Illusion-enhanced Virtual Reality Exercise for Neck Pain A Replicated Single Case Series

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A Replicated Single Case Series

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Objectives: Body illusions have shown promise in treating some chronic pain conditions. We hypothesized that neck exercises performed in virtual reality (VR) with visual feedback of rotation amplified would reduce persistent neck pain.

Methods: In a multiple-baseline replicated single case series, 8 blinded individuals with persistent neck pain completed a 4-phase intervention (initial n = 12, 4 dropouts): (1) "baseline"; (2) "VR" during which participants performed rotation exercises in VR with no manipulation of visual feedback; (3) "VR enhanced" during which identical exercises were performed but visual feedback overstated the range of motion being performed; (4) "follow-up." Primary outcomes were twice-daily measures of pain-free range of motion and pain intensity. During the baseline and follow-up phases, measures were taken but no intervention took place.

Results: No differences in primary outcomes were found between VR and baseline, VR enhanced and VR, or VR enhanced and follow-up.

Discussion: Our hypothesis, that neck exercises performed in VR with visual feedback of rotation amplified, would reduce persistent neck pain was not supported. Possible explanations and future directions are discussed.

Key Words: chronic pain, neck pain, persistent pain, virtual reality, illusion, cortical representation, cortical reorganization, brain training, whiplash-associated disorder, exercise therapy

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Many persistent pain states are not associated with demonstrable tissue pathology.[1–3] One way of conceptualizing this apparent disconnect is that the central nervous system's encoding of the body part is consistent with pathology or vulnerability, even though this does not reflect the actual state of the body part.[4,5] As a result, protective responses including perceptual (eg, pain), endocrine (eg, stress), and behavioral (eg, escape/avoidance behaviors) responses may persist despite their redundancy. In this way, persistent pain could be viewed as the result of a mismatch between the actual body state and its neurally encoded representation—which underpins bodily perception. Indeed, several modern explanations of persistent pain are consistent with this idea.[6–8]

If altered neural representations of the body contribute to persistent pain, then approaches targeting these representations may have utility. That perceptual representations of the body can be dynamically altered utilizing body illusions is well established,[9] confirming that divergence between real and perceived bodily state is possible.[6] The flagship example of a bodily illusion is the rubber hand illusion. Here, simultaneous stroking of the *out-of-view* real hand, and the *in-view* rubber hand, induces the illusions that (1) the participant can feel touch arising from the rubber hand, and (2) that the participant's own hand is closer in space to the rubber hand than it really is[9]—a phenomenon known as "proprioceptive drift," which also occurs in a range of situations of multisensory incongruence.[10,11]

That body illusions can alter attitudes,[12] cognitive performance (eg,[13]), body part-specific temperature,[14] and histamine reactivity[15] points to the integrated biopsychosociality of humans, and the potential to leverage illusions for positive gain in a range of domains. The potential role of multisensory illusions in treating pain has been explored in conditions such as osteoarthritis,[16,17] complex regional pain syndrome,[18] neck pain,[19] and neuropathic pain[20–22] (for reviews see Moseley and colleagues[6,8,23–28]). Several investigations show at least a short-term benefit,[16,17,19–22] but others do not.[29] To date, the only systematic review on body illusions to relieve pain concludes that specific illusions such as mirror therapy, resizing illusions, and prosthetic use (which induces the illusory existence of a missing body part) show promise in reducing pain, but more work needs to be done.[26]

Recently, we developed a virtual reality (VR) illusion known as the MOtor Offset Visual Illusion (MoOVi), which tracks the movement of a body segment, and then provides visual feedback that is multiplied by a chosen factor, creating the perception of greater, or lesser, movement than is actually occurring.[19,30,31] This illusory effect has been confirmed by showing that when neck rotation is combined with bogus visual feedback, people report perceived movement that is different from the amount actually performed.[31] That is, if people rotate consistently to 50 degrees in the real world, but receive visual feedback suggesting as little as 25 degrees, or as much 100 degrees, participants experience on average 31 and 65 degrees, respectively—as demonstrated when participants are asked to reproduce the movements.[31] This illusion also modulates the degree of rotation available before pain onset in people who have neck pain[19] demonstrating a link between visual kinaesthetic cues and pain. However, its therapeutic potential beyond the duration of the application is untested.

