



Pain education and pain management skills in virtual reality in the treatment of chronic low back pain: A multiple baseline single-case experimental design

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ABSTRACT

Chronic lower back pain is a major health problem and current treatments do not always lead to adequate pain control. Virtual reality (VR) is an upcoming technology that has shown to be effective in reducing acute pain. However, the value of VR in reducing chronic pain is still unknown. Therefore, the current study focuses on the effects of a recently developed VR application 'Reducept' using a multiple baseline single-case experimental design in 8 patients ($N = 8$). Reducept is a VR-training program aiming to improve pain management skills and providing pain education in patients with (chronic lower) back pain. Results based on visual and statistical analyses indicated that Reducept has the potential to reduce chronic lower back pain, although its clinical relevance was small. This study is one of the first that focuses on the possible effects of Reducept using sophisticated visual and statistical analyses. Our study shows a detailed overview of individual changes in pain intensity over time. Further research is necessary to investigate the working mechanism of Reducept and its impact on chronic pain conditions.

1. Introduction

Chronic low back pain is a major health problem with a high prevalence (Fatoye et al., 2019) leading to serious physical and psychosocial disabilities (Cherkin et al., 2016; Kamper et al., 2015), high disease burden and huge healthcare costs (Hoy et al., 2014). Globally 540 million people suffered from chronic low back pain in 2015 (Hartvigsen et al., 2018). Despite a variety of available treatments, the majority of patients do not encounter adequate pain relief. Analgesics e.g., opioids are often prescribed for pain management. However, opioids do not always lead to adequate pain control and are also associated with negative side effects (Mallari et al., 2019) such as drowsiness, constipation, headaches, confusion, depression and breathing problems. In case of long-term use of opioids physical dependence, addiction and increasing pain are possible. In addition, long-term use can also lead to overdose, fractures, myocardial infarction, and endocrine dysfunction (Schepens et al., 2019).

Because of these facts (that chronic low back pain is a complex and

major health problem, and the long-term use of analgesics has negative side effects) it is important to understand the development from acute-to chronic low back pain. This, however, remains a challenge in clinical practice and needs to be further investigated (Marcuzzi et al., 2018). Research shows that psychosocial perpetuating factors for chronic pain in general are a high degree of emotional distress such as anxiety and depression, pain catastrophizing (Leeuw et al., 2007; Chou & Schelleke, 2010; Traeger et al., 2015; Martinez-Calderon et al., 2018)), a high pain-related fear and fear of movement (Vlaeyen et al., 2016).

Treating chronic pain using a strict biomedical approach contrasts with the idea of chronic pain as a multidimensional illness; the latter being viewed as the complex interaction of biological, psychological, and social factors (Gatchel, 2005). Therefore, a biopsychosocial approach is widely accepted as the most heuristic perspective to the understanding and treatment of chronic pain disorders (Gatchel, 2004; Gatchel, Peng, Peters, Fuchs, & Turk, 2007). The International Association for the Study of Pain (IASP) and Dutch guidelines (Pijnpatiënten naar één stem, 2022) in the treatment of chronic pain recommend the

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use of a biopsychosocial approach and advice additional pain education and thereby optimization of pain management skills: changes in the behavioral, cognitive, and emotional functioning are effective elements in the treatment of chronic pain. Due to the aforementioned complexity of chronic pain and the sometimes-limited effects of current treatments the development of new treatment methods, using a biopsychosocial approach, is warranted.

Virtual reality (VR) is an upcoming technology that has shown to be effective in reducing acute pain, for instance during medical procedures such as wound care (Hoffman et al., 2000).

Previous research has focused on using VR for acute pain. Studies on the effects of VR on chronic pain are in its infancy but emerging. The results indicate the potential of VR in treating chronic pain, but more research is needed to confirm this (Chuan, Zhou, Hou, Stevens, & Bogdanovych, 2021).

Reviews by Garrett et al. (2014) and Pourmand et al. (2018) indicate that VR treatment is effective in reducing chronic pain through mechanisms of distraction and focus shifting. Using VR, people divert their attention from an unpleasant stimulus (pain) to a pleasant and absorbing virtual world. VR diminishes a patient's subjective pain experience through visual, auditory, and tactile cues engaging higher cognitive and emotional centers of the nervous system (Gold et al., 2007). Garrett et al. (2014) and Pourmand et al. (2018) found only a short-term effect of VR in chronic pain. Reduced pain levels were mostly seen during distraction in VR exposure but no sustained difference in pain levels post-exposure was observed. The aforementioned reviews show that there was no strong evidence for long term pain reduction, however, this finding was partially attributed to limitations of the reviewed studies. Therefore, potential long-term benefits of VR on chronic pain are still uncertain (Pourmand et al., 2018). More research is needed into possible long-term benefits of VR exposure (Ahmadpour et al., 2019; Mallari et al., 2019). Treatment via VR has several advantages such as high engagement due to its immersive nature. For example, participants are less likely to be distracted than during face-to-face therapy. Moreover, VR can be used on the go or at home by allowing patients to complete the program independently, which (if effective) would make treatment accessible to a larger number of patients.

With these considerations in mind, VR could be a promising option for an effective non-pharmacological pain management intervention for acute and chronic pain.

The current study focusses on the effects of a recently developed VR application called 'Reducept'. Reducept provides training in pain education as well as pain management skills for people with chronic pain (Fennema & Zantema, 2019). An important factor in the content of Reducept is pain education. Research from Tegner, Frederiksen, Esbensen, & Juhl (2018) shows that pain education contributes to improvement of pain outcomes; perceived pain intensity and disability. The pain management techniques used in Reducept are derived from evidence-based psychological treatment techniques (Fennema & Zantema, 2019). See section Intervention for more detailed information about the content of Reducept. Despite the fact that the content of the training is derived from existing psychological interventions in the treatment of chronic pain, it is thusfar unknown to what extent Reducept influences pain intensity and their psychosocial perpetuating factors over time during and after a treatment period. There are two important factors in this respect. Firstly, the exact working mechanisms of the content of Reducept are still unknown because of its novelty and further research on that should be done.

Secondly, it is unknown to what extent Reducept succeeds in effectively converting the elements of various psychological treatments into a VR environment and the exact working mechanism of VR in the treatment of chronic pain.

We employed a Single Case Experimental Design (SCED) to investigate whether the VR application Reducept contributes to a decrease in pain intensity and influences perpetuating factors of chronic pain.

A SCED will provide insight into whether and how individual

changes on these variables take place during VR exposure and after the withdrawal of the VR intervention. The Medical Ethics Review Committee (METC Oost-Nederland, registration number: 2019-5750) confirmed that the Medical Research Involving Human Subjects Act does not apply to this study.

2. Methods

2.1. Design

A single-case multiple baseline design ABA was employed and replicated across eight participants. In this design, multiple data series are compared and a treatment is introduced and withdrawn at a different, randomly chosen time point for each participant. Comparisons can be made between and within data series (Kratochwill et al., 2010) meaning that changes at time of introduction and withdrawal of a treatment can be monitored between participants as well as changes within an individual during the treatment period. This type of design is increasingly used in the field of clinical psychology. It has proven to be a scientifically valid method to evaluate individual occurring changes, while introducing a new intervention and also shows to be an efficient method to investigate whether an intervention will work for a particular patient (Morley, 2017). The multiple baseline design is a effective design that uses an empirical sophisticated methodology. Kratochwill et al., (2010). The Oxford Center for Evidence-Based Medicine classified the randomized N-of-1 trial as Level 1 evidence for treatment decision purposes in individual patients, alongside systematic reviews of RCTs" (Krasny-Pacini & Evans., 2018). An important strength of the design is the experimental control it provides for threats to internal validity. Demonstration of a relationship between manipulation of the independent variable and change in the dependent variable is thereby possible (Horner et al., 2005). Another advantage of this design is the fact that it can demonstrate who is benefiting from an intervention (Morley, 2017).

