Virtual Reality (2008) 12:259–267
DOI 10.1007/s10055-008-0100-3

ORIGINAL ARTICLE

Virtual reality with fMRI: a breakthrough cognitive treatment tool

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Received: 29 July 2008 / Accepted: 9 September 2008 / Published online: 30 October 2008

Abstract The impact of virtual reality (VR) has been felt in a wide range of fields over the past 10 years. VR has been shown to be an effective treatment for anxiety, phobia, pain, posttraumatic stress disorder, stress inoculation training, and drug and alcohol addiction. The emerging application of VR in conjunction with functional magnetic resonance imaging (fMRI) is helping to improve upon current VR systems, and in the future will aid in creating more effective treatments for patients. With the advent of fMRI-safe VR goggles, brain activity can be studied in real time as a patient undergoes a VR treatment. The use of brain imaging during a VR session allows for the study of the brain itself as a patient interacts in a real-world environment. Studies are showing that by using VR in combination with fMRI, a new emergence of data about previously-elusive functions of the brain can be expected.

Keywords Virtual reality · fMRI · Brain imaging · Posttraumatic stress disorder · Cue exposure · Physiology · Exposure therapy

1 Introduction

Virtual reality (VR) is an effective tool to assess and treat disorders, rehabilitate after stroke and injury, and improve cognitive function (Wiederhold et al. 1998a; Wiederhold and Wiederhold 2000; You et al. 2005a, b; Grealy et al. 1999). VR creates a striking sense of "presence" for participants when they are in the virtual environment (Wiederhold 1998a, 1998b), and most participants report a complete sense of immersion (Glantz et al. 2003). VR allows investigators to understand, for the first time in a controlled environment, what is occurring when participants perform a near real-world task. Prior to the advent of VR, 2-dimensional videos or still photographs were the tools most often used by researchers, making it difficult to compare across studies or to replicate results.

The Virtual Reality Medical Center (VRMC), a world leader in virtual reality technology, has pioneered the use of VR exposure therapy in combination with physiological monitoring to treat panic and anxiety disorders, to treat posttraumatic stress disorder (PTSD), to create distraction from pain, and to aid in cognitive and physical rehabilitation. Controlled studies have continuously shown that this combination of VR with traditional therapies results in more successful outcomes being achieved in a highly efficient manner to treat a wide range of issues (Hoffman et al. 2000; Oyama 1998). In treating these patients, objective data that confirm the effectiveness of the VR and monitor the patient's response to the treatment are of the utmost importance. The most common measures used today to assess the impact of VR on a patient are self-report, simple cognitive testing, and physiological measurements that include skin conductance, peripheral skin temperature, respiration rate, and heart rate. New research in the field, however, is showing that it is time to take the next step beyond these less direct measurements by directly imaging the brain itself. With research that has recently been done on the impact of adding functional magnetic resonance imaging (fMRI) to VR treatment, the uses of VR are poised to branch into many new directions.

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Uses of virtual reality as a form of treatment
Anxiety disorders
Specific Phobias
Pain distraction
Physical rehabilitation
Cognitive and locomotor rehabilitation
Posttraumatic stress disorder (PTSD)
Stress inoculation training (SIT)
Alcohol and smoking cessation

2 Background

2.1 VR in the treatment of anxiety and, phobia

Results of VR treatments for anxiety and phobias have shown astonishing results. In studies on patients experiencing a fear of flying, VR graded exposure therapy (VRGET) has been shown to not only be effective to combat the fear of flying (Wiederhold et al. 1998a), but it has been shown to be more effective overall than imaginal exposure therapy (Wiederhold et al. 2001a; Wiederhold et al. 2002). In treating patients with agoraphobia, adding a VR aspect to traditional cognitive-behavioral therapy (CBT) to create what has been termed experiential-cognitive therapy allows for an eight-session treatment that gradually exposes the patient to the feared stimuli to desensitize the person, and can reduce or eliminate the fear (Vincelli et al. 2002). In a VR therapy system created by Hanyang University for the treatment of acrophobia (fear of heights), after just six sessions an acrophobic participant was able to visit a 63-story tall building in Seoul with minimal anxiety (Jang et al. 2002.)