In theory, the MoOVi illusion might be applied to target pain in a number of ways. For example, recent theories and evidence suggest that non-nociceptive cues associated with painful noxious events may come to contribute to pain (see *The Imprecision Hypothesis*[32]; and related studies[33–41]). This is not surprising, given that pain is clearly dependent on more than nociception and that cues encoding potential threat may be most relevant.[42] In clinical scenarios, movement frequently causes or increases pain, and thus kinaesthetic cues may become cues that contribute to pain. We recently showed that manipulating kinaesthetic feedback during head rotation changes the magnitude of pain-free movement, the direction of change depending on whether feedback understates or overstates the real movement.[19] This finding suggests that pain-associated kinaesthetic cues may be a viable target for treatment. One way to tackle the apparent contribution of pain-associated kinaesthetic cues to pain would be to reduce their association with pain, thus diminishing their threat value. This might be achieved using extinction protocols, where the kinaesthetic cues normally followed by pain are repeatedly experienced without the expected pain.

In this study, we used a replicated single case series design to investigate whether exercises in VR performed with illusory visual feedback beyond normal pain-free limits would be effectively relative to the same exercises without the illusion. We hypothesized that VR-enhanced (VRE) exercise would be more effective than normal exercise for moderate to severe persistent neck pain, as assessed by changes in movement-evoked pain threshold and pain reports.

METHODS

Participants

Willing participants were included if they had experienced neck pain for longer than 3 months and had pain with head rotation. To avoid including participants with mild pain, only individuals reporting $\geq 3/10$ "average pain over the previous week" were included (on a scale of 0 to 10, where 0 = no pain, and 10 = the worst imaginable pain). Participants with either traumatic (including whiplash-associated disorder) and nontraumatic neck pain were eligible. Participants were required to be between the ages of 18 and 70 and were excluded if they had known or suspected spinal pathology (eg, metastatic disease of the spine); confirmed fracture or dislocation at time of injury (whiplash grade IV); traumatic brain injury; insufficient English fluency for informed consent; intellectual or mental impairment; pregnancy; pain severely exacerbated by movement; epilepsy; or neurological deficit. Ethics was approved by the institutional ethics board (Ethics Protocol Number: GU Ref No: 2016/378) and the trial was registered a priori with the Australian and New Zealand Clinical Trial Registry (ACTRN12617000107325).

Equipment and Software

To facilitate the home-based neck exercises, we used portable head-mounted displays (HMDs) designed for immersive VR (Samsung Galaxy Gear + Samsung Galaxy S8 mobile; Samsung, Seoul, Korea). The Samsung Gear VR system was designed to deliver VR with a 101-degree field of view, with a sub 20 ms motion-to-photon (visual feedback) latency, on a Quad High Definition (QHD) display (1,480×1,440 pixels per eye) updated at 60 frames-per-second (https://en.wikipedia.org/wiki/Samsung_Gear_VR). The HMDs were preloaded with custom-built applications (Wearable Computer Lab, University of South Australia, Adelaide, Australia). These applications were designed to measure and store a range of motion outcome data and guide the neck exercises. Each HMD was preloaded with 3 applications. The first application facilitated the range of motion measures during the baseline and follow-up phases; the second and third facilitated the measures and the range of motion exercises during the VR and VRE exercise phase.

Experimental Design

We used a multiple-baseline replicated single case series design. There were 4 phases: (1) baseline, where outcome data were collected but no exercises performed; (2) VR exercise phase, where outcome data were collected and VR neck exercises performed but with no illusion; (3) VRE exercise phase, where outcome data were collected and the identical VR exercises performed with the illusion applied; and (4) follow-up phase, where outcome data were collected but no exercises performed. The order of phases was consistently applied. The phase length was jittered because statistical power of multiple-baseline replicated case series designs depends on randomization of phase start points/durations, and the number of points available for randomization,[43] so the length of each phase was jittered for each participant within a set range (Fig. 1). In multiple-baseline design, phases can vary in length, on the basis of the expected duration needed to see a change.[44] The duration of the 2 exercise phases was systematically different because the mechanisms of interest in each phase were faster-acting placebo (VR phase) and neuroplastic adaptations requiring sustained repetition (VRE phase). The duration parameters were: baseline phase (jittered between 5 and 14 d), VR exercise phase (jittered between 5 and 14 d), VRE exercise phase (jittered between 21 and 28 d), and follow-up phase (jittered between 5 and 14 d). As participants engaged with VR twice per day, time (morning vs. afternoon) was also randomized. These phase durations/start points were determined a priori and randomly allocated among participants.

