Effects of different virtual reality environments on experimental pain rating in post-stroke individuals with and without pain in comparison to pain free healthy individuals

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Abstract: Virtual reality (VR) is a computer-based, interactive multisensory simulation that occurs in real-time and has been used for pain reduction. The effectiveness of VR in reducing acute procedural pain has been established however the effectiveness of VR for chronic pain has not been tested. In addition, it is not clear whether different VR environments have a differential effect. The objective of this study was to determine whether different virtual environments (VE) had a differential effect on experimental pain rating in stroke patients with moderate to severe persistent clinical pain. Thirty six subjects participated in this study: twelve stroke patients without pain, twelve stroke patients with pain in their upper limb, and twelve pain free control participants. Quantitative sensory testing (QST) was conducted using the method of limits standard test protocol. Thermal stimuli were applied to subjects’ forearms within the range of weak to strong intensities to assess pain ratings of hot and cold stimuli while subjects were immersed in a virtual reality environment viewed through a head-mounted display. The VEs were randomly presented and were: cold (Snow World), Hot (Dante’s Canyon World), Neutral (black and white pillars), and No VR (control condition). After each thermal stimulus, subjects rated their pain perception on the basis of 0-100 scale of intensity. The mean pain ratings for hot and cold stimuli were calculated and used for analysis. Preliminary analysis of results showed that for patients in the stroke group with pain, Dante’s canyon (hot VE) decreased pain rating to both hot and cold stimuli (p<.05), but other VE environments had no effect. For patients with stroke but with no pain, neutral environment decreased pain ratings to both hot and cold stimuli (p<.05). Virtual reality environments differentially influence experimental pain ratings in patients with stroke, depending on the presence or absence of clinical pain.

Stroke is an injury to the brain due to the interruption of the blood supply, which causes destruction of a portion of brain tissue that can lead to weakness, numbness, paralysis, or cognitive problems. According to the World Health Organization 15 million people around the world suffer a stroke each year, with five million of those episodes resulting in death and a further five million people left with a permanent disability. In the U.S there are more than 5 million stroke survivors, and each year about 780,000 Americans suffer a new or recurrent stroke (The Stroke Association, 2008). The majority of people affected are over 65. Stroke is a leading cause of adult disability in the United States and Europe (Feigin, 2005). According to the American stroke association, Americans will pay about $65.5 billion in 2008 for stroke-related medical costs and disability. Pain is a common problem after stroke such that more than 20% of stroke patients have persistent moderate to severe pain (Jonsson, 2006) and about 8% will have central post-stroke pain (Canadian Stroke Network, 2006). The onset of pain may occur at the time of the stroke but often occurs several months later. The precise cause of central post-stroke pain is unknown, but most frequently pain occurs in a part of the body affected by the stroke often in the arm and leg on the stroke side. Movement, changes in temperature, or other unrelated stimuli may intensify the symptoms. Although many treatments are available for pain reduction, a survey conducted by the American Pain Society in 1999 found that more than four out of ten people suffering moderate to severe pain were unable to find adequate pain relief. Untreated chronic pain has a negative effect on an individual’s quality of life, decreasing the ability to concentrate, and work, often leading to depression, and loss of self esteem.
Virtual reality (VR) is a computer-based, interactive multisensory simulation that occurs in real-time and has been used for pain reduction (Weiss, 2006). It is believed that VR can provide a means of attracting attention to a specific virtual environment or alternatively distracting attention from a painful experience. In a series of preliminary studies, Hoffman, has shown that patients with severe burns using VR have reported large reductions in worst pain, pain unpleasantness, and time spent thinking about procedural pain (Hoffman, 2000, 2001a, 2004d) and report having more fun and less anxiety during various painful procedures. VR has also been used in different clinical settings to reduce dental pain (Hoffman, 2001b), prostate thermo-surgery (Wright, 2005), cancer pain (Gershon, 2004), and symptoms from cancer chemotherapy (Schneider, 2004). The effectiveness of VR for chronic pain has not been tested.

The use of immersive VR for post stroke pain has not been previously tested. In addition, it is not clear whether different VEs have a differential effect on pain ratings. This is an important question given that pain is known to be aggravated by heat and cold in (real) environments. The objective of this study was to determine whether different VEs have a differential effect on pain ratings in stroke patients with and without post-stroke (clinical) pain. We hypothesized that all virtual environments would reduce pain perception compared to the control condition. We also hypothesized that there would be a differential effect of thermal pain ratings based on their congruence with the thermal impression of the VE.

Methods

This was a 3x4 (group x VE condition) factorial design. A convenience sample of 36 subjects participated (see table 1): 12 stroke patients without pain, 12 stroke patients with central post-stroke pain (> 2 on a 0 - 10 Numerical Rating Scale) in their upper limb, and 12 pain free control participants. The study procedures were explained to all subjects and an informed consent was signed prior to participation.

