), there were no significant differences in intensity of reported sensations between the mirror incongruence condition and the whiteboard incongruence condition. However, the frequency of reported sensations was significantly higher during the mirror incongruence condition compared to the whiteboard incongruence condition. Additionally, there were no significant differences in perceived sensations between dancers suffering from musculoskeletal complaints and pain-free dancers.[26]

Healthy Individuals. McCabe et al. have demonstrated that during the mirror incongruence condition, which represents experimental SMI, 15% of the 41 healthy individuals reported pain, compared to 2% in the control conditions and 12% during the mirror congruence condition. A total of 59% of the healthy individuals reported all sorts of sensations, such as pain, discomfort, changes in temperature, changes in the perception of limb weight, perceived additional or lost limbs, and disorientation, during the mirror incongruence condition. As the nature of the study was primarily

qualitative, statistical analyses of pain intensity reporting were not part of the protocol. However, the researchers did report that the mean intensity of pain during the protocol for all participants was lower than 2 on a verbal numeric rating scale.[22] In another study of the same research group in which participants with fibromyalgia and healthy controls were investigated, 10% of the healthy controls reported pain during the mirror incongruence condition compared to 3% in the control conditions and 14% in the mirror congruence condition. A total of 45% of the healthy controls reported sensations and/or pain during the mirror incongruence condition. Again, statistical analyses of pain intensity reporting were not part of the protocol, although the mean intensity of pain for all participants was lower than 2 on a verbal numeric rating scale.[17]

The healthy controls in the study of Daenen et al.[23] experienced no pain in response to experimental SMI, but 55% reported sensations different from pain, such as discomfort, a feeling of peculiarity, changes in the perception of limb weight, a perceived loss of an arm or an additional arm, or temperature changes. The mean intensity of the reported sensations was significantly higher during the mirror incongruence condition compared to the whiteboard incongruence and incongruence control conditions. The mean intensity of sensations during the mirror incongruence condition was 1.61 on a numeric rating scale. There was a significant difference in intensity of sensations between the mirror incongruence condition and the whiteboard incongruence condition.[24] The study by Foell et al. demonstrated that 1.8% of the 113 healthy individuals reported pain in the mirror incongruence condition of the arm, and 0.9% reported pain in the mirror incongruence condition of the hand. Pain intensity scores were lower than 0.5 on a numeric rating scale for all conditions. There were no significant differences in pain intensity and pain frequency reports between conditions. The sensation of having an additional limb was the only item with a significant change in intensity and was significantly higher in the mirror incongruence condition compared to the mirror congruence condition and both control conditions.[28]

The study of Roussel et al. used the same protocol as Daenen et al.[23,24]. They report that none of the 44 dancers, of which 18 (41%) suffered from musculoskeletal complaints, experienced pain during the test protocol. In the group of dancers without musculoskeletal pain, 50% experienced sensations during the mirror incongruence condition. The mean intensity score was highest during the mirror incongruence condition: 1.88 on a numeric rating scale. Intensity measures between the mirror congruence and whiteboard congruence conditions and between the mirror incongruence and whiteboard incongruence conditions were not significantly different.[26] The study by Wand et al. included 35 healthy individuals. This study investigated the effect of experimental SMI on pain intensity and pressure pain thresholds, to test whether experimental SMI influenced the pain system in these healthy individuals. Results showed that experimental SMI did not have a significant effect on pain intensity and pressure pain thresholds, as there were no differences between conditions on either outcome. The mean pain intensity score during the mirror incongruence condition was 1.5 on a numeric rating scale. Notably, the mean intensity scores between the test and control conditions were nearly identical (maximum difference of 0.3).[27]

The available evidence (level B) shows that intensity and frequency reports of sensory disturbances are not increased due to the effect of experimental SMI in people with chronic musculoskeletal pain. There are no significant differences between test conditions of the bimanual experiment, although there is a difference in reports of sensory disturbances between the baseline and test conditions. This indicates that patients with chronic pain report more pain and sensations due to visual manipulation. Furthermore, the available evidence (level B) suggests that experimental SMI rarely triggers pain in healthy individuals, and if pain is reported, intensity ratings are very low. The majority of studies found no significant difference in pain reports between the mirror incongruence condition and other test conditions, although sensory disturbances during the mirror incongruence condition were reported most frequently. It is important to note that differences across studies on pain outcomes were equivocal and hard to interpret due to methodological issues (ie, different outcome measures and lack of full description of the methods).

DISCUSSION

The purpose of this study was to systematically review the studies on experimental SMI in people with musculoskeletal pain and healthy individuals, to examine whether experimental SMI triggers or changes pain in these populations.

