# Experimental pain reduction in two different virtual reality environments: a crossover study in healthy subjects

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## ABSTRACT

The literature on unique virtual reality (VR) attributes impacting pain reduction is scarce. This study investigated the effect of two VR environments, with differing cognitive load (CL) demands, on experimental pain levels. Sixty-two students underwent psychophysical thermal pain tests, followed by exposure to tonic heat stimulation under one of three conditions: low CLVR (LCL), high CLVR (HCL), and a control. Significantly greater pain reduction occurred during VR compared to the control condition. Cognitive components predicted pain reduction during HCL only. Cognitive load involved in VR may influence the extent of pain decrease, a finding that may improve treatment protocols and promote future research.

## 1. INTRODUCTION

Distraction is a process in which attention is directed away from the nociceptive stimuli and results in change in the quality and quantity of pain (Van Damme, et al., 2010). Distraction can be achieved when attention is directed towards another sensory modality such as visual, auditory or tactile stimuli (Miron, et al., 1989), and is commonly evoked by various cognitive tasks (Eccleston & Crombez, 1999). Several former studies have suggested that the cognitive load involved in the task impacts the level of pain decrease (Miron et al., 1989).

Virtual reality (VR) is an advanced and useful technology that can be used for distraction from pain (Mahrer & Gold, 2009). Most of the previous studies examining the effect of VR on pain included burn pain patients, demonstrating the effectiveness of the technique in relieving pain during wound care (Hoffman et al., 2004; 2008) and physical therapy (Carrougher et al., 2009). In the laboratory setting, there is also evidence showing the efficacy of VR in reducing experimental evoked pain in healthy subjects; such studies were conducted using diverse methodologies regarding both pain measures and VR paradigms (i.e. Hoffman et al., 2003). However, there is scarce literature examining the specific attribute of VR in reducing pain or relating to the cognitive effort that individuals need to invest in the environment in order to perform the task correctly, a key for implementing the approach as part of individualized medicine.

Therefore, the aims of the present study were to: (1) investigate the effect of participation in two VR environments, which differed in terms of cognitive load (CL) demand on experimental evoked pain scores, in healthy subjects; (2) identify predictive factors affecting pain reduction during participation in VR.

## 2. MATERIALS AND METHODS

### *2.1 Subjects*

Sixty-two healthy subjects (31 males, 31 females, mean age= 24.2 SD=3.7 years), with an age range of 18–35 years, who were Hebrew speakers, free from any type of pain, not taking any medication, and able to communicate and understand the purposes and instructions of the study.

### *2.2 Experimental Pain Models*

*Cold Pressor Test (CPT)* – cold pain threshold, tolerance and intensity. The CPT apparatus (Heto CBN 8-30 Lab equipment, Allerod, Denmark) is a temperature-controlled water bath with a maximum temperature variance of ±0.5 C, which is continuously stirred by a pump. Subjects were instructed to place their right hand in the CPT in a still position. A stopwatch was simultaneously activated, and subjects were requested to keep their hands submerged in the cold water for as long as possible. A cut-off time of 180 seconds was set for safety reasons. Subjects were instructed to indicate the exact point in time when the cold sensation began to elicit pain. The time until the pain was first perceived was defined as time to pain onset (seconds). In the current study, the water temperature of the CPT was 5ºC. Immediately after hand withdrawal, subjects were asked to mark their maximal pain intensity on a 0–100 numerical pain scale (NPS), where 0 represented "no pain" and 100 represented "the worst pain one could imagine." The latency of intolerability (spontaneous hand removal) was defined as pain tolerance (seconds). Tolerance for subjects who did not withdraw their hand for the entire 180 seconds was recorded as 180 seconds.

*Thermal Sensory Analyzer (TSA)* – thermal thresholds and pain intensity. Cold and heat pain thresholds were determined with the method of limits on a Medoc TSA-2001 device (Medoc, Israel). A Peltier thermode (30 x 30 mm) was attached to the skin above the thenar eminence. The baseline temperature was set at 32.0°C and was increased or decreased at a rate of 1°C/s. The stimulator temperature range was 0–50°C. Subjects were instructed to press a switch when the stimulus was first perceived as painful heat or cold. Three readings were obtained for each thermal modality (cold and hot), and their averages were determined as pain threshold scores. The TSA was also used to determine sensitivity to noxious heat stimulation. Subjects were exposed to tonic heat stimulation (46.5ºC, for 120 seconds) on the medial part of their left ankle and asked to report the perceived pain intensity (NPS 0–100).