2.2 VR in the treatment of pain

Additionally, as VR treatments to distract patients from pain mature, results have shown that these measures are continuing to be successful. In a recent study performed on 18 adult heart surgery patients, 2 pregnant women, a teenager, and an infant, a VR head-mounted display (HMD) that immersed patients in one of two virtual worlds—Enchanted Forest or Icy Cool World—increased patients' subjective ratings on a well-being scale and improved physiological characteristics post surgery. The heart surgery patients rated their well-being within 24–48 h post surgery on a scale of 1–10 (10 being the greatest amount of well-being) an average of 3.12 without the HMD and an average 7.25 with the HMD (Mosso et al. 2007). These results suggest that the VR immersion greatly improved their subjective well-being during the experience. In pregnant women, the use of the VR for 5 h during labor increased their subjective well-being ratings for a natural birth from a 1 to a 5, and when an epidural was used, from a 3 without VR to a 10 with VR. These results show that VR is also very effective at distracting from labor pain. The teenager (who was post-kidney transplant) improved his rating from a 1 without VR to a 9 with VR, and the infant's breathing rate decreased with the use of VR to show increased relaxation.

One of the VR environments used in the previous study, Icy Cool World, has been typically used with burn patients experiencing intense pain during treatment. While it has been long thought that the virtual scenario of Icy Cool World distracts burn patients from their original burn trauma by introducing them to an "icy" world, new research is showing that this may not in fact be the case (Mühlberger et al. 2007). While it has been shown that being in a VR environment distracts patients from pain in general (Rizzo et al. 2006; Hoffman 2004), being in a hot environment is not more successful at distracting from pain induced by cold stimuli, and being in a cold environment is not more successful at distracting from pain induced by hot stimuli (Mühlberger et al. 2007). Additional research on what virtual environments are most successful for each individual treatment is an important future direction for this field, and, as this article later discusses in the Hoffman (2004) pain distraction study, it is a question that may best be answered by combining VR with brain imaging.

2.3 VR in the treatment of alcohol dependence

It has recently been shown that addiction is a partially learned behavior. Volkow et al. (2008) propose a treatment model for addiction that strengthens the addict's control in the executive and inhibitory functions in the brain, weakens learned behaviors that have been conditioned in the addict, and minimizes the reward value of the drug while maximizing the reward value of non-drug related reinforcers. Because of this, exposure to cues and contexts that have been programmed in the addict's brain to elicit craving often contribute to relapse of the addictive behaviors. To desensitize addicts to these cues, and to break the link between the cues and the substance itself, cue-exposure therapy (CET) has been used. In a study of eight members of Alcoholics Anonymous (AA), a VR system was used that displayed two environments related to the desire to drink—a Japanese-style pub, and a western bar. After participants spent eight 30-min sessions in the virtual environment with a trained psychiatrist introducing the scenario each time, a reduction in craving was reported by the participants through the Alcohol Urge Questionnaire.

These results suggest that using VR in combination with CET can lead to an effective treatment to reduce craving associated with alcohol addiction (Lee et al. 2007).

2.4 VR in the treatment of posttraumatic stress disorder

The prevalence of PTSD in veterans returning from Iraq and Afghanistan is a concern of both the Veterans Administration and the Department of Defense (Hoge et al. 2004). According to a recent RAND corporation report (2008), 14% of all returning service members suffer from PTSD, with an additional 14% meeting the criteria for depression. This totals approximately 300,000 individuals who currently suffer from depression or PTSD (Tanielian and Jaycox 2008). With the prevalence of this disorder rising as increasing numbers of active duty military are in combat, the need for an effective treatment for this disorder has never been more inherent.

In a case report detailing the use of VRGET in combination with physiological monitoring, Wood et al. (2008) utilized a virtual combat environment to treat a patient diagnosed with combat-related PTSD. The patient was exposed to the environment in a graded fashion, beginning with the least intense stimuli, through a virtual reality HMD. The patient was seated, but could "walk" in the environment, drive a Humvee, or fire an M-16 rifle with the accompanying joystick. Since PTSD is characterized by a heightened state of arousal, levels of physiological arousal were recorded through skin conductance, peripheral skin temperature, respiration rate, heart rate, and heart rate variability as the patient explored the virtual environment. After ten sessions of this VRGET with increasing intensity of stressful stimuli, the patient's arousal was recorded again on the three measures. Results of these physiological measures documented a significant decrease in arousal after the ten sessions were complete (Wood et al. 2008). This use of VR in combination with physiological monitoring shows that through the use of VRGET, patients can experience a decrease in the physiological arousal that is characteristic of the symptoms of PTSD (Wood et al. 2008).