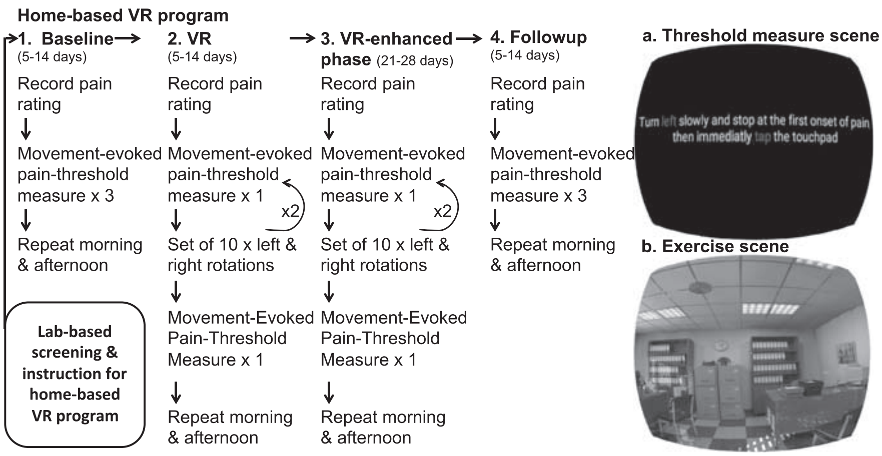

FIGURE 1. Outlines the procedure within the 4 experimental phases. The right of the figure shows the scene used for the pain threshold and calibration measurement (top) and the rotation exercises (bottom).

VRE Exercise

For the VRE exercise phase, left and right head rotation exercises were performed in VR while a progressive visual illusion was applied, giving the appearance of increasing range of motion across each of the 2 sets of 10 (left and right) rotations. Participants performed the 2 sets of 10 rotation exercises twice per day, each session taking ~10 minutes inclusive of measures. To restrict exercises within pain-free limits, the exercise range of motion was individually calibrated at the beginning of each session. This calibration was updated between sets to account for within-session changes. The gain—factor by which real-world movement was multiplied in the world—was individually calibrated according to each participant's range of pain-free movement, such that those with more limited movement would receive more amplified visual feedback, ensuring all participants would receive an illusion of movement substantially beyond their normal limits. Example data are included in Table 1, and the process for determining the magnitude of visual amplification is detailed in Supplementary File 1 (Supplemental Digital Content 1, http://links.lww.com/CJP/A600). Gain values were applied to the axis of movement only, aiding to stabilize the visual field and limit motion sickness. After initial calibration, the user entered a virtual room and was instructed to follow a small circle that guided rotation left and right. The gain was applied in even increments over the 10 repetitions, to reach the maximum gain value by repetition 10.

VR Exercise

For the VR exercise phase, the range of motion calibration and head rotation exercises were performed in precisely the same way as for the intervention phase, including the number of repetitions, however, visual feedback matched the real-world movement. As this in no way challenged the boundaries of participant's normal movement, it was considered a relatively inert control intervention.

Procedure

Participants attended their initial assessment and instruction at Recover Injury Research Centre, Queensland, Australia, with all further measurements and exercises being carried out by participants in their own home using the HMD and a treatment diary. During the initial session, participants provided informed consent and basic clinical information, including pain intensity, duration, and etiology/precipitating event, and completed the Neck Disability Index,[45] Depression Anxiety and Stress Scale (DASS),[46] and Tampa Scale for Kinesiophobia (TSK)[47] for descriptive purposes. Participants were told that we were investigating a new method of exercising in VR that was intended to target the brain's contribution to persistent pain. This was backed up by a short conversation about how when pain persists, an increase in sensitivity in the nervous system may be part of the problem. The example of mirror therapy for phantom limb pain was given as a tangible example of such a treatment. Patients were blinded to the difference between the VR and VRE intervention applications and were not told about the illusion. Following the above, participants were taught how to operate the HMD and to monitor symptoms and promote participation[48] were given a paper-based treatment and symptom diary. The treatment diary was arranged according to date, with space for twice-daily pain

TABLE 1. Example Data, Showing the Relationship Between Movement-evoked Pain Threshold, and the Corresponding Real-World and Virtually Simulated Movement Calibrated for the Exercise Phases

Pain Threshold	Real Motion (All Phases)	Virtual Motion (VR Phase)	Max Gain Value (VR-enhanced Phase)	Virtual Motion (VR-enhanced Phase)
30	28.5	28.5	1.8	51.7
45	42.8	42.8	1.7	71.5
60	57.0	57.0	1.5	87.2
75	71.3	71.3	1.4	98.9

