Get Your Head in the Game

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Get Your Head in the Game: A Replicated Single-Case Experimental Design Evaluating the Effect of a Novel Virtual Reality Intervention in People With Chronic Low Back Pain

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Abstract: **Chronic low back pain (CLBP) is a leading cause of disability worldwide. Contemporary treatment of CLBP is suboptimal, with small-moderate effect sizes and high relapse rates. Virtual reality (VR) is an increasingly accessible technology that can improve adherence to exercise programs through gamification. Using VR to facilitate exercise adherence and enjoyment may improve the clinical outcomes. This study aimed to evaluate the effects of a gamified VR graded activity intervention in people with CLBP, using commercially available and bespoke VR programs. A sequentially replicated, multiple-baseline, randomized AB single-case experimental design was undertaken in 10 people with CLBP. Outcomes were assessed daily and included pain intensity (primary) and pain catastrophizing, pain-related fear, and anxiety/worry (secondary). The effect of the intervention on the primary outcome was evaluated using a multilevel-model, nonparametric randomization test. The VR graded activity intervention resulted in a significant reduction in pain intensity (effect estimate = −1.0, standard error = .27, $P < .0011$) with 4 participants achieving ≥30% pain reduction (minimum important change). There was a significant effect of the intervention on pain catastrophizing but not pain-related fear or anxiety/worry measures. These findings provide preliminary support for a VR graded activity program to reduce pain in people with CLBP.**

Perspective: ***This novel, VR graded activity intervention reduced pain intensity and catastrophizing in people with CLBP. The intervention also had high adherence and enjoyment. Given that this intervention involved 2 freely available VR programs, it can be easily translated into clinical practice.***

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Low back pain is a leading cause of disability worldwide.[1,2] While the majority of people recover from an episode of acute low back pain, some go on to develop chronic low back pain (CLBP).[3] Despite increased health spending,[4] current treatment options for CLBP provide only modest improvements in pain and disability.[5]

Clinical guidelines for the treatment of CLBP typically recommend exercise-based graded activity programs.[6] Graded activity is a well-established intervention that aims to restore functional capacity through operant learning principles,[7] by slowly and consistently increasing one's capacity to engage in a previously limited or feared activity (eg, forward bending). Participants first establish their baseline level of tolerance for an activity, then increase their participation in that activity over time in line with preplanned activity increase quotas. Critically, in graded activity programs, participants are encouraged to adhere to the activity plan (avoid deviation), and these interventions are often performed independently, typically as part of a home exercise program. Graded activity programs are proposed to improve pain and disability through a variety of mechanisms, ranging from neuromuscular to psychosocial.[8] There is evidence that these programs are effective in improving pain and disability in people with CLBP; however, as with all treatments for CLBP, the effect size for pain intensity and disability improvements is moderate.[9]

Graded activity interventions require long-term follow-up, are challenging, and require a plan for managing relapses,[10] with long-term adherence often being poor.[11] Therefore, there is potential to improve the effectiveness of graded activity interventions through enhancing engagement and enjoyment and thus, adherence. Given that the long-term outcomes for pain and disability are mixed for graded activity interventions,[9] optimizing these interventions is needed to improve clinical outcomes.

Virtual reality (VR) is an increasingly accessible technology that has been used across a range of pain conditions.[12] A recent systematic review including 24 studies evaluating the effectiveness of various VR interventions, from virtual hippotherapy (horse-riding simulation) to cognitive behavioral therapy, found that VR interventions significantly decreased pain intensity in people with CLBP, supporting the clinical promise of this technology.[13] Immersion in the virtual environment and the use of exergaming (playing a game that requires physical interaction) have been shown to improve motivation and enjoyment during exercise[14] and thus may provide a way to improve engagement (and adherence) in interventions such as graded activity. Additionally, VR interventions can be completed at home,[15] which may improve long-term adherence and protect against relapse, which is often seen after traditional clinic-based interventions. Past work has explored a VR-based "dodgeball" intervention in people with CLBP,[16] consistent with graded activity principles, and found mixed results. The participants underwent three 15-minute sessions of the immersive VR dodgeball game, which aimed to encourage repeated (and increasing) lumbar flexion. The intervention was safe and enjoyable, with high adherence (98% of the participants completed the intervention). While the intervention increased lumbar flexion during game play, this did not carry over post intervention, and VR dodgeball had no effect on other clinical outcomes including pain intensity when compared to a waitlist control group. Given that traditional graded activity programs typically involve more treatment sessions (eg, 8–10, consistent with a theoretical underpinning of the operant conditioning principles),[7,17] the null clinical effects for VR dodgeball seen in this previous randomized control trial may reflect suboptimal intervention dosage.

Here, we aimed to extend the previous work by determining the effect of a highly immersive, "gamified" VR intervention based on graded activity principles in people with CLBP, evaluating the effect on pain intensity using a dosage more reflective of clinical practice (average of 8 sessions). Additionally, we purposefully assigned different intervention dosages to participants to explore any dose-related effect on the clinical outcome. The VR intervention was designed to implicitly encourage forward bending and enhance engagement with activity occurring in the space in front of the body via gameplay objectives (eg, hitting targets or interacting with objects). Forward bending was specifically targeted in this intervention, rather than general activity, because this movement is commonly feared and avoided in people with CLBP.[18,19] For example, people with CLBP who have high levels of fear avoidance experience higher levels of disability than healthy controls, despite similar objective physical activity levels.[20] Such findings suggest that activity levels are preserved and may not be the best interventional target, and that general activity itself may not be sufficient to improve engagement with a feared movement, resulting in sustained disability. We also evaluated the secondary outcomes of pain catastrophizing, pain-related fear, and pain-related anxiety/worry, as well as both enjoyment of the VR intervention and participant adherence.

Methods

Study Design

A sequential, multiple-baseline single-case experimental design (SCED) was undertaken. The SCED had 3 phases: 1) baseline, lasting 5 to 14 days; 2) intervention, lasting 14 to 23 days (6–9 intervention sessions); and 3) posttreatment period, lasting 7 days. Participants were randomized to a baseline phase duration using a random number table. A value in the table was

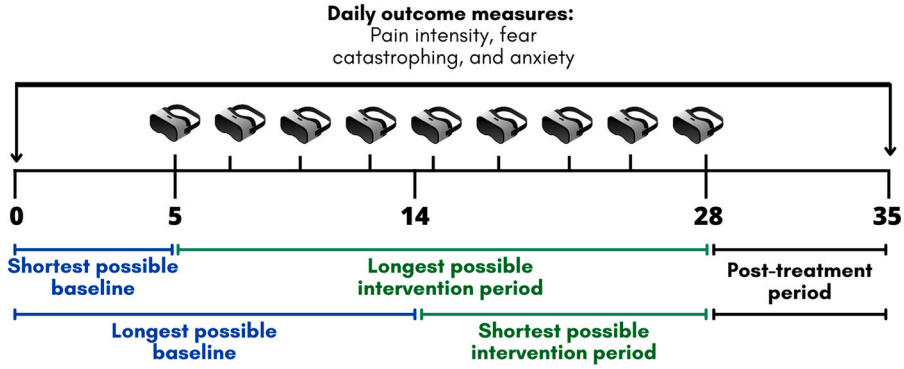

Figure 1. Study timeline and outcome measures.

randomly chosen (pointing with closed eyes), and then the first random number value for which the first 2 digits matched a number within the baseline phase range (total of 10 possibilities given the range of 5–14 days) was considered the baseline duration for participant 1. This process was repeated for each participant. Once a baseline duration was allocated (eg, 7 days), this was no longer an available option such that different baseline durations were used for each participant. Once the baseline duration phase was selected for a participant, their intervention phase was automatically determined in that the combined duration of both phases was 28 days for all participants (Fig 1). This procedure was completed by an investigator not involved in recruitment, data collection, or treatment provision. Phase duration randomization improves the internal validity via reducing the likelihood of maturation bias and regression to the mean influencing the results, and is recommended by the Risk of Bias in N-of-1 Trials Scale (RoBiN-T).[21] Participants completed daily outcome measures throughout the 35-day study assessing pain intensity, pain catastrophizing, pain-related fear, and pain-related anxiety/worry. Pre-post intervention and assessments occurred at day 0 and day 35, evaluating disability, functional capacity, and perceptual measures (Fig 1). A study protocol was created a priori by the research team and is available upon request.