In terms of the design, the recommendations of Dugard et al., (2012) were followed.

Dugard and Todman give a detailed description of the decision-making factors to consider when utilizing a single-case design, and how to collect and analyze the data. Important factors that have determined the choice for an ABA multiple baseline design in this study are: the number of participants (more than two), the fact that we wanted to test the effects of an intervention, the possibility to conduct measurements before, during, and after intervention, and the possibility to determine the start and withdrawal of the intervention randomly. We determined the following prior to data collection:

- The number of measurements per participant, that was set at 42 days.
- The number of participants.
- The minimum number of measurements for baseline.
- The minimum number of measurements for the intervention.
- The minimum number of measurements for the withdrawal phase.

To perform the randomization, we listed the possible intervention-withdrawal pairs. These pairs were numbered so that they could be randomly assigned to participants. We added the difference between the intervention mean and the mean of the baseline- and withdrawal phase and used this as our multiple baseline test statistic in the randomization test.

2.2. Primary outcome measures

Pain intensity. The intensity of the lower back pain was assessed using an 11- point numeric pain rating scale (NRS) (0 = no pain, 10 = worst imaginable pain). NRS has proved to be reliable in assessing lower back pain (Shafshak & Elneimr, 2020). Internal consistency was good ($\alpha = 0.86-0.95$; Ferraz et al., 1990).

2.3. Secondary outcome measures

Pain catastrophizing. Pain catastrophizing was assessed with the Pain catastrophizing scale (PCS; Sullivan et al., 1995) consisting of 13 statements rated on a Likert rating scale (0–4, 0 = not at all, 4 = always). The total score was used where higher values reflected a higher level of pain catastrophizing.

Psychological complaints. The Symptom Checklist 90-R (SCL90-R) is a self-reporting inventory that was used to assess psychological distress and symptoms of psychopathology.

(Arrindell & Ettema, 2005). The SCL 90-R consists of 90 questions rated on a Likert rating scale (0–5, 0 = not at all, 5 = extremely).

The total score of the instrument was used as a measure of overall psychological distress, with higher scores reflecting higher levels of psychopathological distress.

Fear of movement. Fear of movement was assessed with the Dutch version of the Tampa Scale for Kinesiophobia (TSK; Vlaeyen et al., 1995). TSK consist of 17 statements, rated on a Likert rating scale (1–4, 1 = strongly disagree, 4 = strongly agree). The total score was used in this study, with higher values reflecting greater fear of movement.

Pain coping. Pain coping was assessed with the Pain Coping Inventory List (PCI) (Kraaimaat et al., 1997). The PCI consists of 33 items that can be scored on a Likert scale (1–4, 1 = hardly ever, 4 = very often). The total score of the subscales (Pain Transformation, Distraction, Reducing demands, Retreating, Worrying, Resting) was used. Where Pain Transformation, Distraction and Reducing demands reflect an active coping strategy, and Retreating, Worrying and Resting reflect a passive coping strategy.

Quality of life. Quality of life was assessed using the SF 36/RAND 36-item Health Survey (RAND 36; van der Zee & Sanderman, 1993), that was developed as a multi-dimensional instrument. The questionnaire consists of 10 subscales in which limitations in functioning or cognitions about perceived health status are assessed. The way of answering is variable; the measurement level is nominal and ordinal. The total score of the subscales (Physical functioning, Role functioning/physical, Role functioning/emotional, Energy/fatigue, Emotional well-being, Social functioning, Pain, General health) was used where higher values reflect a higher perceived quality of life.

Pain intensity was measured on a daily basis at standardized moments. Self-reported symptoms (quality of life, pain catastrophizing, psychological complaints, fear of movement, pain coping) were assessed at four data points.

The study consisted of three phases: a baseline-(A), an intervention-(B) and a posttreatment phase (A) (ABA). During the baseline- and post-treatment phase there was no intervention. The intervention phase consisted of 9–12 VR sessions (with a frequency of three sessions per week). The start and the end of the intervention phase (and therefore the length of the different phases) were randomly assigned using the following criteria: a minimum baseline period of five days, a minimum intervention phase of 21 days, and a minimum post-treatment phase of 10 days. Due to this randomization process, the length of the baseline varied between five and 10 days, the length of the intervention phase varied between 21 and 26 days, the length of the post treatment phase varied between 10 and 14 days. Randomization of the start- and withdrawal moment of an intervention strengthens the internal validity of the design and makes observed changes more likely to be subscribed to the underlying effect of the intervention (Dugard et al., 2012). All treatment sessions took place at the hospital in a quiet environment.

This study was not subject to the Medical Research Involving Human Subjects Act (WMO), governed by the Human Research Committee Arnhem – Nijmegen region. Approval of the local science committee of the Canisius Wilhelmina Hospital was granted. Written informed consent was obtained from each participant prior to the start of the study.

2.4. Participants

The participants were referred by an anesthetist pain-specialist for additional psychological assessment in a non-academic teaching hospital (N = 8). They were suffering for more than 6 months from nociceptive chronic low back pain and met all ICD-11 criteria of chronic pain (World Health Organization, 2019). Before referral, the anesthetist determined that there were no further options for medical treatment. After referral, participants were screened and selected for the study by an experienced psychologist following the next inclusion criteria: a minimum age of 18 years, a diagnosis of chronic low back pain (>6 months on a daily basis), a mean pain intensity score of 4 on a numeric rating scale between 0 and 10 (NRS, 0 representing no pain and 10 the highest pain intensity imaginable) in the week before inclusion, sufficient knowledge of the Dutch language and willing to follow the study protocol. Participants were excluded when severe psychopathology (e.g., mood, anxiety, or psychotic disorders and/or suicidal risk), cognitive impairment, disorders that are contra-indications for the use of virtual reality (e.g., hearing or visual complaints, and epilepsy) were present. During the screening after referral, the experienced psychologist assessed whether the respondents' met criteria for severe pathology according to DSM 5 using a verbal interview approach. All participants were asked to keep their pain treatment/analgesics stable during the whole study period or if that failed to report changes to the researcher. No changes took place by starting/ending physical therapy and/or a treatment with transcutaneous nerve stimulation (TENS).

2.5. Intervention

Reducept (Zantema & Fennema, 2018) consists of five different parts, namely *Nerves*, *Spinal cord*, *Brain*, *Alarm center* and *Control room*. The total playing time is 40–45 min. The parts can be performed independently of each other, but during the study participants always followed the aforementioned order. This meant that participants were engaged in the same content during all visits to the hospital. During the training, participants see themselves through the VR glasses, for instance, as if they are entering their own brain where they are surrounded by neurons, neural pathways, and pain gates. During the phase *Nerves*, a metaphor is used such as is usual in Acceptance and Commitment Therapy (ACT) or hypnotherapy. Participants visualize their pain sensation as a painful stimulus at which they can shoot with a lasergun. Developers conceptualized this game as: 'a strong visual metaphor for taking control over the threat-related stimuli in the nervous system' (The ultimate guide to the Reducept game, 2022). During the part *Spinal cord* participants focus their attention on visual "pain ports" in the spinal cord and also on their breathing. By doing this, they are taught to visually and metaphorically 'close' pain ports for incoming pain signals to their brain. An important factor in this game element is to learn how a state of relaxation may positively influence perceived pain. The game *Brain* explains how to let your brain react less strongly to pain stimuli. This is visualized by showing participants a pattern of illuminating connection points in the brain which they need to remember. Then they are asked to light them up in the same order again by shooting them. As they do this, they have to focus their attention on the pain. Gameplay in the *Alarm center* focuses on feelings, thoughts, and actions, and how these affect the sensitivity of the brain for pain stimuli. The *control room* is the final exercise of the training and visualizes the inside of your alarm center. In Reducept, the alarm center is defined as the part of the brain that processes pain stimuli and determines to what extent pain stimuli are transmitted to the brain. The experience is similar to sitting in the cockpit of a plane. From this vantage point, participants are inside their brain and can now determine the extent to which stimuli from the alarm center are transmitted. Pain education is given during the whole training and is based on the book 'Explain Pain' from Butler & Mosely (2013). This book discusses the concept that the brain "produces" pain due to a variety of potential harmful input from the tissues which interacts with

memory, emotions, and thoughts. Also, the reaction of the autonomic, motor- and immune systems in your body can contribute to pain which can persist after tissues already seem to be healed (Butler and Mosely, 2013). For more information on the intervention, please refer to: [The ultimate guide to the Reducept game](#) (2022).