Quantitative Sensory Testing

QST was done using the method of limits standard test protocol and the NeuroSensory Analyzer Model TSI-II (MEDOC Ltd., Ramat Yishai, Israel) on the painful and contralateral, pain-free forearm in counterbalanced order to assess pain perception to thermal hot and cold stimuli. The TSI-II uses a 30mmX30mm thermode which was placed on the skin of the patients’ forearm. Thermal stimuli were delivered by 15 brief (700ms) taps of stimuli via the thermode. Rate of temperature changes were between 0.3 °C/sec and 4.0 °C/sec. Temperatures between 36 - 47°C were used for hot stimuli and 30 °C with a rate decrease of 1°C/sec and an automatic safety lower limit of 4.5°C for the cold stimuli. In the methods of limits, stimuli (hot or cold) increased in intensity to a specific temperature for less than 1 second and then immediately returned to neutral temperature, in preparation for the next stimulus. Six clusters of stimuli were given, with up to six stimuli in each cluster, so a mean was taken in order to derive the pain rating. Interval between stimuli started from stimulus end to onset of next stimulus which lasted 6 seconds.

**Table1: Subjects Characteristics**

<table>
<thead>
<tr>
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<th>Subject Group</th>
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<tbody>
<tr>
<td></td>
<td>Control 12 (n=12)</td>
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<tr>
<td>Age</td>
<td>61.83 ± 7.2</td>
</tr>
<tr>
<td>Females**</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Males**</td>
<td>5 (41.6)</td>
</tr>
<tr>
<td>Time after stroke (year)</td>
<td>--------</td>
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</tbody>
</table>

* Values are mean ± SD  ** Values are n (%)
Virtual Reality Environments

The VE conditions (Figure 3) were randomly presented. They were as follows: 1) “Snow World” (cold) is an environment used extensively by Hoffman (2001). It has snowy mountain canyon scenes, 2) Dante’s Canyon (hot) is a modification of “Snow World. It has interesting red canyon scenes, 3) Neutral is comprised of alternating white pillars on a black background and a rolling ball that appears to draw the individual’s attention along the path (Powell, 2006). Since this virtual environment gives neither a hot nor a cold impression, it is likely to be neutral regarding temperature cues, and 4) No VE condition which is considered as the control condition (lights off, eyes closed). Each of the VR conditions lasted approximately 3-5 minutes, and subjects were allowed to rest between each condition. Subjects were passively exposed to each VE just prior to the test and the VE was continued for the duration of the tests followed by hot and cold pain stimuli on both arms. So, participants did not need to do anything with VE conditions and they just viewed the virtual environments while they were presented to the thermal stimulus. The computer was equipped with the ultra-high end NVIDIA Quadro FX 4500 graphics card (512 MB of high-speed GDDR3memory). Each VE was presented through a head mounted display (HMD) (Kaiser Optical Systems, Ann Arbor, MI, USA). To allow the subjects to experience the VE conditions as realistically as possible, we used an ICUBE head-tracking system that provided subjects to look in any direction and different parts of the virtual environments.

Figure 3: Virtual environments used for experiment: (A) Snow World; (B) Dante’s Canyon world; (C) Neutral VE (alternating white pillars on a black background)
Pain rating

To measure pain rating the thermode was fixed at the inner side of the forearm. During each VR period, three hot stimuli and three cold stimuli were delivered via thermode on the participant’s arm. Stimuli (hot or cold) increased rapidly in intensity to a specific painful temperature for less than 1 second and then returned to the baseline temperature (32 °C). After receiving the hot or cold stimulus, participants were asked to rate each stimulus according to their perceived pain intensity on a Numerical Rating Scale ranging from 0 to 100. Zero represented no pain at all and one hundred was the worst pain imaginable. By clicking the mouse, the thermode temperature immediately returned to neutral temperature and the pain rating was recorded. The procedure was repeated six times on the patient’s arm area (three hot and three cold stimuli). The mean pain rating was calculated and used for analysis.

Procedures

Experimental procedures were first explained and informed consent obtained. Group assignment was based on the history of stroke and presence (stroke with pain) or absence of pain (stroke without pain). The control group comprised an age matched convenience sample of pain free healthy subjects. All subjects were familiarized with the VR and QST equipment prior to the study. The experiments took place in a quiet air-conditioned environment in which the ambient temperature was stable and comfortable (22°C). Subjects then underwent psychophysical testing of thermal (hot and cold) stimuli using the method of limits standard protocol in order to determine hot and cold pain ratings. Participants then viewed the VE’s in random order through the HMD. The hot and cold stimuli were applied and pain rating judgments obtained while viewing the VE’s.

Data analyses

Normality of distribution for all data was analyzed with the Kolmogorov-Smirnov test. Summary descriptive statistics (means, minima, maxima and standard deviations) for demographic and outcome variables were computed and compared for all groups to establish group homogeneity. To analyze the significance of the main effects of group, stimulus, and VE condition on heat and cold pain ratings at each limb loca-

tion MANOVA (3 x 2 x 4) was performed using SPSS software, version 15. Data were also analyzed with repeated-measure ANOVAs containing the within-subject factors (VR environments and stimulus). Tukey HSD was used for post hoc analyses as appropriate. The sphericity assumption was checked with the Mauchly test. The level of significance was set at alpha level of p<0.05.