Participants

Participants were recruited from the referral waitlist of the Outpatients Spine Clinic at Haukeland University Hospital in Bergen, Norway, from January to June 2018. Given the limited availability of the treating therapist, recruitment occurred in 3 "recruitment windows" of approximately 1 to 2 weeks duration, whereby people with CLBP on the waitlist at that time were screened for inclusion.

Participants were required to have a low back pain intensity of ≥4/10 on a numerical rating scale (NRS) for the previous 2 weeks, a minimum score of 25 on the Tampa Scale for Kinesiophobia (TSK-11 Norwegian Version, where the maximum score is 52 and ≤23 indicates subclinical levels of kinesiophobia),[22] and normal or corrected to normal vision. The exclusion criteria were ongoing treatment from other clinicians; specific low back pain (LBP) diagnosis (radicular pain, disc herniation, spondylolisthesis, stenosis, modic changes); acute exacerbation of LBP at the time of screening; widespread constant nonspecific pain disorder; active rheumatoid disease; progressive neurological disease; previous surgery involving the lumbar spine; lower limb surgery in the last 6 months; currently pregnant or less than 6 months postpartum; diagnosed psychiatric disorder; self-reported dizziness and/or benign paroxysmal positional vertigo (eg, dizziness associated with loss of balance, nausea, and/or vomiting); serious cardiac or other internal medical conditions; malignant diseases; and contradictions to general exercise. Individuals meeting the eligibility criteria were invited to participate in the trial. Ethical approval was obtained from the University of Bergen and the Regional Ethics Committee of Western Norway (2017/1199/REK vest). All participants provided written informed consent.

Sample Size Considerations

Traditional sample size calculations do not apply to SCED. Instead, statistical power is based on the number of randomizations (eg, potential points at which an intervention can start in a multiple-baseline design), autocorrelation of observations, effect size, and number of replications.[23] In accordance with RoBiN-T[21] and other best-practice SCED guidelines,[24,25] at least 5 reported measures of the primary (pain intensity) and secondary daily outcome measures (pain catastrophizing, pain-related fear, and pain-related anxiety/worry) were collected in each phase. The number of participants recruited for this study was also informed by previous literature, where similar studies (design and intervention) recruited between 6 and 8 participants.[26,27] We therefore aimed to recruit 10 participants.

Intervention

The intervention involved individualized VR exergames, all of which encouraged participants to move into forward bending. The intervention was supervised by a physiotherapist in training (M.S.) who had access to consult with a highly experienced licensed physiotherapist (K.V.F.). An Oculus Rift Head Mounted Display and

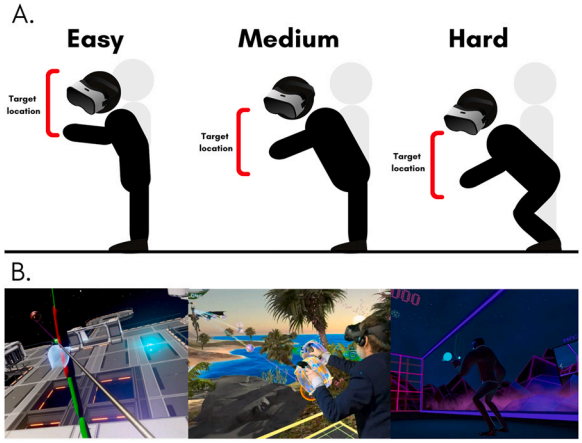

Figure 2. VR intervention games. (**A**) Target location for each level of the VR game. Easy levels provided targets between the head and solar plexus (likely requiring minimal forward bending). Medium levels used provided targets between the shoulder and hip height (likely requiring some forward bending). Hard levels provided targets approximately between the shoulder and mid-thigh height (likely requiring more forward bending and/or knee flexion). (**B**) Screenshots from each VR game; from left to right: RoBow Agent, HoloDance, and Holoball.

hand-held controllers (Oculus VR, Irvine, CA) were used to allow interaction with the exergames, which were provided using SteamVR (Valve Corporation, Bellevue, WA). Three exergames were used in the intervention: HoloBall; HoloDance; and RoBow Agent. HoloBall and HoloDance are commercially developed by Narayana Games (SteamVR), and RoBow Agent was custom designed in Unity (San Francisco, CA) by the research team. During each session, participants played the 3 games each for 10 minutes, with a 2 to 3 minutes break in between games. A minimum of 6 VR sessions and a maximum of 9 VR sessions were completed by the participants (number dependent on randomization of the intervention length). Each session lasted between 30 and 45 minutes and was scheduled to occur approximately 2 to 3 days apart (ie, allowing for weekends) during the intervention phase.

During use of the exergames, participants were encouraged to move as freely as possible through the virtual world. All games had multisensory inputs (vision and sound), high-quality graphics, and head tracking, allowing for a highly immersive experience. All 3 games targeted forward bending, where easy levels required minimal forward bending, and more difficult levels aimed to progressively increase the amount that participants had to move their trunk in order to achieve the objectives of the game (see Fig 2A for location of targets for each level). Gameplay levels were individually tailored to each participant by the treating physiotherapist. Specifically, this was informed by clinical assessment of each participant's active spine movements (forward bending, rotation, extension, side bending), including total range of motion and motion quality (hesitation to move, smoothness of movement, and speed of movement), and with visual observation of facial expressions during movement. This information, particularly forward bending, was used to inform selection and progression of gameplay levels. Further, participant-specific setting of target location levels was undertaken for the bespoke VR game RoBow Agent, with levels adjusted based on participant height and the visually observed forward bending range motion (ie, can set a lower "hard" target location than the other 2 VR games).

In the first session, all participants played the easy level of each game, regardless of clinical assessment findings, to familiarize themselves with the use of the VR system and the different VR games. In subsequent sessions participants played all 3 games for 10 minutes each. The difficulty level was progressed between and within (at the halfway point) sessions, with respect to the participant's reported pain intensity and fear levels. Participant's autonomy and safety were emphasized in the progression through the levels over the course of the intervention; therefore, some of the participants did not reach the most difficult levels of each game. Reenforcement was provided within the VR games via increased points (higher scores), auditory, and written feedback (text such as "well done!") (see Fig 2B for screenshots of each game). The treating physiotherapist observed the participants while engaging with the VR games to monitor safe performance and whether avoidance of forward bending (particularly during more difficult levels) was occurring. If needed, brief feedback regarding lumbar movements was provided to the participants to encourage greater trunk movement (eg, "you are doing great, next time when reaching for some of the lower targets, consider bending a bit less at the knees and a bit more at the back"). A full description of the VR games is contained in Supplementary file 1.