Sensorimotor Incongruence and Pain

Importantly, and contradictory to the healthy individual population, participants with whiplash-associated disorder and fibromyalgia were more susceptible to experiencing sensory disturbances and pain during the experimental protocol; however, no differences were shown between the experimental conditions of the bimanual experiment.[23–26] This implies that people with chronic pain are more susceptible to experiencing sensory disturbances and pain due to visual or experimental manipulations. However, the fact that sensory disturbances and pain were not different across test conditions in people with chronic pain suggests uncertainty about whether SMI triggers or changes pain in these populations. Therefore, the cortical model of pathological pain implying SMI to be linked to the development of chronic pain cannot be supported, based on the results of this systematic review.

A recent and novel study of Harvie et al.[30] investigated the effect of incongruent visual information of the environment during neck movement, applied via virtual reality, on movement-evoked pain in patients with neck pain. They demonstrated that reported pain can change due to the effect of visual feedback; when neck rotation was overstated, proprioceptive sensitivity was enhanced and pain was reported sooner. Interestingly, pain reports decreased, meaning that the pain-free range of motion was larger, when neck rotation was understated. These results support the idea that visual feedback is able to change pain thresholds. However, these results do not support the fact that incongruent visual feedback merely increases pain reports. It is important to note that the difference between the real and virtual range of motion was judged as equal by participants in the experimental setup of Harvie et al. This differs from the larger and obvious mismatch due to experimental SMI of the bimanual experiment. Daenen et al.[24] suggested that high reports of sensations due to modulation of visual feedback indicates that participants with whiplash-associated disorder have a lowered threshold for visually mediated changes. In participants with whiplash-associated disorders and fibromyalgia, there is substantial evidence for altered central pain processing.[31–33] These maladaptive alterations of the central nervous system might contribute to a lowered threshold to visually mediated changes. This can be of great importance, taking into account the development of therapeutic strategies (eg, mirror therapy) that target these underlying mechanisms using visual feedback.

In healthy individuals, the results showed that a sensorimotor conflict triggered no pain in the majority of the participants, although sensory disturbances during the mirror incongruence condition were reported most frequently. This is supported by a study investigating sensory incongruence via illusion of movement. Moseley et al.[34] reported that sensory incongruence did not trigger pain in healthy individuals, although it triggered all sorts of sensations, for example, feelings of peculiarity, foreignness, changes in the perception of limb weight, and swelling. It has been stated that sensory disturbances that occur during experimental SMI are processed by the central nervous system to warn for the abnormalities.[21,22] The authors speculate that if the threat persists and exceeds the individual threshold, pain will occur. As a majority of the healthy individuals experienced sensations during the bimanual experiment, it might be possible that the sensory input during experimental SMI is perceived by the brain as strange or unusual (leading to strange sensations), but it is not threatening enough to trigger pain. This is consistent with the idea that only exafferent input (afferent signals generated by stimuli of an external origin) reaches the level of consciousness, in which case the mismatch between motor output and sensory input can provoke proprioceptive sensations.[35] The increased activity of the right dorsolateral prefrontal cortex during experimental SMI shown by Fink and colleagues also adds to these notions.[29] These findings were recently supported by Nishigami et al.[36], who found increased cortical activity in the posterior parietal cortex during the mirror incongruence condition. Interestingly, this study demonstrated that significantly more brain activity is present in the posterior parietal cortex and anterior cingulate cortex in the group of healthy individuals who perceived more discomfort.[36] This suggests that there may exist subgroups of individuals on the basis of vulnerability to experience discomfort related to a conflict in sensorimotor information processing. However, these differences in brain activity might also reflect the perceived feelings of discomfort or increased resources trying to realign the conflicting afferent feedback.[37–39]

It has been hypothesized that SMI results from cortical reorganization.[16] The proposed link between disturbances in representation and sensory processing supports this notion.[21,40,41] It might be possible that in case of cortical reorganization, the warning signal of incongruence is false and therefore might be responsible for the lasting symptoms and pain experiences.[14,16,22] There is evidence for cortical reorganization in people

with chronic musculoskeletal pain.[9,15,42,43] Perhaps reorganization in the body matrix, an elegant model proposed by Moseley et al.[39], might be related to SMI. This could explain sensations like a third hand reported in the study of Foell et al.[28] This model imposes disruptions of body representations in a spatial manner, related to the space around the body, as well as a somatotopic manner.[39] A possible reorganization within the body matrix might explain clinical features such as tactile dysfunctions,[40,41,44] temperature dysfunctions,[45] and dysfunctions in the sense of body ownership,[46] which were frequently reported during the bimanual experiments. Despite the accumulating evidence for the presence of maladaptive plastic changes, and the fact that a relation between these alterations and sensory deficits seems plausible, the causal relation, and whether or not these plastic changes are related to SMI, in people with chronic musculoskeletal pain remains unclear.