2.6. Assessment timepoints

In this design two different measurement methods were used. Daily measurements and pre-post treatment measurements at four single data points as can be seen in Fig. 1.

Daily measures consisted of pain intensity (NRS). Pre- and post-treatment measures consisted of self-reported symptoms: quality of life (SF 36/RAND36), pain catastrophizing (PCS), psychological complaints (SCL-90-R), fear of movement (TSK), and pain coping (PCI).

3. Data analysis

3.1. Daily measures

Over the past years different methods have been proposed for the analysis of single case designs. There is however still no consensus in this field of research with each method having its own shortcomings (Onghe et al., 2019). Visual analysis is most commonly used to analyze data in single case designs. We used the guidelines from Morley (2017) for visual inspection to determine whether data patterns differed over time and between phases as an indication of an effect of the intervention. Raw data, the central location of the mean of each phase, changes in the central location of the mean between phases, the variability of the data within phases, and the systematic shift in location of the central location within each phase (trend) using the split-middle method developed by White (1972) were displayed. These visual analyses facilitate a detailed inspection of individual changes over time. In line with Morley (2017), we added statistical analysis to detect whether visually observed change is statistically significant and to detect smaller effects and remove potential observer bias in visual analyses. For statistical analysis, randomization tests were conducted. The null hypothesis of randomization tests is that the intervention has no effect. Randomization tests are non-parametric tests that consider the whole distribution of the data against all possible distributions, and are recommended for single case data (Heyvaert & Onghena, 2014; Morley 2017). Randomization tests are distribution-free, and they make no assumptions about the nature of

the error structure in the data (Heyvaert & Onghena 2014). Moreover, clinically important differences were evaluated following the recommendations of Farrar et al. (2002) in which a reduction of approximately two points or a reduction of approximately 30% on the NRS pain intensity scale is considered clinically important. Tau-U was conducted to determine the effect size. Effect sizes are interpreted as follows: 0–0.65 as a small effect, 0.66–0.92 as a medium effect and >0.92 as a large effect (Parker et al., 2011). Standard alpha levels were used ($p < 0.5$) (Parker, Vannest, & Davis, 2011).

3.2. Pre-post treatment measures

To estimate whether individual changes on pre-post treatment measurements (i.e., quality of life, pain catastrophizing, psychological complaints, fear of movement and pain coping) were clinically relevant, pre-, and posttreatment scores were evaluated for each individual using Reliable Change Indices (RCI; Jacobson & Truax, 1991) and Clinically Significant Change criteria (CSC; Jacobson et al., 1984; Jacobson & Truax, 1991). RCI and CSC are procedures that are widely used in evaluating psychological treatments (Lambert & Ogles, 2009; Ogles et al., 2001). RCI provides information on whether the change is statistically reliable and cannot be attributed to random measurement error alone. The RCI is calculated by dividing the difference between pre- and post-treatment scores by the standard error of the difference, at which an RCI score of 1.96 or less is not considered reliable (Jacobson & Truax, 1991). Computing the RCI we used the mean of T1 and T2 as pre-treatment score and T3 as post-treatment score.

The CSC shows whether the change of an individual is large enough to be regarded as clinically meaningful. The cut-off for the CSC is set in such a way that scores after treatment should fall outside the range of the dysfunctional population (i.e., chronic pain patients). This is defined as the extreme end of the dysfunctional distribution (>2 standard deviations in the direction of the 'normal' reference group. CSC is calculated as follows: $a = \text{mean baseline} - 2 \times \text{SD of the dysfunctional group}$. Standard deviations of the dysfunctional group were derived from test manuals. The CSC will be computed for patients who make a reliable change (improvement/deterioration).

Missing values on pre- and post-test on SCL-90 were replaced following the instruction manual (Arrindell & Ettema, 2005), meaning that the missing values were replaced by the subject's average value for the existing items on the subscale of the questionnaire. We used the same procedure for the other questionnaires (TSK, PCI, PCS, RAND 36)

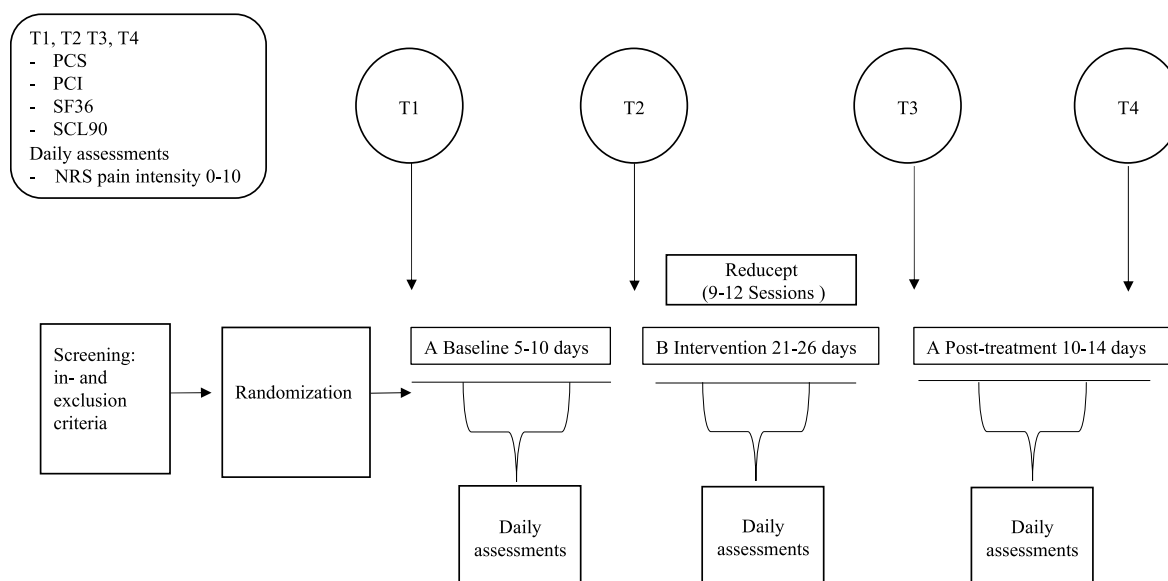


Fig. 1. Schematic representation of the study design.

because no recommendations on this point were provided in the manuals. 75 percent of the participants had no missing values. In total 19 imputations were made. The average imputations that were made per subscale is 1.4 with a maximum of 3 imputations per subscale.

4. Results

4.1. Participant characteristics

All patients referred by the anesthetist were willing to participate and proceed with the study. The original sample consisted of nine participants (three men and six women) with chronic lower back pain. Compliance with the intervention was high. One participant did not complete the study due to personal circumstances and was excluded from further analyses. All other eight participants completed the assessments of all three phases on the primary outcome measure. Table 1 shows the demographic and clinical characteristics of the participants.

Prior to the start of the study, participants were asked to indicate when relevant changes occurred in their ongoing pain treatments during the study that could affect their level of pain intensity (i.e., stopping or starting physiotherapy, a decrease or increase in pain medication). One participant (P2) mentioned that he had tapered his pain medication on his own initiative during the intervention phase due to a decrease of his pain intensity level (10 days after start of Reducept) but had to increase the dose again (7 days) after completion of the intervention phase. No other participants reported a change in treatment during the study. There were no adverse events.