Daily Outcomes

Daily outcomes were collected via a paper diary. Participants were instructed to complete the daily outcome measures at 8 PM every evening, consistent with previous studies.[28] Diaries were returned to the research team at each VR session to minimize the missing data. The primary outcome was daily low back pain intensity (0–10 NRS, where 0 is "no pain" and 10 is "the worst pain"), using a validated Norwegian translation.[29] Secondary daily outcomes consisted of pain-related fear (TSK items 1, 3, and 15), catastrophizing (Pain Catastrophizing Scale [PCS] items 1, 2, and 13), and pain-related anxiety/worry (Pain Anxiety Symptoms Scale [PASS] items 3, 4, 5, and 10). These scale item selections were informed by, and are consistent with, past SCED work evaluating the effect of exposure on pain-related fear, pain catastrophizing, and pain-related anxiety.[28] The TSK items capture activity avoidance (items 1 and 15) and somatic focus (item 3); PCS items capture helplessness (items 1, 2) and rumination (item 13). Both the TSK and the PCS have shown sufficient to good internal consistency in people with chronic musculoskeletal pain (Cronbach alpha of .60 and .72, respectively),[28] suggesting that each scale's items measure one underlying construct (eg, all TSK items capture pain-related fear of

movement). Given this level of internal consistency, a summative score was calculated for the 3 TSK items and the 3 PCS items to create 2 variables representing pain-related fear and catastrophizing, respectively. The PASS items were chosen as they were representative of each of the 4 subscales measured by the PASS (ie, cognitive aspects of threat appraisal [item 3], pain-related fear [item 5], escape/avoidance [item 10], and physiological arousal [item 4]). Pain-related fear and catastrophizing items were obtained from validated Norwegian translations,[30,31] while PASS items were translated by the study team.

Pre-post Intervention Measures

These measures were assessed at baseline (day 0) and at the final follow-up (day 35), and included the following constructs: disability (Oswestry Disability Index)[32]; function (Orebro Musculoskeletal Pain Questionnaire Screening Questionnaire short form [OMPSQ])[33]; and back perception (Fremantle Back Awareness Questionnaire [FreBAQ]).[34] Additionally, implicit motor imagery outcomes of response time and accuracy for identifying the images of back rotation (left versus right) were evaluated using the Neuro Orthopaedic Institute (NOIgroup) Recognise app (https://www.noigroup.com/en/Product/BTRAPP). People with CLBP have previously found to have alternations in implicit motor imagery performance.[35] The accuracy of these judgments is thought to reflect the function of the working body schema (eg, cortical proprioceptive representation) and response time is thought to reflect the allocation of attentional resources.[36,37] Overall, these additional measures were chosen as they provide information about clinically relevant outcomes for CLBP (eg, disability and function) and may represent potential mediators of the intervention effect (eg, back perception, motor imagery performance)[38] that can guide hypothesis generation for future work.

Postexperimental Outcomes

The presence of any adverse effects and participants' feedback/enjoyment of the intervention were assessed via written questionnaires at the final follow-up session (day 35). Participants were asked if they experienced any side effects from the VR intervention (eg, motion sickness). Feedback/enjoyment of the intervention was assessed through 5 open-ended questions (eg, "How did you experience the VR training?" or "In your opinion, how could a VR intervention be tailored to the individual patient during CLBP rehabilitation?"). Adherence was evaluated by the number of intervention sessions attended.

Analysis of Daily Measures

Consistent with SCED reporting guidelines, both descriptive visual and statistical analysis were completed for the daily outcomes.[25] A random-intercept and random-condition multilevel linear mixed model (MLM) was used to estimate the effect of the intervention on daily pain intensity ratings. A fixed effect of baseline duration was included in the MLM analysis as a control variable. The MLM was conducted in R[39] (R Core Team, 2022) using the lmer() function of the lme4 package.[40] The hierarchical multilevel structure induces dependencies within the data—because an individual's daily, repeated measures are non-independent, nesting the data within levels accounts for both within- and between-participant dependencies. The secondary daily outcomes were also used as dependent variables in MLMs (with random intercept, random condition, and fixed effect of baseline duration). The daily measures for pain-related fear items and pain catastrophizing items were each summed (creating 2 variables) and standardized prior to being entered in the MLMs, while the 4 pain-related anxiety/worry items were analyzed independently, as the individual items measured different underlying constructs (ie, physiological arousal, or escape/avoidance) and therefore were unable to be summed.

Consistent with past work[41] and recommended guidelines,[24] a responder and a nonresponder case were selected for formal structured visual analysis, where the mean, variability, and trend were considered over the 3 study phases. A graphical depiction of the mean, variability, and trend is provided for all participants in the Supplementary information. The main goal of the MLM analyses was to test whether the effect of the intervention is statistically significant. As the statistical inference for MLMs relies on statistical assumptions about the error term (eg, normality, homoscedasticity) that are often violated and that may be hard to assess when the sample size is small, we used an MLM-based nonparametric randomization test[42] (RT MLM) to compute the *P*-value for the intervention effect. This randomization test uses the absolute value of the estimated intervention effect of the MLM as a statistic. It computes the reference distribution of the statistic under the null hypothesis by estimating the MLM for each of 5000 randomizations. The randomizations are obtained by randomly sampling (without replacement) the day of intervention for the subjects from days 6 to 15 so that the minimum and maximum baseline length are respected (ie, it uses the randomization schedule adopted to set up the experiment). The *P*-value of the randomization test is obtained as the proportion of statistics in the randomization distribution that are at least as extreme as the statistics obtained for the observed data. We also evaluated if the participants achieved a minimally important change (MIC) for the pain intensity outcome. There is consensus that a 30% improvement in pain and functional status may be considered a MIC.[43]

Analysis of Pre-post Intervention Outcomes

Paired t-tests evaluated the change in non-daily measures from baseline to final follow-up. The data were analyzed using jamovi.[44]

Results

Participant Characteristics

Participants were recruited from January to June 2018. The number of participants screened for inclusion was erroneously not logged. A review of clinic records indicated that approximately 400 new patients with CLBP attended the Outpatient Spine Clinic during this recruitment timeframe, and given 3 recruitment windows (average of 2 weeks), this would likely involve the attendance of 100 patients with CLBP. From the email communication between research team members, it is estimated that approximately 40 people with CLBP were screened for eligibility (ie, those at the top of the waitlist during recruitment windows; capturing 40% of the total patients at the time) and that the most common reason for exclusion was inadequate levels of pain-related fear of movement. Of these, 14 participants met the eligibility criteria and were invited to participate in the study, with 10 participants included (Fig 3). There were no dropouts, although 1 participant was excluded from the analysis because between screening and enrollment their pain intensity rating reduced to 1 out of 10 on the NRS, and therefore they no longer met the eligibility criteria for participation in the trial. Participants were predominantly male (n = 8), with a mean age of 44.1 (SD = 13.2). Full participant demographics are detailed in Table 1. Most participants had complete data sets (1% missing data for daily outcomes).