*Assessment of CPM.* Conditioned pain modulation (CPM) is considered to be a manifestation of pain inhibition. CPM describes a state whereby the response to a given noxious test stimulus is attenuated by another conditioning stimulus that is simultaneously administered to a remote area of the body (Yarnitsky et al., 2010). In order to induce a CPM effect, phasic heat stimulations were given and considered the "test stimulation," whereas cold stimulation was used as a "conditioning" stimulation. For further elaboration see Demeter et al. (2014).

### *2.3 EyeToy*

The current study included two EyeToy (Sveistrup et al., 2003) environments: both environments were taken from "EyeToy Kinetic" (EyeToy games CD). The environments were chosen because of their similar motor requirements. In the first environment, named "Backlash," the subject is required to move his upper limbs and right leg, to avoid contact with four paddles, two paddles on each side of the screen, with a central circle. In the second environment, named "Equilibrium," the subject is required to move his upper limbs and right leg and be precise in touching light beams appearing on the screen in different positions.

### *2.4 Self-Feedback VR Inventory*

For the purpose of the current study, four questions were chosen from the Presence questionnaire (Witmer & Singer, 1998). The questions were chosen based on an analysis conducted by the researchers comparing the differences between the two VR environments, as well as the activity analysis results. The inventory includes a Likert scale of 1–5 (1=not at all, 5=a lot) which evaluates: 1. the ability to predict what will happen in response to the subject's action (anticipation); 2. the feeling of skilled movement and interaction with the VR environment (movement skills); 3. the ability to block external distraction and concentrate on a task (attention and cognitive inhibition); 4. the extent of physical effort demand during task (physical effort).

### *2.5 Activity Analysis Form*

In order to thoroughly analyze and identify different aspects of each VR environment, "expert validity" was conducted with four experts, using an activity analysis form (Murphy & Davidshofer, 1994). This qualitative-based form includes 73 items reviewing general aspects of the activity (16 items, such as: activity description, required preparations or activity structure) and activity performance components: motor (16 items), sensory (16 items), cognitive (14 items), psychological (19 items) and neuromuscular (8 items). The experts rated each item, answering whether the specific attribute is manifested in each of the VR environments. In addition, they provided a qualitative evaluation regarding the VR environments s/he was exposed to (Drake, 1991).

### *2.6 Study Procedure*

*Determining VR Environment Characteristics.* Four experienced Occupational therapists actively participated in each VR environment and completed the activity analysis form immediately afterwards. Intraclass correlations (ICC) as estimates of interrater reliability were calculated using SPSS software version 19. The results showed that in the LCLVR, ICC= .92 $p<.000$, and in the HCLVR, ICC= .95 $p<.000$. Meaning that, there was a high level of agreement between raters regarding the activity analysis of both VR environments. According to the experts' evaluation, the main characteristics of each environment were identified and representative titles were given. Specifically, it was found that although both environments were based on a similar motor task, the "equilibrium" environment involved a higher cognitive load and demanded more cognitive resources (attention, accurate movement, problem solving) compared to the second environment – "Backlash." Consequently, the "Backlash" VR environment was named low cognitive load virtual reality (LCL), whereas the "equilibrium" environment was named high cognitive load virtual reality (HCL).

### *2.7 Study Design*

The study was approved by the ethical committee of the University of Haifa, Faculty of Social Welfare & Health Sciences. Each subject received an explanation of the study, signed an informed consent form to participate in the study, and then underwent a set of pain training tests and an introduction to VR environments. Ten minutes later, a battery of pain tests was performed to determine each participant's baseline sensitivity to pain. The battery included measuring heat and cold pain thresholds (TSA), sensitivity to noxious cold (time to pain onset, tolerance and intensity) and CPM, as explained above. All tests were conducted in a random order with an interval of five minutes between them. Immediately afterward, each subject went through three separate experimental conditions in a random order: A) LCL; B) HCL; or C) heat stimulation without VR (the control condition).