4.2. Primary outcome measure

4.2.1. Pain intensity

Fig. 2 shows the pain intensity for all eight participants during the baseline- (A), intervention- (B) and follow-up (A) phases. For participants 1, 3, 5, and 8 visual inspection (Fig. 2) and mean scores (Table 2) suggest a reduction of pain intensity scores during the intervention phase compared with the baseline phase. For participant 1, 5, and 8, pain intensity further decreased in the during the withdrawal phase.

For participant 6 visual inspection suggests a reduction of pain intensity during the withdrawal phase compared with the baseline- and intervention phase. Visual inspection of data from participant 2 and 4 showed no signs of a significant change in pain intensity during the three phases. The mean pain intensity scores of participant 1 met the criteria of a reduction of approximately two points or a reduction of

approximately 30% during the withdrawal phase compared to the baseline phase. In addition, the mean pain intensity scores of participant 3 met the criteria of a reduction of approximately two points or a reduction of approximately 30% during the intervention phase compared to the baseline phase. Altogether, for two out of eight participants a clinically relevant decline was observed during the study period (Farrar et al., 2002). Besides visual inspection of pain intensity scores, a one-tailed randomization test was applied. This randomization test combines the results of all 8 participants and is therefore unable to distinguish on an individual level what has changed. A statistically significant decrease in pain intensity ($p = 0.0086$) was shown across all the eight participants.

The results of the Tau U shows that differences between baseline and intervention phases were statistically significant, though the effect size was small (Tau-U = -0.35 $P < 0.05$). No baseline correction was needed.

4.3. Secondary outcome measures

4.3.1. Pre- and posttreatment measures

All eight participants completed the pre-post treatment questionnaires. Unfortunately, due to a technical error the assessment of pre-post treatment T1 of participant 2 and T3 of participant 5 could not be used. Table 3 shows pre-post treatment test scores, RCI and CSC.

4.3.2. Pain catastrophizing

Two out of eight participants (P3, P8) showed a reliable reduction (based on the RCI), although not clinically significant (based on the CSC) in pain catastrophizing from baseline phase compared to post intervention (PCS total score).

4.3.3. Psychological complaints

None of the participants showed a reliable change (based on the RCI) in psychological complaints (SCL90-R total score) from the baseline phase compared to post intervention.

4.3.4. Fear of movement

None of the participants showed a reliable change (based on the RCI) in fear of movement (TSK total score) from the baseline phase to compared to post intervention.

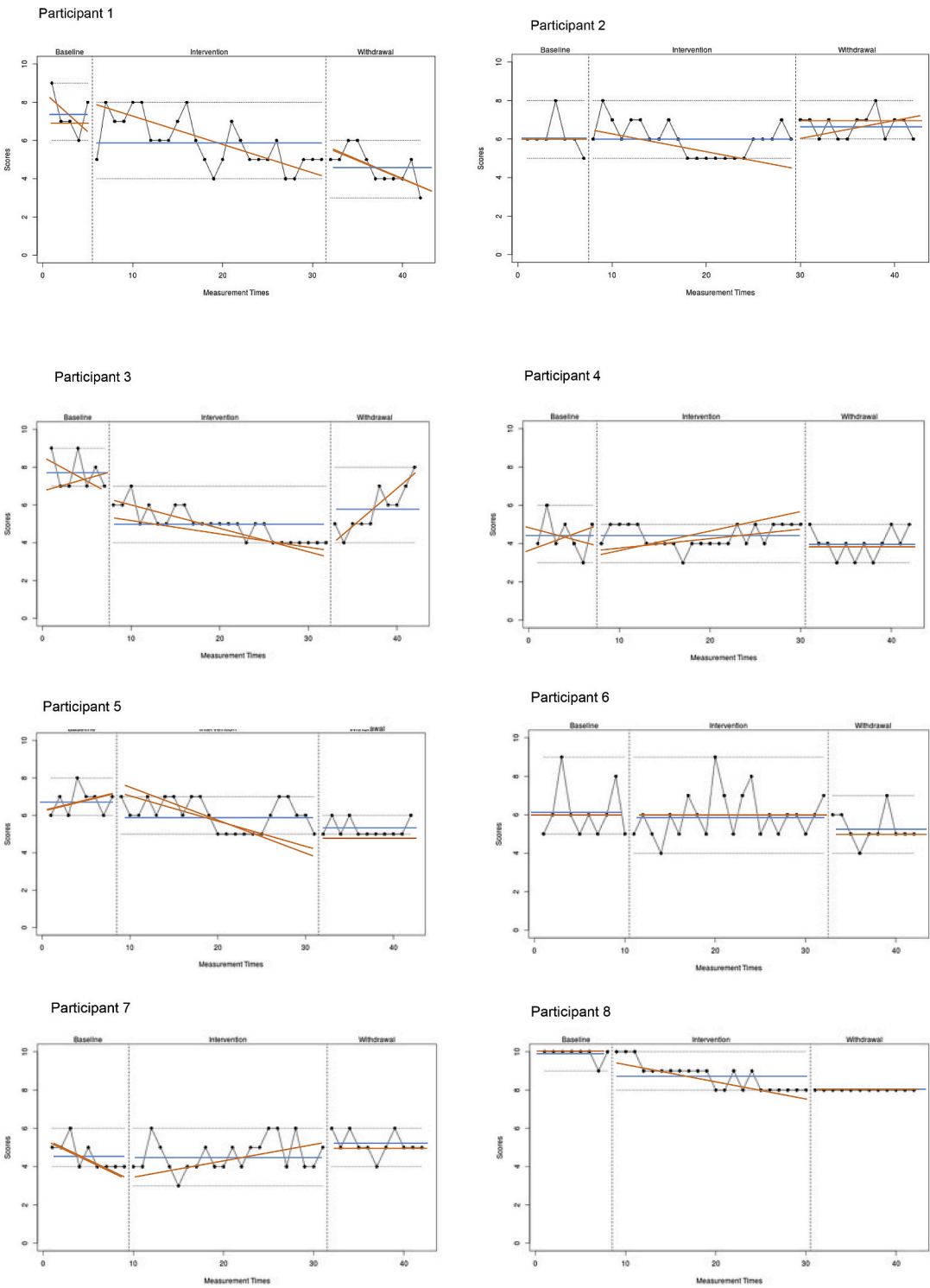
4.3.5. Pain coping

Active coping strategies (total scores PCI subscales: Pain

Table 1
Participant characteristics (N = 8).

Participants (P)	P1	P2	P3	P4	P5	P6	P7	P8
Age (years)	79	22	73	45	62	87	72	80
Gender	Man	Man	Man	Woman	Woman	Woman	Woman	Woman
Nationality	Dutch	Dutch	Dutch	Dutch	Dutch	Dutch	Dutch	Dutch
Duration of the pain complaints	7 years	3 years	5 years	12 years	4 years	10 months	3 years	6 months
Type pain complaints	nociceptive	nociceptive	nociceptive	nociceptive	nociceptive	nociceptive	nociceptive	nociceptive
Other medical complaints	None	None	None	None	Amblyopia	Basal cell carcinomas	Obstructive sleep apnea Adiposity	Leukemia Stable curative phase None
Current ongoing pain treatments	None	Pain medication	Pain medication	TENS*	Pain medication	TENS* Physiotherapy Pain medication Paracetamol	TENS*	
Type pain medication		Paracetamol	Paracetamol		Paracetamol opioid, NSAID			
New treatments or treatment changes during the study	None	Decrease of pain medication	None	None	None	None	None	None

Note: * Transcutaneous Electrical Nerve Stimulation.