Treatment Characteristics

All participants received their randomized number of treatment sessions within the planned timeframe. All but 2 participants completed the duration of the baseline phase as randomized (participants ID25 and ID22 were delayed by 1 and 2 days, respectively). The duration of the posttreatment phase was increased in 5 participants, due to unforeseen events (work-related scheduling conflicts, illness, and vacation), resulting in this phase being extended by 1 to 5 days.

Postexperimental Outcomes

No adverse effects were reported during use of the VR intervention. One participant expressed doubts about the treatment and its relevance to their specific

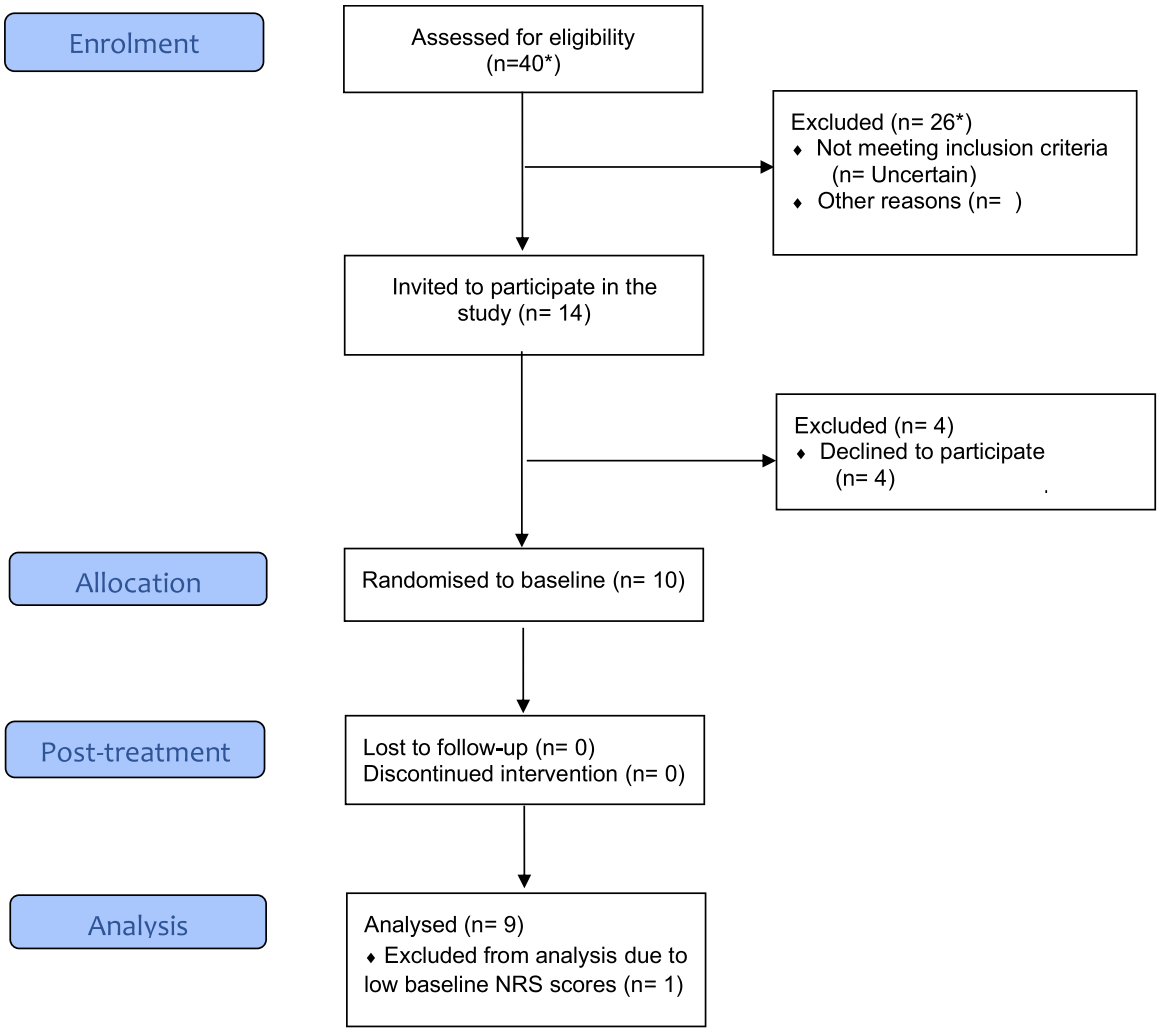

Figure 3. Participant flow diagram. *Number estimated from the email communication between the research team.

Table 1. Participant Characteristics

ID#	Demographic factors	Baseline pain intensity (NRS)	Marked painful areas	Pain in other body areas	Pain-related fear (TSK)	Disability (ODI) (%)	Function (OMPQ)	Implicit motor imagery (NOI-App recognise)	Perception (FREBAQ)	Function (PSFS)
ID22	Male, 63 y, married, 2 children. Works as a plumber. On full sick leave for 5 mo. Been sick listed for the same complaint 2 to 5× before.	5.91	Lumbar spine, bilateral	Yes: leg and foot, both 9/10	25/52 (mild)	56	74/100	Speed (L/R): .95/ 2.95 s Accuracy (L/R): 25/85%	8/36	Lifting heavy: 4 Carrying heavy: 3 Vacuuming: 4
ID23	Male, 38 y, married, 4 children. Primary school (runs own company). Partial sick leave for 5 mo. Has been sick listed for the same complaint more than 10× before.	4.83	Lumbar spine, bilateral, but most pain on the left side. Pain on both sides of the buttocks	Yes: leg and foot, both 8/10	37/52 (mod)	48	57/100	Speed (L/R): 1.2/ 2.0 s. Accuracy (L/ R): 80/75%	16/36	Sitting in excavator: 3 Sitting in truck: 3 Sitting in office: 3
ID24	Male, 31 y, single. Primary school (maintenance worker). Full sick leave for 3 mo. Never been sick listed for this complaint before.	3.87	Right side lumbar spine and buttocks, and right anterior thigh and testicle	Yes: leg and foot, both 8/10	35/52 (mild)	38	46/100	Speed (L/R): .8/ 1.3 s. Accuracy (L/ R): 75/90%	7/36	Driving far: 7 Certain tasks at work: 5 Strength training: 7
ID25	Female, 54 y, divorce, 1 child. Profession-based education (working in health care). On full sick leave for 1 y. Been sick listed for the same complaint 2 to 5× before.	5.14	Lumbar spine, bilateral	Yes: leg and foot, both 7/10; neck and shoulder, both 7/10	28/52 (mild)	54	35/100	Speed (L/R): 2.5/ 1.55 s. Accuracy (L/R): 35/30%	24/36	Sitting: 2 Walking uphill: 2 Shower: 4
ID26	Male, 47 y, married, 2 children. Profession-based education (off-shore). On full sick leave for 5 mo. Been sick listed for the same complaint more than 10×.	6.11	Lumbar spine, bilateral, but mainly right side with radiating pain on posterior right leg	Yes leg and foot, both 8/10	32/52 (mild)	70	66/100	Speed (L/R): .8/ 1.2 s. Accuracy (L/ R): 90/90%.	4/36	Walking: 4 Sitting: 4 Bending forwards: 2
ID27	Male, 28 y, single. Primary school (truck driver). Not sick listed. Been sick listed for the same complaint 2 to 5× before.	2.00	Lumbar spine, slightly more pain on the right side	No	34/52 (mod)	36	24/100	Speed (L/R): 1.5/ 1.1 s. Accuracy: (L/ R): 95/100%	10/36	Working: 4 Hiking: 6 Lifting: 6
ID28	Male, 48 y, married, 3 children, car salesman and mechanic. Not sick listed. Have never been sick listed for the same complaint before.	2.07	Lumbar spine, bilateral, but slightly more pain on the left side	Yes: leg and foot, both 8/10	25/52 (mild)	30	21/100	Speed (L/R): .9/ 1.2 s. Accuracy (L/ R): 90/95%	0/36	Missing