During each condition, the subject was exposed to tonic noxious heat stimulation (46.5°C, for 140 sec) applied to the medial part of the left ankle. Heat pain intensities (NPS 0–100) were reported six times: 10, 40, 70, 100, 130 seconds from the beginning of the heat stimulation, as well as 10 seconds after the stimulation was completed. The exposure to each VR environment lasted 120 seconds parallel to the heat stimulation, beginning 10 seconds following the commencement of the heat application (right after the first NPS report). Consequently, four NPSs were measured during participation in VR. Immediately after participating in each VR environment, subjects completed the self-feedback VR inventory, providing feedback regarding their experience in VR as commonly used in other VR studies (Yarnitsky et al., 2010).

### *2.8 Statistical Analyses*

Descriptive statistics were used to describe subjects and study variables. Interrater reliability of the activity analysis form was examined by Intraclass correlations (ICC). Repeated measure ANOVA was performed to examine differences between the three study conditions in the extent of pain decrease. In order to examine differences between six measurements, the Bonferoni post hoc test was conducted. In order to examine interaction effect, repeated contrast was conducted. The maximal pain decrease from baseline was calculated for each study condition separately (i.e., Δ LCL, ΔHCL, ΔControl). The Spearman correlation test was performed to examine correlations between all pain measurers taken before the three study conditions and pain decrease following VR. Hierarchical regression was performed for examining the variables predicting pain decrease following VR. Results were considered significant at the 0.05 level. Findings are presented as mean±SEM.

## 3. RESULTS

All pain measures that were taken before the three study conditions are depicted in Table 1.

The mean (±SEM) scores of the self-feedback VR Inventory (1–5) were as follows: (1) following LCL: anticipation 3.8±.91; movement skills 3.9±.80; attention and cognitive inhibition 4.2±.64; physical effort 3±.87; (2) following HCL: anticipation 3.3±1.11; movement skills 3.1±.92; attention and cognitive inhibition 4.1±.85; physical effort 1.8±.85.

### *3.1 Effect of VR Participation on Pain Intensity – Within-Session Results*

*LCL Environment.* The mean BL heat pain score taken before exposure to VR was 63.6±3.3; 30 seconds after the heat stimulus was administered, the mean pain score dropped to 32.8±3 (test 1), 29.0±2.7 (test 2), 30.0±2.9 (test 3), and 33.0±3.2 (test 4). In the last heat measurement following 120 seconds from the beginning of the stimulation and right after VR was discontinued (test 5), the mean pain score increased to 47.8±3.5 (RM ANOVA, $F(5, 305) = 73.54$, $p<.001$, $\eta^2=.55$).

*HCL Environment.* The mean BL heat pain score taken before exposure to VR was 65.6±3.3; 30 seconds after the heat stimulus was administered, the mean pain score dropped to 33.2±24.9 (test 1), 32.7±3.2 (test 2), 35.4±3.6 (test 3), and 33.6±3.6 (test 4). In the last heat measurement 120 seconds from the beginning of the stimulation and right after VR was discontinued (test 5), the mean pain score increased to 45.4±3.9 (RM ANOVA, $F(5, 305) =58.92$, $p<.001$, $\eta^2=.49$).

**Table 1**. *Descriptive values of pain parameters examined before the study conditions.*

| | Heat pain intensity | Cold pain intensity | Cold tolerance (sec) | Cold threshold (Sec) | Cold threshold (°C) | Heat threshold (°C) | CPM |
|---|---|---|---|---|---|---|---|
| Mean±SEM | 51.6±3.7 | 83.4±1.7 | 33.8±5.2 | 4.9±.4 | 9.3±.9 | 46.5±.4 | 28.9±2.4 |
| Median | 53.5 | 85 | 20.5 | 4.0 | 8. 6 | 47. 6 | 25 |
| Range | 0–100 | 40–100 | 6–180 | 1–19 | 0.3–25.6 | 36.9–50 | 0–70 |

*Control Session.* The mean BL heat pain score, was 63.9±3.2, which decreased to 48.4±3.2 at test 1 (RM ANOVA, $F(5,305) = 17.26$, $p<.001$, $\eta^2=.22$). During this session, across the following four measurements, pain ratings were similar: 48.0±3.3, 52.6±3.5, 56.4±3.7 and 55.3±4 (tests 2, 3, 4 and 5 respectively).