Results

Pain ratings

Data of pain ratings for the stroke side in each group of study were averaged separately for hot and cold stimuli and for each VR condition. MANOVA was significant for main effects of group and VE condition (2-way interactions) (Wilk’s lambda p= 0.039), but there was no interaction among VE condition, group, and type of stimulus (3-way interactions) (Wilk’s lambda p= 0.54). Moreover, the interaction between environment and temperature was not significant (Wilk’s lambda p= 0.64). For patients with stroke and pain, Dante’s canyon decreased pain rating to both hot and cold stimuli (p < .05), but other VE environments had no effect (Figure 4). For patients with stroke but no pain, Neutral environment decreased pain rating to both hot and cold stimuli (p < .05) (Figure 5). For healthy subjects there was no significant effect of VE albeit there was a trend towards Snow world decreasing pain ratings to hot stimuli, and Neutral environment decreasing pain ratings to cold stimuli (Figure 6). Finally there was no differential effect of VE condition on pain rating to thermal, warm and cool stimuli across the three groups (p > .5) when tested on the non-stroke arm in patients with, and without pain as well as one arbitrary arm of the control subjects (see table 2).
Figure 4: Mean pain ratings of the cold and hot pain stimuli of the patients in stroke group with pain during presentation of the virtual worlds.

Figure 5: Mean pain ratings of the cold and hot pain stimuli of the patients in stroke group without pain during presentation of the virtual worlds.

Figure 6: Mean pain ratings of the cold and hot pain stimuli of the patients in healthy group during presentation of the virtual worlds.
<table>
<thead>
<tr>
<th>Virtual Environments</th>
<th>Control</th>
<th>Stroke without Pain</th>
<th>Stroke with pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stimulus</td>
<td>Stimulus</td>
<td>Stimulus</td>
</tr>
<tr>
<td>Hot</td>
<td>Cold</td>
<td>Hot</td>
<td>Cold</td>
</tr>
<tr>
<td></td>
<td>41.36±7.5</td>
<td>38.05±6.8</td>
<td>45.59±8.1</td>
</tr>
<tr>
<td>Cold</td>
<td>35.97±7.1</td>
<td>32.66±7</td>
<td>41.20±6.6</td>
</tr>
<tr>
<td>Neutral</td>
<td>43.69±8</td>
<td>38.41±7</td>
<td>45.01±7.2</td>
</tr>
<tr>
<td>No VR</td>
<td>40.8±7.5</td>
<td>36.97±6.4</td>
<td>48.86±6.6</td>
</tr>
</tbody>
</table>

Table 2: Data of pain ratings for the non-stroke arm in patients with, and without pain as well as one arbitrary arm of the control subjects were averaged separately for hot and cold stimuli and for each VR

Discussion

This study compared the relative effectiveness of different VR conditions on subjective pain ratings to thermal (hot and cold) pain stimuli in stroke patients, with and without pain in comparison to healthy pain free control individuals. In line with our hypotheses, the results indicated that all VR conditions decreased pain ratings compared to the control condition (no VR). In addition, virtual reality appeared to differentially influence experimental pain rating to both hot and cold stimuli in patients with stroke. Dante’s canyon (Hot environment) in stroke group with pain and black and white pillars (Neutral environment) in patients with stroke but with no pain were the most effective environments. Moreover, there was no significant difference between hot and cold stimuli on experimental pain rating across groups when tested on the symptom free side.

In the present study, subjects in both stroke groups with and without pain reported a significant decrease in their pain rating during VR exposure, which is consistent with previous reports in subjects using an experimental pain paradigm (Hoffman, 2004c, 2004d). In addition, the results are generally consistent with the results of Mublberger (2007) who showed the pain experience was reduced in both the warm and the cold virtual environments compared to the control condition. Mublberger (2007) also indicated that hot stimuli were always perceived as less painful than cold stimuli, regardless of which VR condition was presented. This is contrary to the results of the present study which showed no difference between hot and cold stimuli. However, in both studies the interaction between environment and temperature was not significant. The differences may be due to the subject differences.

The small sample size in this study limits the generalizability of VR analgesic efficacy to larger populations of stroke patients. Individual differences and personal characteristics such as degree of ability to concentrate and immerse in VR environment may also mediate the effectiveness of VR. In addition, interactivity of VR environments may influence effectiveness. More research is needed on whether different types of chronic pains respond differentially especially if the level of interaction is different.

Conclusion

Results revealed that all virtual environments reduced pain ratings for hot and cold pain stimuli compared to a control condition. There was a differential effect of VE in individuals with stroke, based on the presence or absence of pain. Dante’s canyon was most effective in the stroke group with pain and a Neutral environment was most effective in patients with stroke but with no pain.

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References