Table 1 (*Continued*)

ID#	DEMOGRAPHIC FACTORS	BASELINE PAIN INTENSITY (NRS)	MARKED PAINFUL AREAS	PAIN IN OTHER BODY AREAS	PAIN-RELATED FEAR (TSK)	DISABILITY (ODI) (%)	FUNCTION (OMPQ)	IMPLICIT MOTOR IMAGERY (NOI-APP RECOGNISE)	PERCEPTION (FREBAQ)	FUNCTION (PSFS)
ID29	Male, 59 y, divorced, 2 children. Primary school (technician). On full sick leave for 5 mo. Been sick listed for the same complaint 2 to 5× before.	8.20	Lumbar spine, bilateral, both buttocks, left anterior thigh (numb sensation)	Yes: leg and foot, both 6/10	25/52 (mild)	62	58/100	Speed (L/R): 1.35/1.9 s. Accuracy (L/R): 100/95%	8/36	Doing the dishes:0 Dressing: 4 Bowling: 2
ID30	Male, 29 y, single. University education (working in IT). Partly sick listed for 3 mo. Never been sick listed for the same complaint.	8.07	Lumbar spine and lower thoracic spine/Radiating to the buttocks each side	No	38/52 (mod)	44	56/100	Speed (L/R): .8/1.0 s. Accuracy (L/R): 85/95%	0/36	Sitting: 2 Lifting: 3

Abbreviations: ODI, Oswestry Disability Index; PSFS, Patient-Specific Functional Scale.
NOTE. Mean ± SD or count, %: female: 1 (11.1%); age, mean ± SD (range): 44.1 ± 13.2 (28–63); pain intensity (NRS) baseline mean ± SD (range): 4.96 ± 2.33 (range: 1–9).
Demographic factor: Is the pain intensity present all the time? ID30: "yes," other participants: "no."
Demographic factor shift work: ID26: "yes," other participants: "no."

complaints. All other participants expressed satisfaction with the intervention. They found the VR to be motivating, engaging, and enjoyed the sessions. Full responses to the open-ended questions are contained in Supplementary file 2. There was 100% adherence to the intervention: all participants attended all scheduled intervention sessions and completed all interventions in full (ie, played all 3 exergames for the planned amount of time).

Daily Outcomes

Primary Outcome: Pain Intensity

The visual analysis for pain intensity showed a somewhat variable response pattern between participants, although most showed improvement after the VR intervention (Fig 4). Two cases were selected for a formal visual analysis, one representing a responder (ID25, Fig 5A) and the other a nonresponder (ID30, Fig 5B). ID25 had a relatively stable baseline (mean = 5.14) with a slight downward trend. Their intervention phase shows a decrease in pain scores (mean = 2.57), with an increased slope of improvement. There is overlap between the baseline and intervention phases; however, this occurs during the first half of the intervention. Their posttreatment shows increasing pain scores once the intervention was removed; however, this is still well below the baseline (mean = 1.5), and there is no overlap between baseline and posttreatment phases. ID30 is a nonresponder. They had a slight trend toward worsening in baseline (mean = 8.07). They then had stable intervention (mean = 7.80) and posttreatment phases (mean = 7.00), both of which had minimal trends in the data. Accordingly, there is overlap between all 3 phases of the trial. Individual participant graphs displaying the level, variability, and trend for all stages of the intervention are contained in Supplementary file 3.

Across all participants, 4 met the MIC for pain intensity over the course of the intervention period (days 0–28; see Table 2). Of these, 3 participants had consistent decreases in pain over the course of the study, while 1 participant (ID29) had highly fluctuating pain levels throughout the study, but with an overall reduction in pain over the intervention period (vs baseline). Of interest, all those participants attaining the MIC for pain intensity were randomized to receive a greater number of VR interventions (n = 8–9; Table 2). For the remaining 5 participants, while all had reduced pain intensity over the course of the intervention period, the MIC threshold was not met. Two of these participants (ID27 and ID28) had low mean pain intensity scores through the baseline phase, so their small changes in pain may indicate a floor effect. However, another participant (ID30) had high pain intensity ratings during the baseline phase and showed little change in their pain levels throughout the intervention, ultimately having a small reduction of pain during the posttreatment phase.

Consistent with the visual analysis, the randomization test (using 5000 randomizations) for the MLM analysis revealed a statistically significant reduction in pain