The maximal pain reduction was found to be between test 1 (BL) and test 2. Therefore, the difference between these two measures was calculated and the value, named ΔVR (Δ LCL= Δ low cognitive load VR), ΔHCL= (Δ high cognitive load VR, was used for further statistical analyses.

**Table 2**. *Mean ±SEM and F values of repeated measures for each study condition separately*.

| | BL | Test 1 | Test 2 | Test 3 | Test 4 | Test 5 | F |
|---|---|---|---|---|---|---|---|
| LCL | 63.6±3.3 | 32.8±3 | 29.0±2.7 | 30.0±2.9 | 33.0±3.2 | 47.8±3.5 | 73.54** |
| HCL | 65.6±3.3 | 33.2±24.9 | 32.7±3.2 | 35.4±3.6 | 33.6±3.6 | 45.4±3.9 | 58.92** |
| Control | 63.9±3.2 | 48.4±3.2 | 48.0±3.3 | 52.6±3.5 | 56.4±3.7 | 55.3±4 | 17.26** |

*** p<.001*

### *3.2 Effect of VR Participation on Pain Intensity – Comparison between Sessions*

No significant differences were found between the three pain scores at baseline (RM ANOVA, $F(2,122) =.64$, $p=.53$). However, the reduction in pain intensity across the entire 140 seconds was significantly different between study conditions [$F(10, 610) = 14.53$, $p<.001$, $\eta^2=.19$]. Repeated contrast tests showed a significantly greater reduction in pain in VR conditions compared with control conditions between BL and test 1 [$F(2, 183)=14.97$, $p<.001$, $\eta^2=.14$). In addition, there was a significant increase in pain ratings in test 5 in VR conditions only ($F(2,183) =21.92$, $p<.001$, $\eta^2=.19$). (Figure 1).

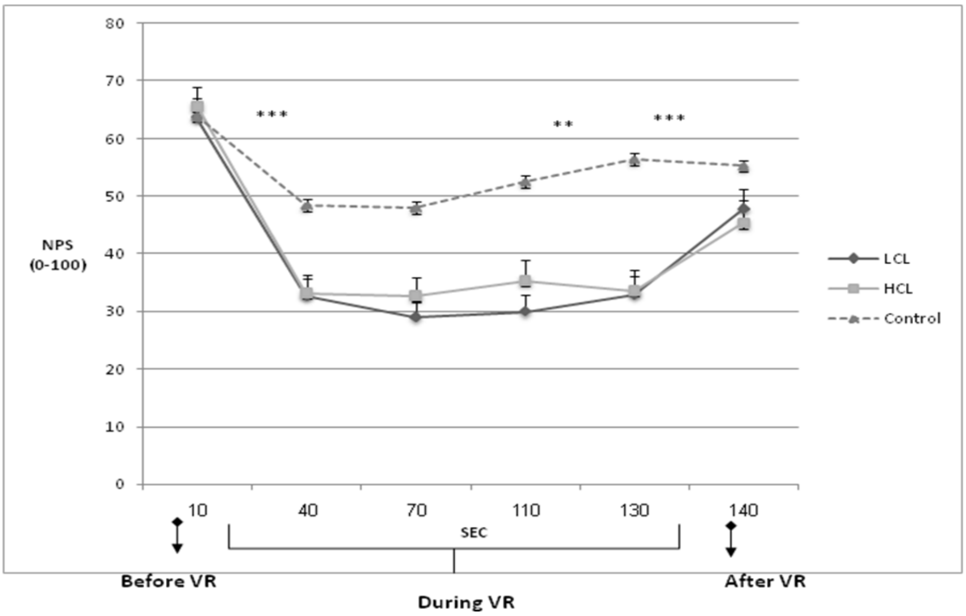
*Correlations between the Battery of Pain Measures and Maximal Pain Decrease in Three Study Conditions.* In the LCL environment, the Spearman correlation showed a negative correlation between ΔLCL and heat pain threshold ($r=-.27$, $p=.03$), and a positive correlation with heat pain intensity ($r=.33$, $p=.01$). In addition, there was a positive correlation between ΔLCL and CPM ($r=.39$, $p=.002$). In the HCL environment, only one correlation was found to be significant; this was between ΔHCL and CPM ($r=.40$, $p=.001$). All other correlations were not found to be significant.