For detailed calculations and explanation see Supplementary File 1 (Supplemental Digital Content 1, http://links.lww.com/CJP/A600).
VR indicates virtual reality.

ratings. At the top of each page, a 0-10 numerical rating scale was displayed, with the anchors *no pain* and *worst possible pain* and the central marker *moderate pain* (diary structure is presented in Supplementary File 2, Supplemental Digital Content 2, http://links.lww.com/CJP/A601). Participants were asked to "select one number that best describes your pain before using VR" and "select one number that best describes your pain after using VR." Space was provided for ratings at both morning and afternoon sessions. The diary also indicated which of the VR applications were to be used in concert with the experimental phases. The applications were labeled 1, 2, 3, and 4, so as to not imply their content.

At the beginning of each home session, participants recorded their pain intensity and opened the application appropriate to the phase. They then applied the VR headset while sitting in a supportive chair to limit thoracic rotation. Participants followed the on-screen instructions for calibration to: "turn to the left (then right) and stop at the very first onset of pain, then immediately tap the touch pad." During the baseline and follow-up phases, this was repeated 3 times, followed by the message "your session is complete." In the exercise phases, an initial measurement of range of motion was followed by the 2 sets of 10 rotations, each set was preceded and followed by the threshold measurement, and finally, a message stating "your session is complete." The pain threshold measures were performed against a black background, whereas the participants performed the exercise in an office scene (Fig. 1). A room scene was chosen because such scenes offer clear and familiar spatial cues that were thought to support the illusion.

Outcomes

The primary outcomes were movement-evoked pain threshold (total range of motion to pain threshold in degrees) and self-reported pain intensity. The 3 threshold measures from each session were combined only after confirming no systematic differences. Pain ratings from the beginning of the session were used because we were interested in cumulative/sustained analgesia, rather than immediate effects. Outcomes were assessed twice daily throughout the study. Measures were enabled by the motion sensors onboard the Samsung Gear VR headset and Galaxy smartphone. At each session, 3 measures were taken for the left and right rotations. Each rotation pain threshold was recorded automatically in a digital log on the mobile phone hard drive, along with a time and date stamp. We have previously shown highly precise axial measures using data from HMDs.[30,35]

Statistical Data Analysis

The data were analyzed with a randomization test specifically designed for randomized multiple-baseline designs.[43] This approach was used to improve confidence in our ability to attribute the effects to the intervention, relative to other case series designs.[43] The multiple-baseline design chosen involved regular assessments throughout experimental phases. This enabled the stability and trajectory of symptoms across time to be better accounted for statistically, and therefore the intervention effects to be better isolated.

A target sample size of 12 was determined using a priori sample size calculation. The sample size was required to achieve power at least 80% using a 5% significance level and was calculated through a simulation study approach. For an estimate of the expected treatment effect, we used the effect size estimate of 1.06 reported for a graded motor imagery treatment.[49] In the simulation study, we generated the data patterns of individual cases using a first-order autoregressive (AR1) model with a positive autocorrelation of 0.3. The use of this model seemed feasible as it has been shown that this level of autocorrelation is usually present in data from multiple-baseline designs.[50]

Our analyses followed recommendations for multiple-baseline designs.[43] The initial analysis involved visual inspection of the consistency of intervention effects among participants. The randomization test analysis was conducted using the SCRT-R package from the statistical analysis suit R. Randomization tests are free from the assumptions of random sampling and are free from distribution and variance assumptions. Further, serial dependence and trends over time do not invalidate results.[43] In a randomization test, some aspects of the experimental design need to be randomized. This is generally the timing of the introduction of each phase or intervention. The randomization test is then on the basis of permutations that mirror the random assignment used in the experiment.[43] The null hypothesis, that there is no effect of the intervention, is then tested by locating the observed value of the test statistic in the randomization distribution. The randomization test's P-value is equal to the proportion of test statistics that exceed or equal the observed test statistic.[43] The null hypothesis is rejected when this value is ≤ 0.05. Notably, the order of the phases must be constant, as the randomization cannot be applied to the treatment order.