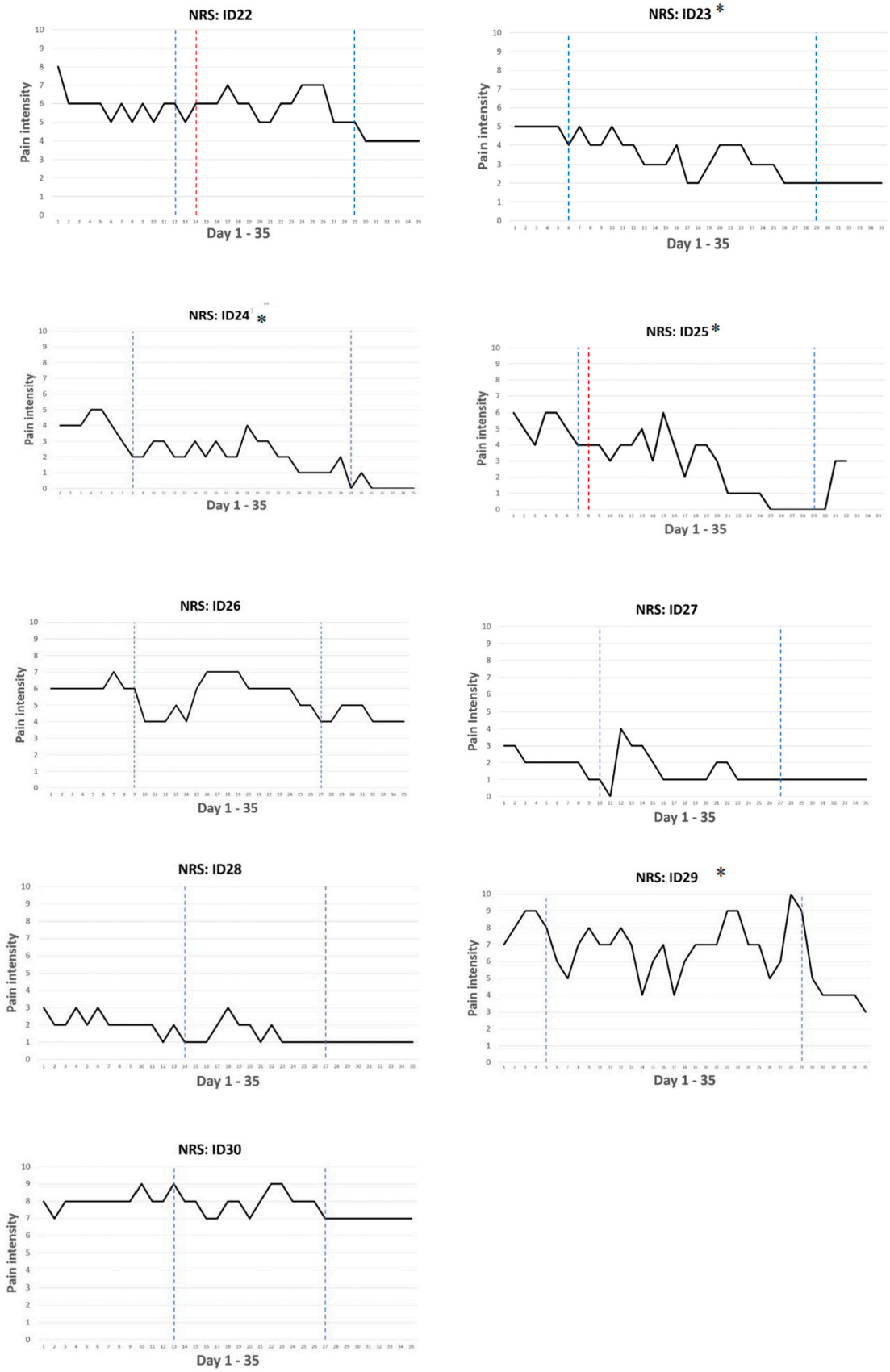

Figure 4. Daily pain intensity ratings (NRS) for each participant throughout the study. The dashed black vertical lines represent the changes between experimental phases: baseline, treatment, and posttreatment period. The red line indicates that the baseline was extended. An asterisk indicates that the pain reduction reached the MIC threshold.

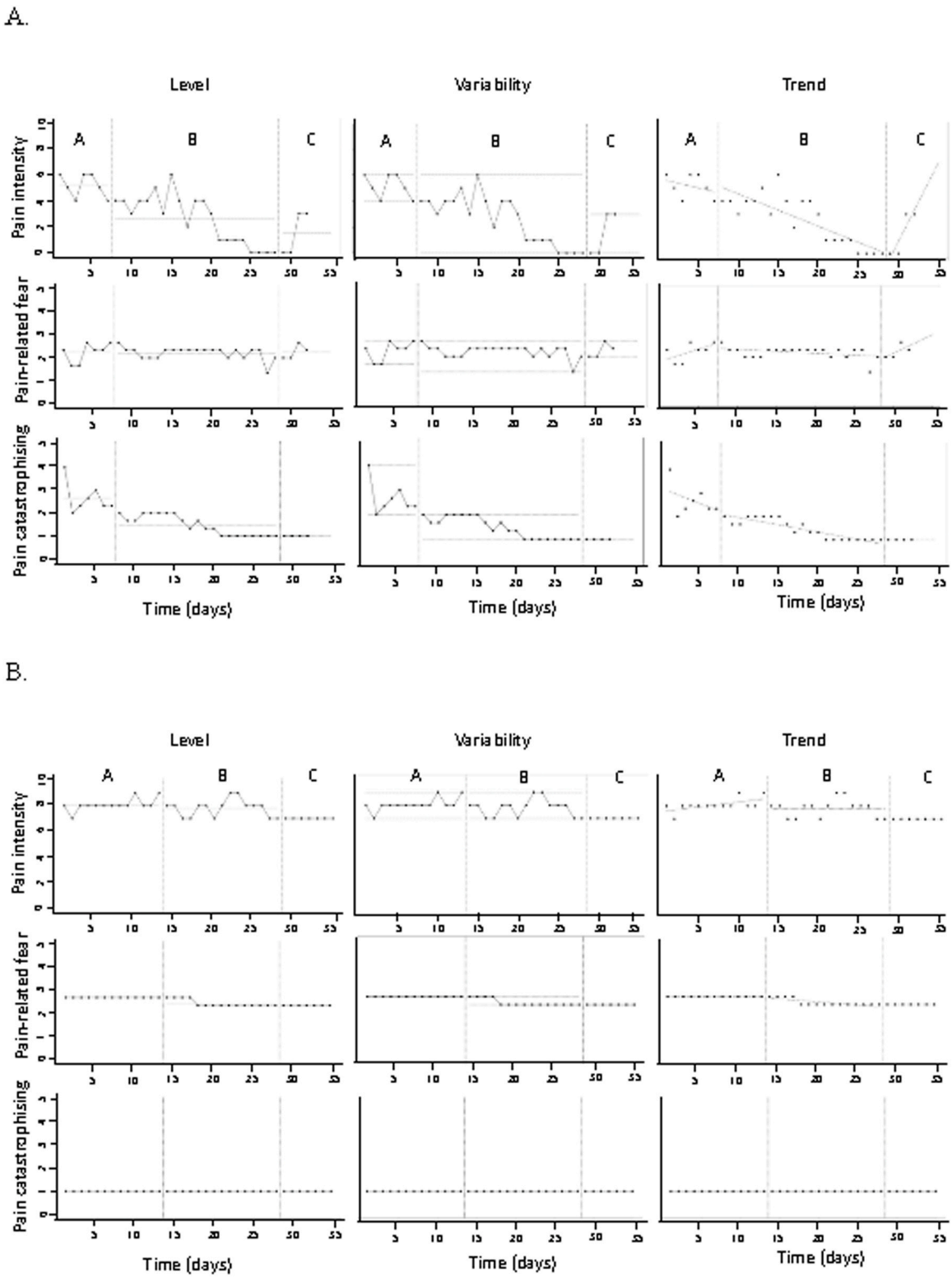

Figure 5. Visual analysis depicting the level (mean), variability (range lines), and trend (least squared regression) for pain intensity, pain-related fear, and pain catastrophizing. Phase A is baseline, B is intervention, and C is posttreatment. (**A**) is a responder (ID25) and (**B**) is a nonresponder (ID30).

intensity levels over the course of the intervention ($P = .016$). The effect estimate for pain intensity was −1.0 (SE = .27), indicating that the pain intensity ratings decreased by an average of 1 point on an 11-point NRS during the intervention period. Given the low baseline pain scores in 2 participants (ID27 and ID28), a sensitivity analysis was run excluding these participants. The results of the MLM-based randomization test (using 5000 randomizations) were similar, showing a significant intervention effect ($P = .01$, effect estimate = −1.13 [SE = .34]), indicating that the pain intensity decreased on average by 1.13 points between the baseline and

Table 2. Change in Pain (NRS) Scores

PARTICIPANT	MEAN SCORE OVER THE BASELINE PERIOD	MEAN SCORE OVER THE INTERVENTION PERIOD	MEAN SCORE OVER THE POSTTREATMENT PERIOD	CHANGE FROM BASELINE PERIOD TO THE INTERVENTION PERIOD (%)	CHANGE FROM BASELINE PERIOD TO THE POSTTREATMENT PERIOD (%)	NUMBER OF VR SESSIONS
ID22	5.91	5.94	4.14	+.03 (+.35)	−1.77 (−30.0)	7
ID23*	4.83	3.32	2.00	−1.52 (−31.3)	−2.83 (−58.6)	9
ID24*	3.88	2.20	.14	−1.68 (−43.2)	−3.73 (−96.3)	8
ID25*	5.14	2.57	1.50	−2.57 (−50.0)	−3.68 (−70.8)	9
ID26	6.11	5.42	4.43	−.69 (−11.3)	−1.68 (−27.5)	8
ID27	2.00	1.50	1.00	−.5 (−25.0)	−1.00 (−50.0)	7
ID28	2.07	1.43	1.00	−.64 (−31.0)	−1.07 (−51.7)	6
ID29*	8.20	6.78	4.71	−1.42 (17.3)	−3.49 (−42.5)	9
ID30	8.08	7.80	7.00	−.27 (−3.42)	−1.08 (−13.3)	6

*MIC for pain intensity (NRS from baseline to intervention phases).

treatment phases. Pain reductions were maintained or decreased further at the end of the 7-day posttreatment phase (Table 2).