### *3.3 Regression Analyses*

In order to identify predicting variables for pain reduction, hierarchical regression analysis was conducted for each of the study conditions. The following variables were examined as possible predictors: gender, all pain measures, and four statements of self-feedback VR inventory (anticipation, movement skills, attention and cognitive inhibition, physical effort). In the LCL condition, hierarchical regression showed that gender explained 6.1% of the pain decrease variance, meaning that pain was less decreased in women than in men ($\beta=0.25$, $p=0.05$). CPM added another 7.5% of the explained variance, meaning that the extent of CPM predicted pain decrease ($\beta=0.28$, $p=0.03$). (See Table 3).

Hierarchical regression showed that gender predicted 10% of the explained variance in the HCL condition, as well, meaning that pain was less decreased in women than in men ($\beta=0.31$, $p=0.01$). CPM predicted 11.6% of the explained variance, meaning that the extent of CPM predicted pain decrease ($\beta=0.35$, $p=0.01$). In addition, two statements of the self-feedback questionnaire (anticipation + attention and cognitive inhibition) added another 20.2% of the explained variance, meaning that the higher the score for abilities of anticipation; attention and cognitive inhibition, the more the pain decreased ($\beta=0.40$, $p=0.001$). (See Table 4).

In the control condition, no predicting variables were found (F (4, 56) = 1.89, p=.13).




**p<.01, ***p<.001

**Figure 1.** *Heat pain intensity during three study conditions (mean±SEM). Asterisks represent differences between the two VR conditions and control within two adjacent time points. LCL=low cognitive load VR, HCL=high cognitive load VR.*

**Table 3**. *Hierarchical regression for predicting variables of pain decrease in an LCL environment.*

| | *Model 1* | | | *Model 2* | | |
|---|---|---|---|---|---|---|
| Variable | B | SE B | β | B | SE B | β |
| Gender | 9.21 | 4.70 | .25* | 6.53 | 4.70 | .18 |
| CPM | | | | .29 | .13 | .28* |
| | | .061 | | | .136 | |
| F for change in $R^2$ | | 3.84* | | | 5.01* | |

*p≤.05 Note: male:0, female: 1

**Table 4**. *Hierarchical regression for predicting variables of pain decrease in an HCL environment.*

| | *Model 1* | | | *Model 2* | | | *Model 3* | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | B | SE B | β | B | SE B | β | B | SE B | β |
| Gender | 14.33 | 5.65 | .31* | 10.24 | 5.51 | .22 | 14 | 5 | .31** |
| CPM | | | | .44 | .15 | .35** | .33 | .14 | .27* |
| A+CI | | | | | | | 10.91 | 2.9 | .40*** |
| ant. | | | | | | | -5.03 | 2.19 | -.24* |
| $R^2$ | | .10 | | | .21 | | | 41.2 | |
| F for change in $R^2$ | | 6.42* | | | 7.88** | | | 9.95*** | |

*p≤.05 **p≤.01 ***p≤.001

Note: CPM: conditioned pain modulation; A+CI: attention + cognitive inhibition;

ant.: anticipation; male: 0, female: 1

## 4. CONCLUSIONS

The findings of the current study show that: (1) during VR with two different cognitive load tasks, pain ratings were significantly reduced with no difference in the reduction extent between the two virtual environments; (2) attention and cognitive inhibition, as well as anticipation, predicted pain reduction in the HCL environment only.