RESULTS

Twelve participants met eligibility criteria for inclusion and underwent training for participation. Participants had moderate pain (3-6.5/10), and had no (0% to 8%, n = 1), mild (10% to 28%, n = 5), moderate (30% to 48%, n = 5), or severe (50% to 68%, n = 1) disability, as assessed by the Neck Disability Index (NDI).[45] Patients reported either no or mild depression, anxiety, and stress, as measured by the DASS (mean(SD) = 4.5(3.7), 4.1(3.1), and 7.4(4.7), respectively).[46] Participants generally showed low levels of fear of movement, according to the TSK (mean(SD) = 39.3(4.2)),[51] with the exception of participants 1, 9, and 10, who scored over 42 classifying them as having high levels of kinesiophobia.[52]

Two participants withdrew because of unrelated illness (participant 9) and personal events (participant 12, Table 2), 1 participant used the applications in the wrong order (participant 10, Table 2), as detailed by the VR headsets automated log, and 1 participant withdrew because of motion sickness in the initial exercise phase (participant 11, Table 2). Another participant withdrew because of motion sickness that coincided with the onset of the intervention phase, however, data to that point were still included in the analysis (participant 5, Fig. 2). Thus, 8 participants correctly completed at least 3 phases of the experiment (participants 1 to 8, Table 2).

Manipulation and Data Checks

Across all sessions and participants, virtually all calibrated ranges of motion were between 30 and 85 degrees. As a result, the intervention phase visual feedback overstated true movement by a maximum of 30% to 80%. Measures that were under 10 degrees were assumed the result of the erroneous triggering of the sensitive touch panel and were immediately deleted. Before combining the 3 rotation measures taken at each time point, we performed an analysis of covariance to confirm stability across the 3 trials, and determine if the

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TABLE 2. Descriptive Data on the 8 Included Participants

	Initial Trauma	Pain NRS	Pain Months	Age	Sex	Pre-NDI	Post-NDI	TSK	DASS D	DASS A	DASS S
1	Chiropractic	4.0	24	60	M	24%	14%	47	0	0	1
2	MVA	4.0	384	47	F	20%	18%	37	4	3	6
3	Fall on head	5.5	18	41	F	40%	16%	37	10	2	11
4	Fall on head	4.0	36	60	M	22%	6%	34	3	2	9
5	MVA	3.0	240	70	F	26%	20%	35	0	3	3
6	MVA	3.5	36	26	M	34%	18%	40	7	9	8
7	Sports injury	4.0	276	69	M	6%	12%	37	0	1	0
8	MVA	5.0	300	69	M	24%	14%	39	6	9	12
9	MVA	5	132	52	M	54%	NA	42	7	8	12
10	MVA	3	360	62	M	48%	40%	47	6	5	13
11	MVA	6.5	5	45	F	38%	NA	37	10	2	11
12	MVA	5	204	67	M	42%	NA	40	1	5	3

Participants below the line were not used in the analysis.
DASS indicates Depression Anxiety Stress Scale; F, female; M, male; MVA, motor vehicle accident; NA, not applicable; NDI, Neck Disability Index; NRS, numerical rating scale; TSK, Tampa Scale of Kinesiophobia.

consistency of the measure varied according to phase. Results confirmed no overall difference between the 3 threshold measures within each session, $F_{(2,\ 1054)}=0.98$, $P=0.4$, and no interaction with phase, $F_{(2,\ 1054)}=0.48$, $P=0.6$. Inclusive of erroneous data, and data absent because of participant non-completion, there was a total of 16% missing data among the 8 participants included in the analysis. As such 688 data points remained for analysis.

Pain Outcomes

No significant between-phase differences were found for movement-evoked pain threshold, or pain intensity (all $P\text{s}>0.05$). Descriptive data confirmed no meaningful change in pain-free range during the VR exercise phase relative to the baseline phase (−0.1 degrees), during the VRE phase relative to the VR exercise phase (−2.4 degrees), or in the follow-up phase relative to the VRE phase (+2.8 degrees). Phase comparisons for each participant are shown in Table 3 and Figure 2. Observation of each individual's data suggested that there was some variability between participants with respect to symptom responses within the study phases, but there was no support for the existence of a subgroup of responders.

DISCUSSION

We aimed to determine whether neck exercises performed in VR with visual feedback of rotation amplified, would reduce persistent neck pain. We hypothesized that the exercises with enhanced visual feedback would have a greater effect on pain-free movement and self-reported pain intensity than VR exercises without the illusion. Contrary to our hypothesis, there were no significant differences across the experimental phases. That is, VRE rotation exercises did not result in improvement relative to VR exercises. These data suggest that moderate persistent neck pain is not responsive to an illusory intervention on the basis of overstated movement or that the intervention configuration was otherwise flawed.