Analgesic Effects of Visual Feedback

Conclusions from intervention studies targeting pain reduction and restoring motor function may support the hypothesis of SMI being related to pain.[47] In mirror visual feedback experiments, participants perform congruent exercises while looking at the reflection of their unaffected limb. Previous studies have reported positive results of mirror visual feedback in participants with chronic limb pain[47–52]; however, results vary among patient groups, and the underlying mechanisms behind the effect of mirror therapy remain unclear.[53] It is proposed by McCabe and colleagues that no effect of mirror therapy on restoring sensorimotor function might be explained by "the chronicity of their disease and other peripheral drivers of pain" in people with chronic regional pain syndrome.[54] Perhaps SMI is not a main driver of pain in those particular subgroups. Another possibility is that the effect of visual feedback of the body is a result of central inhibitory mechanisms due to enhanced connectivity between the visual body network—a bilateral network of posterior regions activated when seeing one's own body vs. a neutral object—and the pain matrix.[55] Perhaps this mechanism of enhanced connectivity between the visual body network and the pain matrix is impaired in subgroups of people with chronic pain. Nevertheless, it still remains plausible that mirror therapy reduces SMI by restoring sensorimotor integration, resulting in pain and symptom relief in a subgroup of people with musculoskeletal pain.

In line with the idea that mirror therapy might be effective in restoring sensorimotor integration for some people with chronic pain, there is preliminary evidence that visual feedback of the body has analgesic effects in people with chronic musculoskeletal pain. In people with chronic low back pain, movement-related pain intensity ratings were lower, and time to ease after movement was shorter, while viewing the lower back in a mirror.[56] This is supported by the analgesic effects of visual feedback in people with chronic musculoskeletal pain and healthy individuals.[57–59] Nevertheless, in line with the results of this systematic review, and contradictory to the results in healthy individuals, in people with chronic regional pain syndrome, visual feedback has a pain- or symptom-enhancing effect.[60–62] In the future, it might be interesting to further explore treatment strategies targeting improvement of sensorimotor integration via visual feedback, together with the different responses to visual feedback in participants with musculoskeletal pain.

Limitations and Recommendations for Further Research

The main limitation of this systematic review was the heterogeneity across studies in patient populations, outcome measures (eg, pain was reported as a continuous or a categorical variable, or pain was part of all sensory disturbances combined and not an outcome measure on its own), and the lack of a full description of methods. Therefore, it is was not feasible to conduct a meta-analysis on the included studies. The methodological quality of the included studies varied. In the majority of the included studies, assessors were not blinded (or this was not described) and allocation of concealment was not reported. Furthermore, other factors such as hypervigilance, somatization, and anxiety were not taken into account and might have contributed to some of the study findings. Therefore, it is not possible to draw firm conclusions on the relation between SMI and pain.

Further research is needed to investigate the cause-and-effect relationship between SMI and pain in participants with chronic musculoskeletal pain. Current studies in people with musculoskeletal pain have investigated the effect of experimental SMI on all sensory disturbances combined, which makes it difficult to draw conclusions on the effect of SMI on pain. Therefore, more robust studies are warranted to investigate the effect of experimental SMI on pain intensity in people with musculoskeletal pain. Furthermore, it might be

interesting to investigate the effect of experimental SMI on other groups of people with musculoskeletal pain (eg, people with low back pain and nontraumatic neck pain). Additionally, it might be interesting to investigate SMI in a more functional and less clinical environment using virtual reality.

CONCLUSIONS

Due to the lack of reporting concealment of allocation and blinding assessors and differences across studies on pain outcomes, it is not possible to draw firm conclusions on the relationship between experimental SMI and pain. Nevertheless, the current results are not in line with the cortical model of pathological pain implying SMI to cause pain. The available evidence suggests that experimental SMI rarely triggers pain in healthy individuals and pain intensity ratings are very low. Reports of sensory disturbances were more frequent, and intensity ratings were higher during all experimental conditions compared to baseline conditions in participants with musculoskeletal pain. As results did not differ across the experimental conditions, it is unlikely that SMI is solely responsible for these higher reports of sensory disturbances including pain. Nonetheless, the results of this study indicate that people with musculoskeletal pain are more susceptible to experiencing sensory disturbances and pain during visual manipulation.

ACKNOWLEDGEMENTS

The authors are especially grateful for the help of Wichor Bramer (information specialist of Erasmus Medical Centre) for designing the literature search and Maarten Venema, Vincent Sluiters, and Marieke Breed for commenting on the article.

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