The effectiveness of the VR technique on pain relief was shown in various clinical pain conditions (i.e. Hoffman et al., 2004), and in the laboratory setting, demonstrated its alleviating effect on experimental evoked pain (i.e. Hoffman et al., 2003). Yet, the data is limited in examining the VR environment attributes that impact pain reduction. One study compared the effects of two different environments (warm and cold) on thermal pain intensities in healthy volunteers (Mulhberger et al., 2007). The authors hypothesized that a cold environment would reduce heat pain and vice versa. Nevertheless, this hypothesis was refuted when no differences were found in the effect of each environment on pain in both models. Law et al. (2010) examined whether increasing the demand for central cognitive processing (e.g., working memory and emotional control) involved in a distraction task would increase tolerance for cold pressor pain. They compared interactive versus passive distraction tasks via a VR-type helmet, and demonstrated that the effect of distraction on cold pain tolerance was significantly enhanced when the distraction task included greater demands for central cognitive processing.

The fact that the settings of these laboratory studies are diverse in many aspects points to the barriers that limit the generalization of conclusions from one study to another. The current study adds the knowledge that participation in VR reduces experimental pain intensity regardless of a specific cognitive demanded environment. While the fact that VR is an efficient pain distracter is not novel, the similarity of those two chosen environments in their ability to reduce pain was surprising. We believe that although a distinction in the cognitive load between the two tasks was verified, the cognitive load per se was not distinguished enough in this study. When we initially chose the VR environments we wished to minimize bias as much as possible by choosing similar tasks through the means of general presentation and motor activity. Even though the main parameter that was identified as diverse was the amount of cognitive load involved, it could be that the variation between environments was not sharp enough. Therefore, no difference in their impact on pain was found. Hence, the contribution of the cognitive load on pain reduction as was shown in previous studies (Eccleston & Crombez, 1999) cannot be ruled out due to the negative results of the present study; further studies are warranted in order to address this issue.

The present study also identified predictive factors affecting pain reduction during VR. Three predictors were identified. The first two predictors, including gender and CPM, are discussed in a previous publication (see: Demeter et al., 2014). The last and best predictor identified in this study as an efficient pain reducer under VR included the following cognitive components: (1) attention and cognitive inhibition and (2) anticipation. These cognitive components made an impact only when a high cognitive effort was required within the HCL VR environment.

The link between pain and cognitive performance has been previously observed in experimental and clinical settings (i.e. Coen et al., 2008). Attention constitutes the most studied cognitive component in relation to pain. While attending to a painful stimulus generally increases perceived intensity (Van Damme et al., 2010), previous studies have found that only a sufficiently attention-demanding cognitive task can divert attention away from pain (Eccleston & Crombez, 1999). The current study identified not only attention but also cognitive inhibition and anticipation as possible predictors for pain reduction during a task with a high cognitive load. Cognitive inhibition represents the ability to suppress irrelevant information and is considered a component of executive functions (EF). Other components of EF include the ability to formulate and maintain goals and strategies and to retain information for further processing (Connor & Maeir, 2011). To the best of our knowledge, there is sparse evidence relating to the link between EF and pain inhibitory control. One study evaluated these links with healthy volunteers exposed to a cold pain model (Oosterman et al., 2010); better cognitive inhibition (as measured by the Stroop test), but not other EFs, were found to be associated with less sensitivity with pain. Similarly, the current study showed that high perceived cognitive inhibition, as reported by the participant, predicted pain reduction.

Anticipation of action is another EF component (Barkley, 1997). When a task is performed repeatedly, it is more likely to be more automatically processed, which in turn reduces the accompanying cognitive load. This renders the task less effective in competing with pain for attention resources (Eccleston & Crombez, 1999). Our findings revealed that multiple task repetitions induce familiarization, which in turn enhances an individual's ability to anticipate more accurately the outcomes of his or her action. Thus, when a subject anticipated the outcome of his or her own actions, the subject was less distracted from pain.

**Study limitations:** The difference in cognitive load between the two VR environments was identified using a qualitative analysis process based on an activity analysis form as well as clinician's impressions. Further research is recommended in order to examine the cognitive load difference in quantitative measures.

In conclusion, this novel study obtained evidence for significant pain reduction during exposure to two VR environments as a function of the respective levels of cognitive demand. This aspect needs to be considered when customizing pain treatment protocols for patients coping with pain.

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