Implications for Illusory Movement as Therapy

To date, persistent pain treatments targeting suspected tissue pathology have shown limited ongoing benefits.[53,54] The quest for better treatments is marked by a shift towards targeting central mechanisms.[23,24] Although cognitive and behavioral approaches targeting beliefs, emotions, and behaviors might also be considered brain-based, the current approach represents a fundamentally different approach. This approach tested in this study, assumed that pain can become a learned response, an idea detailed by the Imprecision Hypothesis of chronic pain.[32] Using a Pavlovian/classic conditioning model, the Imprecision Hypothesis suggests that kinaesthetic (and other) cues associated with noxious events, by virtue of contingent pairing, can come to independently elicit responses native to noxious events, including pain and that imprecise encoding of the non-nociceptive aspects of the event can lead to generalization of the conditioned effect.[32] The current evidence for this theory has been reviewed[34] and although associative learning seems able to modulate pain[35,40] and pain thresholds,[33,34] a painful conditioned response has not been evidenced by laboratory experiments.[55]

The approach to addressing learned pain responses in this study, was designed according to the principles of extinction learning[56]—the process whereby a decrease in learned responses ensues when a stimulus, in this case, visual feedback of a "large movement," is presented without the expected outcome, in this case, pain. Experiences that violate expectations are known to be powerful drivers of learning,[57] and alter (prior) expectancies thought to drive perception.[58] When a certain cue is expected to follow another but does not, there is a discrepancy between predicted and actual outcomes. This discrepancy can be thought of as a prediction error and is related to cortical responses linked to novelty detection, attention, reward, and learning.[59] With the VRE exercise, it was thought that the visual signals of movement beyond a range that would normally evoke pain would result in prediction error and extinction of the movement-pain association.

Although the null result may reflect incorrect theoretical assumptions, it is important to consider alternate explanations. Indeed, it is possible that it is the intervention configuration, rather than the underpinning assumptions, that is flawed. For example, possible adjustments include the implementation of a virtual avatar and virtual mirrors, which might enhance the illusion by providing an intrinsic bodily reference and additional overstated external cues. Moreover, techniques such as change blindness might be