Secondary Daily Outcomes: Pain-Related Fear, Pain Castastrophizing, and Pain-Related Anxiety/Worry

The visual analysis for the secondary daily outcomes was completed similarly to the primary, daily outcome. The same 2 participants (ID25 and ID30) were selected for a formal visual analysis, with full individual participant graphs contained in Supplementary file 2. ID25 had a baseline trend of increasing pain-related fear. This reversed during the intervention phase to a slight decreasing trend, before a second reversal in trend during the posttreatment phase (increasing pain-related fear). They had overlap between all 3 phases of the trial, with a similar level throughout (baseline = 2.23, intervention = 2.21, posttreatment = 2.25). In contrast, their pain catastrophizing baseline had a decreasing trend (mean = 2.67). This trend continued over the intervention phase (mean = 1.46), before stabilizing to a zero trend during the posttreatment phase (mean = 1.00). There was no overlap between the baseline and intervention or the baseline and posttreatment phases. In contrast, ID30 had limited change through the entire trial for both secondary measures. Their pain-related fear was stable (zero trend) during the baseline and posttreatment phases. They had trend toward decreasing pain-related fear during the intervention phase. However, the levels were similar during all 3 phases (baseline = 2.67, intervention = 2.42, post-intervention = 2.33). They had consistent pain catastrophizing scores for the entire trial. There was no change in level, trend, or variability (mean = 1.00).

The RT MLMs found that the effect of the intervention on pain-related fear was not statistically significant, with an effect of −.24 (SE = .11, $P = .07$). Two participants had a greater than 30% decrease in TSK scores from baseline. The intervention reduced pain catastrophizing significantly, with an effect of −.22 (SE = .15, $P = .03$), and 3 participants had a greater than 30% decrease in PCS score from baseline. RT MLMs were nonsignificant for all 4 items from the PASS (P values ranging from .64 to .83). Complete results are available in Supplementary file 3.

Pre-post Intervention Outcomes

There were no differences between baseline and final follow-up for most measures, with the exception of function, as measured by the OMPSQ, which showed a statistically significant improvement at follow-up ($P = .004$; Table 3). While Patient-Specific Functional Scale (PSFS) was intended to be completed by the participants, differing versions of the form between baseline and follow-up precluded data comparison, and thus the PSFS was excluded from analysis. Across all 9 participants, there was high variance in perceptual measures (FreBAQ scores), with no consistent direction of change. Four participants had a > 30% reduction in FreBAQ scores, while 2 participants had > 25% increase in scores. The implicit motor imagery scores showed no changes from baseline to follow-up.

Discussion

This study aimed to evaluate the clinical effect of an immersive VR gamified graded activity intervention in people with CLBP. We found that the VR intervention significantly reduced pain intensity, with 4 participants

Table 3. Results of Pre-post Intervention Measures

	BASELINE		FOLLOW-UP		PAIRED T-TEST			
	MEAN	SD	MEAN	SD	T	P	COHEN'S D	95% CI
Disability (ODI)	24.3	6.52	21.2	6.70	1.87	.10	.62	–.11 to 1.33
Functional capacity (OMPSQ)	50.0	19.6	42.9	18.1	4.06	.004	1.35	.41 to 2.26
Perceptual awareness (FreBAQ)	8.56	7.63	4.67	3.77	1.70	.13	.56	–.16 to 1.26
Implicit motor imagery accuracy (Laterality)	78.6%	24%	79.4%	13%	–.347	.74	–.11	–.77 to .54
Implicit motor imagery speed (Laterality)	1.33	.47	1.19	.52	1.07	.32	.36	–.33 to 1.02

Abbreviation: ODI, Oswestry Disability Index.

reaching the threshold for a minimally important change, and this improvement was maintained over a 7-day posttreatment period. Pain catastrophizing improved significantly over the intervention period, but pain-related fear, and pain-related anxiety/worry symptoms did not. There were no changes in the non-daily pre-post intervention outcomes, barring significant improvements in functional capacity (via OMPSQ). These results provide preliminary evidence for the efficacy of an immersive, gamified VR intervention to reduce pain in people with CLBP.

Our findings are in contrast to previous work that showed no effect on pain of a 3-sessions (each 15 minutes duration) VR "dodgeball" intervention that was similarly based on the graded principles of increasing forward bending.[16] Specifically, our findings suggest that the null findings of previous work may be related to the inadequate intervention dose. In our study, we saw a dose-response relationship for pain, with the participants who achieved a greater than 30% reduction in their pain all randomized to a longer intervention phase (receiving 8–9 sessions) and those who had minimal pain reduction randomized to the shortest intervention phase (6 sessions). While our study design precludes a formal analysis of this finding, that participants receiving more VR interventions had greater improvement in pain is consistent with results from traditional graded exposure intervention studies in CLBP that show effects on pain intensity with 8 to 12 sessions.[27,28] Future work is warranted to determine the minimum dose of graded activity/exposure VR interventions required to induce a clinically meaningful change in CLBP, as well as the maximum dose (ie, the number of sessions at which further improvements are negligible).

The intervention did not reduce pain-related fear or pain-related anxiety/worry. While we did see statistically significant reductions in pain catastrophizing, the visual analysis of this measure was less compelling (ie, no obvious improvements across participants), making any reductions in catastrophizing uncertain. This is in contrast to past CLBP studies where fear has been shown to have both a direct influence on pain and an indirect influence on pain via increased self-efficacy.[45] Participants in our study had only mild-moderate pain-related fear at baseline, suggesting that floor effects may have precluded a meaningful change. Although pain and fear levels were sufficient to meet the inclusion criteria, overall, our baseline levels were low compared to previous studies.[27,46] In addition, pain-related fear was assessed via questions from the TSK, which assess pain-related fear of movement in general, not situational pain-related fear. While some research has indicated that the TSK is associated with reduced forward bending in people with acute/sub-acute low back pain[47] and experimentally induced pain,[48] there is mixed evidence in the CLBP population.[49,50] Therefore, our use of items from the TSK as a measure of pain-related fear may not have been sensitive enough to detect change given that our intervention aimed to target forward bending. Indeed, recent work has shown that task-specific fear (relating to forward bending) is associated with lower peak angular velocity during lumbar flexion in people with CLBP, but that general fear of movement (via TSK) is not.[51] Future research should consider using more targeted measures, such as reported fear of forward bending or evaluation of behavioral measures (eg, lumbar flexion kinematics).