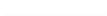
Note:  Central tendency, split level method (White (1972))
 Trend
 Variability
 Raw pain scores

Fig. 2. Graphical display of visual analyses of pain intensity across study phases.

Table 2

Means for the primary outcome pain intensity (N = 8).

Participants	P1	P2	P3	P4	P5	P6	P7	P8
Mean baseline phase	7,4	6,2	7,7	4,4	6,8	6,1	4,6	9,8
Mean intervention phase	5,5	6,0	5,0	4,4	6,0	6,0	4,6	8,7
Mean post-treatment phase	4,6	6,7	5,8	4,0	5,3	5,3	5,2	8,0
Mean baseline- and post-treatment phase	5,9	6,5	6,6	4,2	5,9	5,7	4,9	8,8

transformation, Distraction, Reducing demands).

Two out of eight participants (P3, P4) showed a reliable increased pain transformation, indicating that people can re-interpret their pain, (RCI) from the baseline phase compared to post intervention. This change was only clinically significant (CSC) in one participant (P3). Four out of the eight participants (P1, P6, P7 & P8) showed a reliable decline in pain transformation (RCI). For one of these four participants (P6), the change met the criteria of clinical significance.

Two out of eight participants showed a reliable change from the baseline phase compared to post intervention in distraction (RCI). One participant showed a decline in distraction (P3) and one participant an increase in distraction as coping strategy (P2). Both participants met the criteria of clinically significant change (CSC).

On the subscale 'Reducing demands', the RCI showed a reliable change from the baseline phase compared to post intervention for four out of eight participants. One participant showed a decline in reducing demands (P7) and three participants an increase in reducing demands (P2, P4, P8). All four participants met the criteria of clinically significant change.

Passive coping strategies (total scores PCI subscales: Retreating, Worrying, Resting).

Four out of the eight participants (P1, P2, P4 & P6) showed a reliable increase on the subscale Retreating from the baseline phase compared to post intervention (RCI). One out of eight participants (P7) showed a reliable decline on the subscale Retreating (RCI). All five participants met the criteria of clinically significant change (CSC).

Four out of eight participants (P3, P4, P7 & P8) showed a reliable increase on the subscale Worrying from the baseline phase compared to post intervention. One out of eight participants (P6) showed a reliable decline on the subscale Worrying. Three out of this five participants (P3, P6, P8) met the criteria of clinically significant change (CSC).

On the subscale Resting, the RCI showed a reliable change from the baseline phase compared with post intervention for five out of eight participants (RCI). Three out of eight participants showed an increase on the subscale Resting (P1, P3 & P4). Two out of eight participants (P2, P8) showed a reliable decline on the subscale Resting. Two out of these five participants (P1, P3) met the criteria of a clinically significant change (CSC).

4.3.6. Quality of life

None of the participants met the criteria of a reliable change on the subscales *Physical functioning*, *Emotional well-being*, *Pain* and *General health*.

One out of eight participants (P4) showed a reliable, but not clinically significant, increase in perceived quality of life on the subscale *Role functioning/physical* and a reliable, but not clinically significant, decline in perceived quality of life on the subscale *Energy/fatigue* (RCI, CSC).

On the subscale *Role functioning emotional*, the RCI showed a reliable increase of perceived quality of life for two out of eight participants (P1, P3). For one participant this change was clinically significant (CSC). For one out of eight participants (P2) the RCI showed a reliable, but not clinically significant, decline in perceived quality of life on the subscale *Role functioning/emotional*.

The RCI showed a reliable, but not clinically significant, increase in perceived quality of life for three out of eight participants (P3, P5, P6) on

the subscale *Social functioning*.

One out of eight participants (P4) showed a reliable, but not clinically significant decline in perceived quality of life on the subscale *Social functioning*.

5. Discussion

Visual inspection shows that the use of Reducept for chronic pain resulted on average in a decrease of pain intensity during the intervention phase, for four out of eight participants. Our results on the reduction of pain intensity using VR are in line with the findings in previous studies into the effects of VR training in chronic pain that show that VR has only shown short-term effects due to mechanisms of distraction to reduce pain intensity and anxiety (Mallari et al., 2019; Pourmand et al., 2018). Building on these earlier findings, a return of pain intensity to baseline level after withdrawal of the intervention could be expected. However, contrary to that, for four patients an additional reduction in pain intensity was observed during the post-treatment phase. Our additional randomization test confirms the changes observed in visual analyses and indicates a statistically significant reduction in pain intensity.

This study is a first step in investigating the use of the VR application Reducept on chronic low back pain. The design we used (SCED) has several advantages compared to more traditional designs in scientific practice, such as Randomized Controlled Trials (RCTs). The most important advantage is that individual participants are intensively followed and evaluated over different time periods (phases ABA) in which they act as their own control condition. The use of frequent measurements facilitates a detailed monitoring of individual changes over time (Morley, 2017; Dugard et al., 2012). Moreover, by randomly picking the start and withdrawal points of the intervention, the risk of bias is reduced (Dugard et al., 2012).

In this study we examined a new virtual reality application aimed at reducing pain (Reducept) in patients with chronic low back pain.

Our results could be an indication that the use of Reducept goes beyond mere distraction as a longer lasting reduction in pain intensity was seen in 50% of the participants during the post-treatment phase. However, it is important to note that only one participant benefited significantly from a clinical perspective (i.e., a reduction of about two points or a reduction of about 30%).

Also, the fact that reliable changes were observed in some participants in pain catastrophizing, pain coping strategies, and perceived quality of life that are indicated as perpetuating factors in chronic pain, could also be an indication that possible beneficial effects of Reducept cannot be explained by distraction alone. We hypothesize that Reducept changes the attitudes and beliefs about pain resulting in the above-mentioned positive findings. Although the observed changes were small, only one participant reached a decline of clinical significance. Because of the fact that the content of Reducept is newly developed and it is still unclear what the exact working mechanism are, it is important for both science and clinical practice to get more insight in these changes and the possible underlying mechanisms for example by investigating separate elements of the intervention.

Interestingly, the effects that emerged were among participants 3 and 8, who had the highest pain intensity score compared to the other participants as well as the highest mean one the PCS (including catastrophizing).

Consistent with fear-avoidance models, we hypothesize that their higher levels of perceived pain and catastrophic interpretation of pain stimuli also account for higher levels of avoidance of activities that may cause pain or thinking about pain. Avoidance is a factor that may contribute to maintenance of chronic pain symptoms (Claes et al., 2015).

It is possible that using Reducept can prevent avoidance. Participants are invited to the intervention, in a calm and friendly way, to turn their attention specifically to the pain and formulate helpful thoughts regarding their pain (Control room).

Table 3

Outcome measures pre-post treatment measurements.