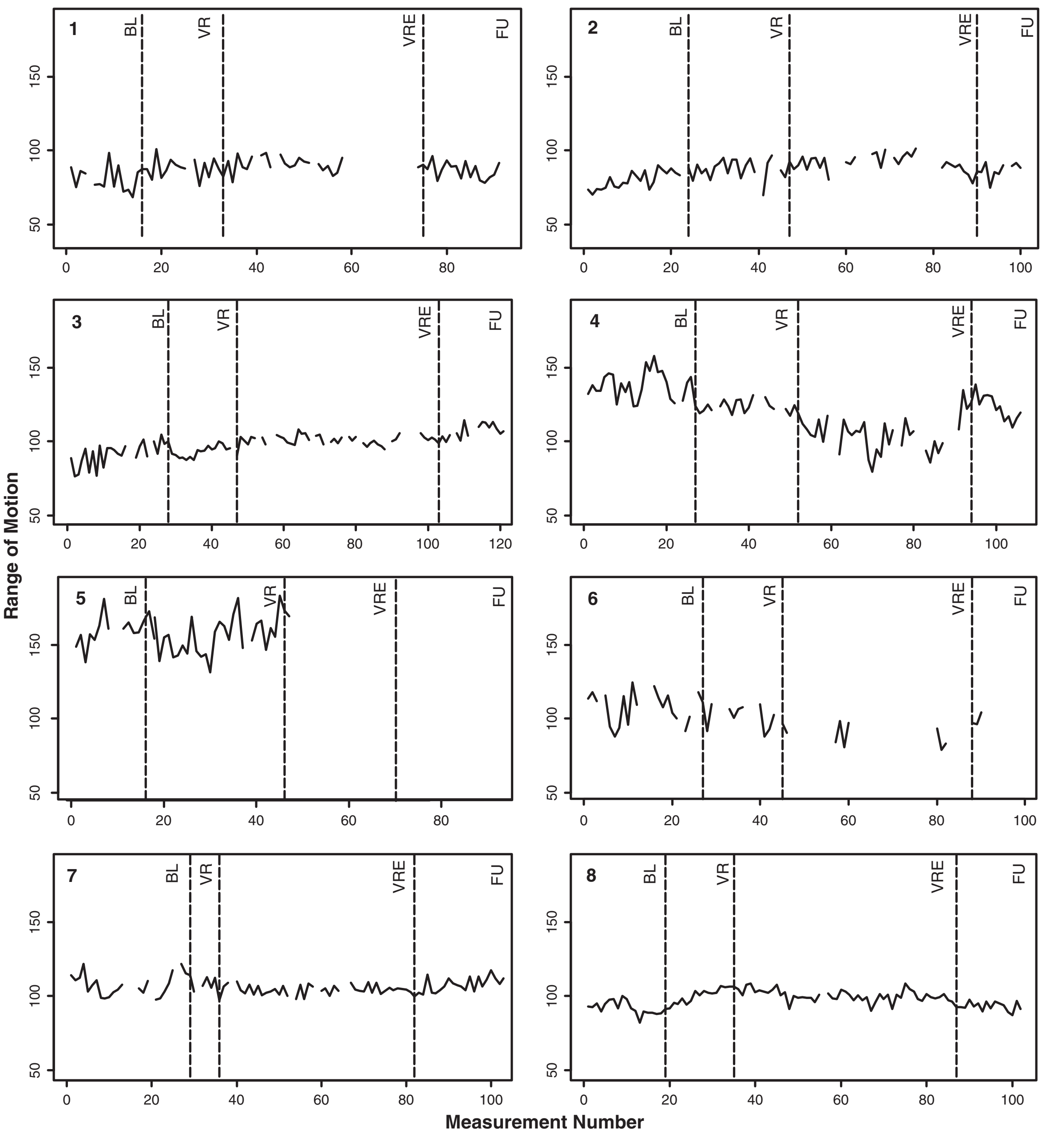

FIGURE 2. The movement-evoked pain threshold data across the 4 study phases for participants 1 to 8. Phase keys: BL, FU, VR, and VRE. BL indicates baseline; FU, follow-up; VR, virtual reality; VRE, VR enhanced.

used to enhance the illusion.[60] Adjustments to the dosage of illusory movement can also be made. In the current study, the illusion was applied progressively over the 10 repetitions of each set, the number of repetitions where real-world movement was sufficiently overstated may have fallen short of an unknown therapeutic dose threshold. Also of note, within the Graded Motor Imagery paradigm,[61] some authors suggest that mirror therapy-type interventions should be preceded by implicit motor imagery strategies, such as left/right judgments and imagined movements, with the results of 1 trial suggesting the order of interventions is important.[62] Thus, future studies might investigate VRE exercise after a period of implicit motor imagery.

Another approach worth considering is one where the kinaesthetic feedback is understated, rather than overstated. Indeed, we have previously shown a real-time improvement in movement-evoked pain while using VR programmed to understate visual feedback.[19] If used repeatedly, it is possible that during VR improvement in movement will translate to post-VR improvement, however, this remains to be validated. This would represent a theoretically different approach, in that understated visual feedback would facilitate physical exercise through an extended real-world pain-free range of motion, rather than the extended perceived pain-free range of motion facilitated by overstated visual feedback. The understated approach can be conceptualized

TABLE 3. Individual Participant and Overall Results for Change in Pain-free Movement and Pain Intensity

Phase	P1	P2	P3	P4	P5	P6	P7	P8	Av.
Change in pain-free movement (deg.)									
VR (VR—baseline)	8	5	2	−15	2	−6	−5	8	0
VR enhanced (VRE—VR)	4	5	7	−18	NA	−10	−4	0	−2
Follow-up (follow-up—VRE)	−4	−4	6	17	NA	9	3	−8	3
Change in pain intensity (0-10 NRS)									
VR (VR—baseline)	−1	−1	0	0	0	0	0	0	0
VR enhanced (VRE—VR)	0	0	0	0	0	0	0	0	0
Follow-up (follow-up—VRE)	0	0	−1	−1	NA	−1	0	0	0

NA indicates not applicable; NRS, numerical rating scale; VR, virtual reality; VRE, virtual reality enhanced.

within a broader danger-safety framework, whereby credible cues of danger to body tissue increase pain and credible cues of safety decrease it.[63,64] According to this line of thinking, during a usually painful magnitude of movement, understated visual feedback might provide a strong safety cue, which is sufficient to turn a painful movement into a pain-free one. In this way, the conditioned stimulus—the movement of a painful range—is not coupled with a conditioned response that is pain.