Using VR to treat PTSD has proven to have a 66–90% success rate in more than 15 studies of diverse populations, and the use of VRGET shows promising results. Because this method places a patient in a virtual environment where a trauma has occurred through a controlled situation that slowly exposes the patient to the traumatic situation, it best allows them to habituate to their PTSD symptoms and emotionally process the situation well enough to regain a sense of control (Wiederhold and Wiederhold 2006). In recent years, VRGET has been shown to improve the efficacy of treatment for PTSD in survivors of motor vehicle accidents, war combat, the 9/11 World Trade Center attacks, and others (Difede and Hoffman 2002; Rothbaum et al. 1999; Walshe et al. 2003; Wiederhold and Wiederhold 2000, 2004; Wiederhold et al. 2001a, 2001b, 2002).

This successful treatment of PTSD with VR has lead to the study of methods of PTSD prevention. VR is now actually contributing to the *prevention* of stress-related reactions to situations such as combat or medical emergencies through the advent of stress inoculation training (SIT). SIT is a type of training that prepares an individual for a stressful situation, which in effect can decrease the person's potential to experience a negative psychological reaction to the situation. SIT is accomplished in CBT through gradual, controlled, and repeated exposure to a stressor. The goal of this use of VR with CBT is to create a desensitization to the stressful stimuli, which in turn helps the person avoid either panicking or experiencing a fight-or-flight response when the situation occurs in real life. This type of "inoculation" against the possible psychological consequences of stressful environments both helps the individual more effectively accomplish the task at hand (whether it be a combat or a medical emergency), and aids in prevention of the long-term effects of stress, which may include PTSD (Wiederhold and Wiederhold 2008).

3 From physiology to neuroscience

Physiological monitoring of responses to VR scenarios meant to assess and treat phobias and anxiety disorders works by monitoring the participant's physiological responses to stressful stimuli. While phobias, anxiety disorders, and PTSD create physiological responses that can be easily recorded and measured, there are many more applications of VR for which physiology is not a good indicator of condition. For the use of VR in navigation tasks, pain distraction, rehabilitation, and alcohol and smoking cessation, a more comprehensive, objective method of measurement has been greatly needed. The effectiveness of treatment in these areas has often been evaluated with self-report data or simple cognitive tests. Not only are these methods often subjective and highly variable, they are only a second-hand assessment of functioning of the brain, and offer only limited knowledge about how, and why, the brain itself is working in each of these conditions.

Recently, the use of fMRI in conjunction with VR in navigation tasks, pain distraction, anxiety and PTSD treatment, rehabilitation, and alcohol and smoking cessation has opened a new pathway for the study and treatment of a wide range of diseases. By combining treatment with imaging of the brain itself, not only can the severity of the disorder be evaluated, and the treatment adjusted accordingly, but outcomes will be greatly improved through the creation of VR scenarios tailored to how the brain responds to stimuli. The use of brain imaging with VR provides an opportunity to see what is actually occurring in the brain before, during, and after treatment in a way that has never been possible in the past. The use of fMRI with VR is bringing the scientific community one step closer to completing the mapping of the neural correlates of addiction and disease, and, therefore, paving the way for more effective and more appropriate treatments in the future.

3.1 fMRI

The use of fMRI is a necessity in the world of cognitive research today. Because fMRI records the changes in blood flow and blood oxygenation linked to neural activity through detecting magnetic signal variation, this technology is able to study the complete brain. There are limitations to fMRI technology, however, and VR is a tool uniquely suited to work with the inflexibilities of the MRI machine. Current MRI technology limits the participant to lying on his/her back in the confines of the machine while a scan is being performed, and because of this position, the sense of reality that the participant would be experiencing while performing simple 2-dimensional tasks is greatly compromised. Some people become anxious when undergoing an MR scan (Evers 1999; Grey et al. 2000), and it may be difficult to accurately study the functioning of the brain in a situation with such limitations. VR, however, has been shown to distract patients from the MRI environment, and can even reduce feelings of claustrophobia (Garcia-Palacios et al. 2007). The combination of VR with fMRI is a breakthrough tool to use for studying the brain because it allows for the systematic presentation of 3-dimensional images, allowing neuronal activity to be examined as a patient performs a near real-world task.