Participant	P1	P2	P3	P4	P5	P6	P7	P8
Measure	PCS (SD = 12.50, $r = 0.92$)							
Mean baseline	30(M)	50 (T)	49(M)	20(M)	40(M)	40(M)	27(M)	46(M)
Post intervention	31(T)	42(T)	39(T)	15	–	39(T)	30(T)	26(T)
RCI	–.20	1.60	2.00*	1.00	–	0.20	–0.60	4.00*
Measure	SCL-90 (SD = 48.51, $r = 0.81$)							
Baseline	124 (M)	159 (T)	178(M)	104(M)	110(M)	166(M)	114(M)	161(M)
Post intervention	112 (T)	158 (T)	130 (T)	99 (T)	–	165 (T)	122(T)	144(T)
RCI	0.40	0.03	1.60	0.17	–	0.03	–0.27	0.56
Measure	TSK (SD = 6.6, $r = 0.77$)							
Mean baseline	54 (M)	36 (T)	45(M)	38(M)	35(M)	48(M)	40(M)	45(M)
Post intervention	51(T)	36(T)	38(T)	33(T)	–	46(T)	38(T)	42(T)
RCI	0.67	0	1.56	1.12	–	0.45	0.47	0.67
Measure	PCI Pain Transformation (SD = 0.64, $r = 0.70$)							
Mean baseline	10(M)	7(T)	12(M)	10(M)	10(M)	10(M)	8(M)	8(M)
Post intervention	11(T)	7(T)	9(T)	9(T)	–	12(T)	9(T)	9(T)
RCI	–2.04*	0	6.12*(**)	2.04*	–	–4.08*(**)	–2.04*	–2.04*
Measure	PCI Distraction (SD = 0.64, $r = 0.67$)							
Mean baseline	15(M)	16(T)	11(M)	11(M)	11(M)	16(M)	18(M)	12(M)
Post intervention	14(T)	13(T)	16(T)	12(T)	–	16(T)	17(T)	13(T)
RCI	1.92	5.77*(**)	–9.6*(**)	–1.92	–	0	1.92	–1.92
Measure	PCI Reducing demands (SD = 0.59, $r = 0.62$)							
Mean baseline	7(M)	9(T)	8(M)	7(M)	7(M)	6(M)	10(M)	10(M)
Post intervention	8(T)	7(T)	9(T)	5(T)	–	6(T)	12(T)	7(T)
RCI	–1.96	3.92*(**)	–1.96	3.92*(**)	–	0	–3.92*(**)	5.88*(**)
Measure	PCI Retreating (SD = 0.55, $r = 0.71$)							
Mean baseline	12(M)	13(T)	17(M)	11(M)	10(M)	11(M)	9(M)	14(M)
Post intervention	8(T)	9(T)	17(T)	9(T)	–	9(T)	13(T)	14(T)
RCI	9.52*(**)	9.52*(**)	0	4.76*(**)	–	4.76*(**)	–9.52*(**)	0
Measure	PCI Worrying (SD = 0.55, $r = 0.81$)							
Mean baseline	15(M)	18(T)	26(M)	13(M)	15(M)	25(M)	15(M)	27(M)
Post intervention	15(T)	18(T)	20(T)	12(T)	–	27(T)	14(T)	23(T)
RCI	0	0	17.65*(**)	2.94*	–	–5.88* (**)	2.94*	11.76* (**)
Measure	PCI Resting (SD = 0.64, $r = 0.71$)							
Mean baseline	14(M)	13(T)	14(M)	8(M)	12(M)	12(M)	15(M)	16(M)
Post intervention	11(T)	14(T)	10(T)	7(T)	–	12(T)	15(T)	17(T)
RCI	7.32*(**)	–2.43*	9.75* (**)	2.43*	–	0	0	–2.43*
Measure	SF 36 Physical functioning (SD = 27.42, $r = 0.93$)							
Mean baseline	20(M)	25(T)	58(M)	68(M)	75(M)	23(M)	28(M)	5(M)
Post intervention	15(T)	40(T)	75(T)	70(T)	–	25(T)	35(T)	15(T)
RCI	0.49	–1.95	–1.65	–0.20	–	0.29	0.68	–0.97
Measure	SF 36 Role functioning/physical (SD = 40.78, $r = 0.84$)							
Mean baseline	0(M)	25(T)	0(M)	0(M)	175(M)	0(M)	0(M)	0(M)
Post intervention	0(T)	0(T)	25(T)	50(T)	–	25(T)	0(T)	0(T)
RCI	0	1.08	–1.08	–2.17*	–	–	0	0
Measure	SF 36 Role functioning emotional (SD = 40.71, $r = 0.83$)							
Mean baseline	50(M)	100(T)	17(M)	100(M)	100(M)	0(M)	100(M)	0(M)
Post intervention	100(T)	33(T)	100(T)	100(T)	–	0(T)	100(T)	0(T)
RCI	–3.54*	4.75*	–5.88* (**)	0	–	0	0	0
Measure	SF 36 Energy/fatigue (SD = 22.39, $r = 0.86$)							
Mean baseline	65(M)	55(T)	42.5(M)	77.5(M)	52.5(M)	42.5(M)	42.5(M)	17.5(M)
Post intervention	60(T)	50(T)	35(T)	50(T)	–	50(T)	30(T)	30(T)
RCI	0.42	0.42	–0.22	2.32*	–	–0.63	1.05	–1.05
Measure	SF 36 Emotional well-being (SD = 21.97, $r = 0.90$)							
Mean baseline	80(M)	52(T)	52(M)	90(M)	86(M)	42(M)	96(M)	52(M)
Post intervention	84(T)	36(T)	56(T)	92(T)	–	48(T)	92(T)	60(T)
RCI	–0.41	1.63	–0.41	–0.20	–	–0.61	0.41	–0.81
Measure	SF 36 Social functioning (SD = 25.43, $r = 0.85$)							
Mean baseline	43.75(M)	37.50(T)	50(M)	75(M)	62.50(M)	12.50(M)	37.5(M)	12.50(M)
Post intervention	50(T)	37.50(T)	87.50(T)	87.50(T)	–	37.50(T)	50(T)	12.50(T)
RCI	–1.41	0	–8.44*	8.44*	–	–5.63*	–2.82*	0
Measure	SF 36 Pain (SD = 25.46, $r = 0.78$)							
Mean baseline	28.75(M)	45(T)	27.50(M)	67.5(M)	57.5(M)	5(M)	26.25(M)	5(M)
Post intervention	45(T)	35(T)	57.50(T)	67.50(T)	–	0(T)	45(T)	30(T)
RCI	0.96	0.59	–1.78	0	–	0.30	–1.11	–1.48
Measure	SF 36 General health (SD = 21.11, $r = 0.78$)							
Mean baseline	60(M)	45(T)	62.50(M)	62.50(M)	45(M)	55(M)	25(M)	45(M)
Post intervention	60(T)	65(T)	50(T)	65(T)	–	55(T)	20(T)	35(T)
RCI	0	–1.43	0.89	–1.18	–	0	–0.71	0.71

Note: in **bold*** RCI Significant reliable change. (**) CSC Clinically significant change. M = Mean T1, T2, T = Total score.

A factor in this study that might have played a role in the lack of clinical relevance among/with each participant, might have been the duration of the pain complaints.

This study especially concerns long-suffering chronic back pain patients for whom there is no further medical treatment available.

Patients in this study all fit into the last step of the stepped care model from the *NHG standaard Pijn* (2015). Stepped care starts with the least intensive form of adequate treatment and, if necessary, takes it one step further. The steps in the model are as follows: Step 1: prevention and self-care; Step 2: monodisciplinary diagnosis, pain education and treatment in primary care; Step 3: multidisciplinary diagnosis, pain education and treatment in primary care in collaboration with the second line; Step 4: multidisciplinary diagnosis, pain education, and treatment in the second or third line.

It is likely that the effect of Reducept is more significant in the population of chronic pain patients who fit the first steps of the model rather than the last. Reducept could possibly be a more stand-alone therapy in the first step and an add-on therapy in the steps that follow.

An important question is whether our results (concerning pain intensity, psychological complaints, pain catastrophizing, fear of movement, pain coping skills and quality of life) could be more significant with different “dosages” of VR sessions. Little is known about the optimal dosage level of VR in chronic pain patients. It is suggested that there is a need for a larger dose of VR therapy to impact chronic pain conditions than acute pain conditions (Mallari et al., 2019). However, this suggestion is based on two studies and more research is needed to draw firm conclusions about the optimal dosage. This study used 45-min VR sessions three times a week for 21–26 days. An important consideration here was the fact that the training did not take place at home but in a hospital setting and we tried to minimize the participants’ burden. Although the developers of Reducept recommend a month of VR home based training on a daily basis, there is a lack of scientific evidence and consensus on the optimal dose of VR for chronic pain. It is therefore possible that more frequent sessions can produce a reduction in pain intensity that has a more clinically relevant duration.