Past work evaluating VR exercise interventions has shown that the immersive environment and gamified intervention can induce dissociation between exercise intensity and how you feel.[52] That is, using VR people feel better (eg, improved affect and engagement) despite working harder. While such findings would predict pain reductions during our VR intervention, dissociation alone would not predict sustained clinical reductions in pain (eg, outside of the VR intervention). Instead, the increased dose of forward bending throughout the intervention sessions and the increased engagement with activities/movement in the space directly anterior to the body may explain the improvements in pain. Our intervention aimed to have participants increase their trunk movements implicitly by meeting game demands, rather than directly and consciously expose themselves to a movement that is often perceived as threatening. Over the course of the intervention, participants were encouraged to increase the amount of forward bending by progressing to the more difficult levels of each game, and were monitored by the treating therapist, who encouraged trunk movement if needed. Previous work indicates that a variety of VR programs can be used to induce spinal flexion, but that the game demands influence factors such as flexion velocity and peak range of motion.[53] Here, we had participants complete 3 different games, to vary the demands and therefore the type of spine movements required. This

progressive increase in forward bending and exposure to many types of movement over the course of the intervention may have reduced the pain via a number of proposed mechanisms, including neuromuscular changes (ie, improved strength or motor control); modulating central nervous system activity; or psychosocial factors (ie, increased self-efficacy).[54,55] However, these possibilities remain speculative as they were not directly measured over the course of the intervention. Future work exploring the mechanisms behind the effect of VR interventions, based on known theoretical underpinnings, is warranted to further elucidate the effects on clinical outcomes. Perceptual outcomes (FreBAQ, implicit motor imagery) measured here as potentially relevant mediators of the treatment effect did not change with the VR intervention, suggesting that further exploration of these outcomes as mediators may not be warranted.

Our intervention also showed clinical promise given the high levels of participant adherence. There was 100% adherence to the program—all participants completed our intervention as planned, attending all sessions. This is particularly notable given the number and frequency of sessions completed over a relatively short timeframe (eg, attending 9 sessions in 23 days). Together with the absence of adverse effects and the participants' qualitative responses consistent with positive feedback and enjoyment of the VR program, these findings support clinical utility of this VR intervention.

This study comes with important caveats. The generalizability to a wider CLBP population may be limited. An unintended consequence of sampling patients entering the Outpatient Spine Clinic from Haukeland University Hospital is that the majority of participants that met our inclusion criteria were male (n = 8, 89%). Previous research shows sex-based influences on VR experiences, with females more likely than males to experience adverse events (eg, cyber sickness) during the use of VR,[56] suggesting that our results may not generalize to a female population. An additional sampling limitation is that we did not collect race and ethnicity data. Given the census data suggesting predominantly white populations in Norway (our sampling location), our results may not generalize to racially diverse populations. Replication of our findings in more diverse CLBP populations is warranted, including potential partnering with stakeholders from racialized groups to inform research questions, data collection, and recruitment procedures (see Letzen et al[57] for further discussion). Further, due to error, we did not collect detailed eligibility screening details, and this, combined with the use of recruitment windows (consecutive sampling during the recruitment window but not across the total recruitment period), means that we cannot be entirely certain that our population is representative of all patients attending the Haukeland University Hospital Outpatient Spine Clinic. Our results are therefore limited to people with CLBP who have moderate pain and pain-related fear of movement and are likely most generalizable to those attending tertiary care centers.

We also did not test our intervention against a control phase (eg, immersive VR, which does not encourage forward bending), and thus cannot be certain about the degree to which nonspecific effects (eg, therapeutic alliance)[58] or general VR effects (eg, immersion/distraction) contributed to the positive results seen here. However, given the minimal clinical interaction once the VR program was initiated and that general effects via distraction would predict pain relief only during VR use, the sustained effects reduce the likely impact of these features. An additionaly limitation is that participant diaries were collected at each intervention session by the treating therapist (although not discussed with the patient). While a pragmatic decision to ensure minimal missing data for the daily primary outcome, it raises the possibility of response bias. Use of online data collection in future work would avoid this potential issue and could even track timing compliance with daily outcome completion via timestamps. Another limitation is the lack of behavioral outcomes, such as measures of lumbar kinematics (flexion excursion, velocity), during our VR interventions to determine the lumbar movement achieved by participants. Our target locations (and game levels) were informed by Thomas and France's[47] past work that confirmed increased lumbar flexion range of motion during VR game play, but given the lack of assessment in our sample, we are unable to conclude that increased lumbar flexion range of motion was a primary contributing factor to the present results. Rather, our results are limited to suggesting that engagement with game play in the anterior frontal place of the body (space in front of the body, with focus on lower levels) had beneficial effects on pain and pain catastrophizing in those with CLBP. Further, past work has shown that higher pain-related fear of movement (via TSK) in people with CLBP is associated with avoidance of lumbar spine motion.[47] Such findings raise the possibility that our VR game interventions may not have sufficiently targeted spinal flexion, but rather participants used other movement strategies (hip/knee) to engage with VR game play. However, despite the lack of an objective measure of trunk kinematics with game play, therapist supervision and feedback (when needed) of trunk movement during VR game play ensured that forward bending movements were not avoided in our sample. Finally, while the use of VR is growing, and high-quality equipment is becoming more affordable, it does require individuals to purchase a headset. Thus, while gamification of the intervention may increase adherence by improving engagement in graded activity, there are still barriers to accessing this treatment independently.

Evaluation of the methodological quality of this study was performed using the RoBiN-T scale (Supplementary file 4).[21] Interval validity was 7/15 and external validity was 11/16. The lower internal validity score was due to lack of blinding and interobserver agreement. However, due to the nature of the intervention blinding was not possible, and interobserver agreement of outcomes was not possible due to the use of self-reported outcome measures. Importantly, our study included measures

such as randomization of baseline length[25]; use of daily sampling of outcome measures (and minimal missing data); and numerous case replications,[21] which fulfill the design criteria of the scale.[21] Further, that adherence to the VR intervention was high, with no dropouts, suggests that these findings and this intervention may hold clinical importance. Despite a wide participant age range (28–63 years), all were able to complete the intervention without adverse effects. The intervention was patient-centered and flexible, with participants able to autonomously control their level of difficulty throughout the intervention. Finally, 2 of the evaluated games are commercially available, which means that they are accessible for both clinicians and people with CLBP. Together, this supports the potential scalability and reproducibility of this intervention across clinical settings.

The findings of this study provide several directions for future research. First, this study should be replicated in a more representative cohort and with a longer follow-up period. The VR intervention should also be compared to a within-subject active control phase, such as an educational program discussing the benefits of exercise or an immersive VR intervention that does not target forward bending. Future interventions could also be further tailored to the individual by targeting movements that are most relevant to that person, rather than the forward bending program used here. Future work should not only evaluate the clinical utility of these VR programs but also endeavor to understand the mechanisms through which clinical effects are mediated. Such knowledge will allow for future refinement and targeting of the treatment, hopefully further improving the clinical outcomes.

Conclusions

The present study found that an immersive gamified VR intervention based on principles of graded activity resulted in significant reductions in pain intensity and pain catastrophizing, but had no effects on pain-related fear or pain-related anxiety/worry symptoms in people with CLBP. Forty-four percent of the sample had pain reduction considered clinically significant and there was 100% adherence to the intervention. These findings of preliminary effectiveness of this VR intervention in reducing CLBP symptoms merits replication.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.03.013.

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