3.2 fMRI-compatible head-mounted display

The recent development of the fMRI-compatible HMD has made it possible to examine the functions of the brain during virtual tasks (Ku et al. 2003). Because VR glasses have typically contained metal parts that are incompatible with the powerful magnet contained in the MRI machine, a cost-effective, compatible device had to be created before the use of VR with fMRI would be widely available. The Virtual Reality Medical Center, in response to a solicitation from the National Institute on Drug Abuse (NIDA), has developed a low-cost, fMRI-safe VR device for use in clinical research and treatment. Because these glasses are low in cost, easy-to-use, and fully integrated for use inside an MRI magnet, a wide range of clinicians, researchers, and cognitive investigators will have access to this increasingly relevant tool.

3.3 VR/fMRI applications on tasks of navigation

In two studies that pioneered the use of fMRI with VR to study alcohol intoxication, Calhoun et al. (2004a, 2004b) studied the effects of "driving" while under the influence of alcohol that results in different blood alcohol concentrations (BACs). The use of a virtual driving simulator allowed the study of a realistic driving experience while the participants were in the MRI scanner, and as they "drove," neural activity was recorded. Driving simulators are one of the most common tools used in the study of intoxication and its effects on driving, and now, with the advent of fMRI-compatible HMDs, the study of the brain itself while a participant "drives" under the influence is possible. The study found that when compared to the sober baseline condition, participants with a lower BAC (mean 0.41) actually performed slightly better on driving performance and reduced average speed. The higher BAC condition (mean 0.96), however, resulted in driving at higher speeds as well as a trend toward an increased number of collisions (Calhoun et al. 2005). The results obtained from the fMRI data displayed activation in visual areas as well as frontal eye fields, the dorsolateral prefrontal cortex, and the supplementary motor area (SMA) while driving, as expected. Results from fMRI also found a decreased correlation of all neural components for the higher BAC, which suggests that brain activation is in fact disrupted when a participant is under the influence (Calhoun et al. 2005).

In another study that combined VR with fMRI, a VR version of an 8-arm radial maze was used to assess the integrity of the hippocampus (HPC) in adults. It has been long known that rodents with HPC damage display severe spatial memory impairments during this task, but the maze has never been studied on humans with a neural monitoring component. Astur et al. (2005) hypothesized that hippocampal activation during performance of this task would be evident in MR scans performed while the participant was navigating the maze through a HMD. If hippocampal activation in tasks of navigation is applicable to humans as well, the frontal lobes would be activated during the working memory aspect of navigating the maze. When 13 healthy undergraduate volunteers were tested with fMRI, scans showed bilateral HPC deactivation as well as activation in the middle frontal gyrus (an area responsible for working memory). This imaging data confirmed the hypothesis, and it is now known that the hippocampus is involved in performing the radial arm maze in humans as well as in rats (Astur et al. 2005).

3.4 VR/fMRI applications of rehabilitation through neuroplasticity

In a study in which participants were immersed in a virtual prototype of the moving room paradigm (Lee and Aronson 1974) while undergoing fMRI in both a sitting down and a standing up condition, researchers found that subjects experienced egomotion (self-motion) and reported vection (sensation of egomotion induced by a moving background). The results of fMRI in the laying-down condition found activation in the prefrontal and parietal cortices, as well as in the bilateral cerebellum. These results suggest that being immersed in a virtual moving room actually activates parts of the brain associated with balance and motion (Slobounov et al. 2005). These fMRI results confirm that VR not only causes participants to "feel" like they are in a virtual world, but that it actually causes their brains to activate in places reserved for movement in response to physical stimuli. This phenomenon, known as Visual Field Motion, is explained by the fact that a person's perception of optic flow contributes to the sense of balance over the body because it indicates a change in posture relative to the environment or a change in body position (Slobounov et al. 2005). Because of this phenomenon, VR is able to "trick" the brain into perceiving a physical movement, even when the only stimulation that would indicate movement is the visual stimuli through the HMD. As this study shows, the advent of the HMD in conjunction with fMRI will allow the advance of research into the neural correlates of movement and balance in a way that has not previously been possible.