Another important question is which specific elements of the Reducept VR application contribute to the reduction of pain intensity and reported improved quality of life.

Seven out of eight participants indicated that they had ‘the impression’ that the element ‘Control room’ was helping them the most. It may be that the level of participation in VR plays an important role in this experience. Research comparing psychological treatments such as CBT and MBCT in the treatment of chronic pain suggests that the degree of participation could be more important than the specific psychological technique used in the treatment of chronic pain (Burns et al., 2022). Reducept encourages participants to actively participate in the virtual environment which could explain the positive therapy outcome. Further research should therefore investigate whether or not certain features of the VR training Reducept are more effective than others by investigating its five different parts (see description of Reducept in Methods section) separately.

In terms of the feasibility of Reducept in practice, it is remarkable to note that the multiple visits to the hospital to engage with the same content were not a problem for our participants.

However, it is plausible that this may be the case in other settings. One option would be to use Reducept at home, as the intervention can be delivered with little to no additional instructions. This would allow for use on a larger scale. Further research could replicate this study in a different setting to determine its feasibility or could focus on the effects of Reducept when used at home.

It is noteworthy is that compliance to the intervention was high. Seven out of the eight participants reported that they would recommend Reducept to other patients with chronic low back pain. Although participants showed no significant difference in perceived quality of life on the RAND 36, they all reported that, during an oral evaluation at the last session, Reducept helped them to cope better with their pain and

thereby improved their quality of life. Even though this study contributes to the knowledge of the impact of Reducept on chronic low back pain some limitations must be noted. Firstly, this study focusses only on chronic low back pain and uses a small sample size ($N = 8$). We therefore need to take restrictions to generalizability of our findings to other patients and pain conditions into account. Next to that, age may be an important variable. Chronic low back pain is a health condition that is common among the elderly people. Most of our participants were aged above 60, with the median age at 73 years old. Although all our participants reported enjoying VR and did not experience problems with it, they were less familiar with technology than most younger people. Different effects may be seen in a younger population. To investigate the generalizability of our findings in different populations further research is needed.

Secondly, all data was collected using self-reports, a common limitation of this kind of data is the occurrence of self-reporting bias, meaning that results can be influenced by factors such as social desirability, recall period or selective recall. Lastly, the fact that no active control or placebo treatment was offered makes it impossible to determine whether results can be attributed to Reducept alone. Factors such as personal attention during the study or positive treatment expectations may as well have played a role in observed effects. Future research should use controlled conditions to further elucidate the effect of Reducept in addition to distraction during VR exposure.

This study showed that Reducept can be feasible and may have the potential to positively contribute to the treatment of chronic pain. Further investigation regarding its clinical relevance and external validity is needed. In line with Morley (2017), replication of SCEDs is recommended. In this context larger scale research (Randomized Controlled Trials) would be needed. The effect of Reducept in patients with shorter lasting chronic pain conditions are of particular interest. In addition, the use of other outcome measures such as Quebec Back Pain Disability Scale (QBPDS), Brief Pain Inventory (BPI), or more idiosyncratic measures in further research might yield compelling results, especially due to the fact that idiosyncratic measures are more sensitive to individual changes.

As for the intervention, it would be interesting to determine the effects, in any, when complemented with homework assignments. This may contribute to the transfer of pain management skills to everyday life.

6. Conclusion

Despite the limitations, the current study demonstrated the positive effects of Reducept on pain intensity in two out of eight participants.

The data in this study pointed to the positive effect of Reducept on perpetuating factors such as chronic pain in some participants. However, the results relating to these factors were mixed and only small indications of a clinical relevance were found.

Further testing using a larger cohort and a good distribution by age is warranted. By itself, Reducept is not able to treat chronic low back pain, but it could be used as a complementary treatment to predominant treatments. The mixed results highlight the fact that Reducept could be helpful for individual patients. Therefore, further investigation into this innovative new treatment is recommended in order to gain more insight into its working mechanisms, the duration of the optimal treatment period, predictors of treatment success, and its potential contribution for the treatment of different chronic pain conditions.

CRedit author statement

Froukje S. de Vries: Writing - Original Draft, Conceptualization, Methodology, Data curation, Visualization, Investigation. Robert T.M. van Dongen: Conceptualization, Writing- Reviewing and Editing. Dirk Bertens: Conceptualization, Writing- Reviewing and Editing Supervision.

Declaration of interest

Declarations of interest: none.

Data availability

Data will be made available on request.