Sensory-Motor (SM) Incongruence

It has been proposed that disrupted sensory information after injury that leads to incongruence between movement intentions and subsequent sensory feedback might cause pain.[27] This SM incongruence theory has been experimentally tested in both healthy participants and patients, but has not been validated (see Don et al for review[65]). So far, however, studies have only exposed participants to a single session of incongruent visual kinaesthetic feedback, whereas repeated or sustained incongruence might be required for an effect. The current study exposed participants to repeated SM incongruence over time. If the SM incongruence hypothesis holds, then one might expect that participants would get worse during the VRE exercise phase (the incongruent visual feedback condition), relative to the VR exercise condition (the congruent visual feedback condition). Although an overall 2-degree reduction in the pain-free movement was noted during the incongruent phase, this was neither significant nor meaningful, thus providing no support for that theory. Further evidence against the SM incongruence hypothesis comes from the observation of the within-session movement-evoked pain threshold data. Here, if the SM incongruence theory would hold, we would expect a relative increase in sensitivity across each exposure in the VRE exercise phase. Instead, there was no significant difference across the 3 threshold measures within any of the 3 phases.

Between-participant Variation

The quantity of assessments over time enables some capacity to observe trends within and between participants. When factoring in the trend towards improvement or worsening in the preceding phase, there was little indication that a subgroup of patients may benefit from the regime. Further, the magnitude of any trend was insignificant. For example, the randomization test shows that participant #3 had a 7-degree improvement in the VRE exercise phase relative to the VR phase. As this is the total range of motion, this represents an average of +3.5-degree rotation to the left and right, which would have little functional relevance. Only participant #4 seemed to show meaningful variation across the phases. This participant appeared to show worsening movement across both exercise phases, and resolution in the follow-up phase. Notwithstanding the possibility that the interventions may have negatively impacted pain thresholds, it is notable that this person reported training for a marathon during the intervention period, which may have influenced symptoms by virtue of the associated physical and physiological stress. Notably, the changing movement-evoked pain thresholds of participant #4 were not paralleled by changes in pain reports. Interestingly, while there was no apparent overall improvement in movement, 7 of 8 participants for whom data were analyzed, finished with less disability, with the average NDI improvement meeting the 10% criterion for minimal important, and minimal detectable change (mean(SD) = 10 (9)%).[66,67] Although the methodology precludes the ability to interpret this as an effect of the intervention, these data at least support the safety of protocol.

Limitations

The current study was powered *a priori* to detect an improvement similar to that shown for graded motor imagery.[49] That 4 participants withdrew meant that the study was underpowered to observe the expected effect. However, on the basis of the collected data we greatly overestimated the effect, which seems to be virtually zero, and therefore additional participants could not plausibly change the result—at least without changing the intervention or population. Therefore, we are confident in accepting the null hypothesis. This position is further supported in that none of the 8 participants showed an effect in the expected direction.

Although the intervention as it stands did not show an effect in the specific population tested, it is possible that other populations may benefit from this intervention or that different applications of similar interventions may be effective. Therefore, it may be premature to close this avenue of research altogether. For example, the included participants had moderate average pain (3 to 5.5/10) and mild-moderate disability. As a result of the lack of representation of people with severe neck pain, we cannot rule out the possibility that the current study failed to match a centrally directed treatment to patients with a more centrally dominant problem. Future studies investigating such brain-based techniques might consider selecting patients on the basis of demonstrable signs of nociplastic contributions to their pain, for example, using the Central Sensitisation Inventory[68] or on the basis of significant changes in movement-evoked threshold when presented with altered visual feedback.[19] Also, we cannot rule out the possibility that the MoOVi has utility in combination with other approaches, such as when preceded by implicit motor imagery, and followed by graded

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activity or exposure, in the same way that mirror therapy is applied as part of Graded Motor Imagery.[47,58] Variations of the treatment or the way it is applied may also justify further interrogation. Notably, we have previously shown a temporary analgesic benefit of understating kinaesthetic feedback.[17] Although the current study used overstated movement, in-line with the study paradigm, a future study might investigate whether repeated exercise in an environment of virtually understated movement could lead to clinical gains.

A further limitation of the current study is that the overstated visual feedback was applied incrementally. This may have had 2 relevant confounding effects: first, it may have reduced the overall dosage of sufficiently amplified visual feedback and Second, sensorimotor adaptation because of altered sensory feedback, which may be enhanced if the feedback is applied gradually,[66] may have reduced the degree to which overstated movement was perceived. This may be important because the treatment was designed to violate the expectation of pain with movement, alter implicit pain expectancies, and thereby alter pain.[54,55]

CONCLUSIONS

Incorporating a visual illusion of increased pain-free neck range of motion does not seem to be effective in improving movement-evoked pain thresholds or general pain intensity ratings in people with moderate neck pain. This is the first attempt at an exercise intervention on the basis of augmented kinaesthetic feedback using a take-home VR device. Although the current approach is not supported, VR provides a highly configurable platform that may facilitate the testing of additional novel approaches.

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