References

- Ahmadpour, N., Randall, H., Choksi, H., Gao, A., Vaughan, C., & Poronnik, P. (2019). Virtual reality interventions for acute and chronic pain management. *The International Journal of Biochemistry & Cell Biology*, 114, 105568–105568. <https://doi.org/10.1016/j.biocel.2019.105568>.
- Arrindell, W. A., & Ettema, J. H. M. (2005). *Symptom checklist: Handleiding bij multidimensionale psychopathologie-indicator*.
- Burns, J. W., Jensen, M. P., Thorn, B., Lillis, T. A., Carmody, J., Newman, A. K., & Keefe, F. (2022). Cognitive therapy, mindfulness-based stress reduction, and behavior therapy for the treatment of chronic pain: Randomized controlled trial. *Pain*, 163(2), 376–389.
- Butler, D. S., & Moseley, G. L. (2013). *Explain pain* (2nd ed.). Noigroup Publications.
- Cherkin, D. C., Sherman, K. J., Balderson, B. H., Cook, A. J., Anderson, M. L., Hawkes, R. J., & Turner, J. A. (2016). Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: A randomized clinical trial. *JAMA*, 315(12), 1240–1249.
- Chou, R., & Schelleke, P. (2010). Will this patient develop chronic persisting low back pain? *JAMA*, 303, 1295–1302. <https://doi.org/10.1001/jama.2010.344>.
- Chuan, A., Zhou, J. J., Hou, R. M., Stevens, C. J., & Bogdanovych, A. (2021). Virtual reality for acute and chronic pain management in adult patients: A narrative review. *Anaesthesia*, 76(5), 695–704.
- Claes, N., Crombez, G., & Vlaeyen, J. W. (2015). Pain-avoidance versus reward-seeking: An experimental investigation. *Pain*, 156(8), 1449–1457.
- Dugard, P., File, P., Todman, J., & Todman, J. B. (2012). *Single-case and small-n experimental designs: A practical guide to randomization tests*. Routledge.
- Farrar, J. T., Young, J. P., Lamoreaux, L., Werth, J. L., & Poole, R. M. (2002). Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*, 94(2), 149.
- Fatoye, F., Gebrye, T., & Odeyemi, I. (2019). Real-world incidence and prevalence of low back pain using routinely collected data. *Rheumatology International*, 39(4), 619–626. <https://doi.org/10.1007/s00296-019-04273-0>.
- Fennema, M., & Zantema, L. (2019). *Reducept guidelines for the treatment of chronic pain (Version 1.0)*. Medical Center Leeuwarden.
- Ferraz, M. B., Quaresma, M. R., Aquino, L. R., Atra, E., Tugwell, P., & Goldsmith, C. H. (1990). Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. *Journal of Rheumatology*, 17(8), 1022–1024.
- Garrett, B., Taverner, T., Masinde, W., Gromala, D., Shaw, C., & Negraeff, M. (2014). A rapid evidence assessment of immersive virtual reality as an adjunct therapy in acute pain management in clinical practice. *The Clinical Journal of Pain*, 30(12), 1089–1098.
- Gatchel, R. J. (2004). Comorbidity of chronic pain and mental health disorders: The biopsychosocial perspective. *American Psychologist*, 59(8), 795.
- Gatchel, R. J. (2005). *Clinical essentials of pain management*. American Psychological Association.
- Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological Bulletin*, 133(4), 581.
- Gold, J. L., Belmont, K. A., & Thomas, D. A. (2007). The neurobiology of virtual reality pain attenuation. *CyberPsychology and Behavior*, 10(4), 536–544.
- Hartvigsen, J., Hancock, M. J., Kongsted, A., Louw, Q., Ferreira, M. L., Stéphane, G., Hoy, D., Karpunen, J., Pransky, G., Sieper, J., Smeets, R. J., Underwood, M., Buchbinder, R., Cherkin, D., Foster, N. E., Maher, C. G., van Tulder, M., Anema, J. R., Chou, R., & Woolf, A. (2018). What low back pain is and why we need to pay attention. *The Lancet*, 391(10137), 2356–2367.
- Heyvaert, M., & Onghena, P. (2014). Randomization tests for single-case experiments: State of the art, state of the science, and state of the application. *Journal of Contextual Behavioral Science*, 3(1), 51–64. <https://doi.org/10.1016/j.jcbs.2013.10.002>.
- Hoffman, H. G., Patterson, D. R., & Carrouger, G. J. (2000). Use of virtual reality for adjunctive treatment of adult burn pain during physical therapy: A controlled study. *The Clinical Journal of Pain*, 16(3), 244–250.
- Horner, R. H., Carr, E. G., Halle, J., McGee, G., Odom, S., & Wolery, M. (2005). The use of single-subject research to identify evidence-based practice in special education. *Exceptional Children*, 71(2), 165–179.
- Hoy, D., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., Williams, G., Smith, E., Vos, T., Barendregt, J., Murray, C., Burstein, R., & Buchbinder, R. (2014). The global burden of low back pain: Estimates from the global burden of disease 2010 study. *Annals of the Rheumatic Diseases*, 73(6), 968–974.
- Jacobson, N. S., Follette, W. C., & Revenstorf, D. (1984). Psychotherapy outcome research: Methods for reporting variability and evaluating clinical significance. *Behavior Therapy*, 15, 336–352.
- Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology*, 59(1), 12–19.
- Kamper, S. J., Apeldoorn, A. T., Chiarotto, A., Smeets, R. J., Ostelo, R. W., Guzman, J., & van Tulder, M. (2015). Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis. *Bmj*, 350.
- Kraaijaat, F. W., Bakker, A. B. H., & Evers, A. W. M. (1997). *Pijncooping-strategieën bij chronische pijnpatiënten: De ontwikkeling van de Pijn-Coping-Inventarisatielijst (PCI)*.
- Krasny-Pacini, A., & Evans, J. (2018). Single-case experimental designs to assess intervention effectiveness in rehabilitation: A practical guide. *Annals of Physical and Rehabilitation Medicine*, 61(3), 164–179.
- Kratochwill, T. R., Hitchcock, J., Horner, R. H., Levin, J. R., Odom, S. L., Rindskopf, D. M., & Shadish, W. R. (2010). *Single-case designs technical documentation*. <http://ies.ed.gov/ncee/wwc/pdf/wwc.scd.pdf>.
- Lambert, M. J., & Ogles, B. M. (2009). Using clinical significance in psychotherapy outcome research: The need for a common procedure and validity data. *Psychotherapy Research*, 19(4–5), 493–501.
- Leeuw, M., Goossens, M. E., Linton, S. J., Crombez, G., Boersma, K., & Vlaeyen, J. W. (2007). The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *Journal of Behavioral Medicine*, 30(1), 77–94.
- Mallari, B., Spaeth, E. K., Goh, H., & Boyd, B. S. (2019). Virtual reality as an analgesic for acute and chronic pain in adults: A systematic review and meta-analysis. *Journal of Pain Research*, 12, 2053.
- Marcuzzi, A., Wrigley, P. J., Dean, C. M., Graham, P. L., & Hush, J. M. (2018). From acute to persistent low back pain. *PAIN Reports*, 3(2). <https://doi.org/10.1097/PR9.0000000000000641>.
- Martinez-Calderon, J., Meeus, M., & Struyf, F. (2018). The role of psychological factors in the perpetuation of pain intensity and disability in people with chronic shoulder pain: A systematic review. *BMJ Open*, 8, Article e020703. <https://doi.org/10.1136/bmjopen-2017-020703>.
- Morley, S. (2017). *Single case methods in clinical psychology: A practical guide*. Routledge.
- Ogles, B. M., Lunnen, K. M., & Bonesteel, K. (2001). Clinical significance: History, application, and current practice. *Clinical Psychology Review*, 21, 421–446.
- Onghena, P., Tanious, R., De, T. K., & Michiels, B. (2019). Randomization tests for changing criterion designs. *Behaviour Research and Therapy*, 117, 18–27.
- Parker, R. I., Vannest, K. J., & Davis, J. L. (2011). Effect size in single-case research: A review of nine nonoverlap techniques. *Behavior Modification*, 35(4), 303–322.
- Pijn, N. W. (2015). NHG-Standaard pijn. *Huisarts en Wetenschap*, 58(9), 472–485.
- Pijnpatiënten naar één stem. (2022, 11 november). Zorgstandaard Chronische Pijn. <https://www.pijnpatiëntennaar1stem.nl/zorgstandaard-chronische-pijn/>.
- Pourmand, A., Davis, S., Marchak, A., Whiteside, T., & Sikka, N. (2018). Virtual reality as a clinical tool for pain management. *Current Pain and Headache Reports*, 22(8), 1–6.
- Schepens, M. H. J., Leusink, M., Eleveld, H., Prenger, A., & Berger, M. Y. (2019). Increase in opioid prescribing in extramural care in The Netherlands: Assessment of use and prescription behaviour, based on claims data. *Nederlands Tijdschrift voor Geneeskunde*, 163.
- Shafshak, T. S., & Elnem, R. (2020). The visual analogue scale versus numerical rating scale in measuring pain severity and predicting disability in low back pain. *Journal of clinical rheumatology: Practical reports on rheumatic & musculoskeletal diseases*.
- Sullivan, M. J., Bishop, S. R., & Pivik, J. (1995). The pain catastrophizing scale: Development and validation. *Psychological Assessment*, 7(4), 524.
- Tegner, H., Frederiksen, P., Esbensen, B. A., & Juhl, C. (2018). Neurophysiological pain education for patients with chronic low back pain. *The Clinical Journal of Pain*, 34(8), 778–786.
- The ultimate guide to the Reducept game. <https://www.reducept.com/blog/ultimate-guide-reducept-game>. (Accessed 28 November 2022) Accessed on.
- Traeger, A. C., Hübscher, M., Henschke, N., Moseley, G. L., Lee, H., & McAuley, J. H. (2015). Effect of primary care-based education on reassurance in patients with acute low back pain: Systematic review and meta-analysis, 2015 *JAMA International Medicine*, 175(5), 733–743. <https://doi.org/10.1001/jamainternmed.2015.0217>.
- Van der Zee, K., & Sanderma, R. (1993). RAND-36. Northern Centre for health care research. *University of Groningen*, 28(6). the Netherlands.
- Vlaeyen, J. W., Crombez, G., & Linton, S. J. (2016). The fear-avoidance model of pain. *Pain*, 157(8), 1588–1589.
- Vlaeyen, J. W., Kole-Snijders, A. M., Boeren, R. G., & Van Eek, H. (1995). Fear of movement/(re) injury in chronic low back pain and its relation to behavioral performance. *Pain*, 62(3), 363–372.
- White, O. R. (1972). *The split-middle: A quickie method of trend analysis*. Eugene, OR: Regional Center for Handicapped Children.
- World Health Organization. (2019). *International statistical classification of diseases and related health problems* (11th ed.) <https://icd.who.int/>.
- Zantema, L., & Fennema, M. (2018). *Reducept protocol for pain education*. White Paper Reducept <https://www.reducept.com/sites/default/files/documents/Whitepaper-Reducept-Mar2021-CE.pdf>.