By helping to create positive neuroplastic changes in deficient areas of the brain, VR works as a form of therapy to improve cognitive and motor functioning. VR-induced cortical reorganization is looked at here with the use of fMRI in two types of locomotor functioning deficiencies—cerebral palsy and stroke.

In a study of VR therapy in a child with hemiparetic cerebral palsy performed by You et al. (2005a, b), fMRI results suggested evidence of neuroplasticity. The child, who suffered from underutilization of an arm because of having never-learned-to-use it (known as NLTU), was given a series of VR games that strengthen motor skills in the brain. The games were given to the child for 60 min a day, 5 days a week, for 4 weeks. At the conclusion of the therapy, motor function tests showed that motor performance increased by 43% for the shoulder, elbow, and forearm regions, 67% for the wrist, and 18.2% for the digits (You et al. 2005a, b). The fMRI results show cortical reorganization following VR therapy that coincides with the increased use of the affected arm, and supports the hypothesis that VR therapy creates positive neuroplastic changes by facilitating development of neural pathways related to locomotor recovery.

In the first fMRI study in the literature that offers evidence for locomotor recovery after VR sessions, ten stroke patients with hemiparetic stroke had significantly increased motor function after VR sessions. VR exercise programs called Stepping up/down, Sharkbait, and Snowboarding were given to stroke patients. These programs focused on exercising the trunk, pelvis, hip, knee, and ankle. This increase in motor function was confirmed by fMRI results in which the group that underwent VR had an increased laterality index (LI) in the primary sensorimotor cortex (You et al. 2005a, b).

3.5 VR/fMRI to relieve pain and assess its neural correlates

It has long been known that there is a strong psychological component to pain, and new VR data with fMRI are confirming this. In a study of healthy volunteers who received pain through an electrically-heated probe to the foot while inside an MRI machine, the control group reported a high degree of pain intensity and unpleasantness, and their fMRI scans confirmed this. A large increase in activity occurred in the areas of the brain known to be involved in perceiving pain: the primary and secondary somatosensory cortex, the insula, the thalamus, and the affective division of the anterior cingulate cortex. However, the VR group showed significantly different results. With the use of fMRI-safe VR goggles, the participants not only self-reported decreased levels of pain, but their fMRI scans actually showed a decrease in pain-related brain activity (Hoffman 2004). These results suggest that while a patient is undergoing VR treatment, their subjective levels of pain decrease not just because they are "distracted," and therefore not paying attention to their physical pain, but also because the introduction of VR actually decreases the amount of neural activity in regions associated with pain (Hoffman 2004). This finding suggests a strong tie between the psychological and neurological components of pain: When a person pays less attention to pain, pain intensity in the brain itself will decrease.

3.6 VR/fMRI to treat anxiety and assess PTSD

Undergoing an MR scan can create a high level of anxiety in some patients (Evers 1999; Grey et al. 2000), and in one large-hospital study, it was found that 14% of MRI patients had to be sedated in order to be able to undergo the required scan (Murphy and Brunberg 1997). Since VR is able to reduce anxiety and to create a "calming" effect by transporting users to gain a sense of being in a virtual environment, using VR to reduce anxiety while a patient is undergoing an MR scan is the logical next step. In a study of two patients who met the DSM-IV criteria for claustrophobia, both experienced such high levels of anxiety while inside a mock MRI machine for a 10-min "scan" that both asked to leave the scan early. Then, the patients were randomly assigned to either calming music or immersion in a virtual world known as SnowWorld. On the second mock MR scan, the patient who was assigned to the SnowWorld condition was able to complete the whole 10 min scan. Afterwards, this patient reported low levels of anxiety and an increased sense of self-efficacy. However, the patient who received the calming music on the second scan was not able to complete the entire scan and again asked to terminate the procedure early. The results of this study show that immersing patients in VR can lead to decreased anxiety as related to claustrophobia while the patient is in the VR environment (Garcia-Palacios et al. 2007).

Data from fMRI studies is proving increasingly relevant in confirming on a neurological level what has been observed with self-report and physiological data. For PTSD, physiological data has recently confirmed that VR immersion can reduce physiological arousal associated with this disorder (Wood et al. 2008). The next step for monitoring of PTSD symptoms, however, is to bring assessment and treatment into the realm of brain imaging through fMRI. In a study in progress using brain imaging to confirm the effects of VR therapy, Roy, et al report mild decreases in the Clinician-Administered PTSD scale (CAPS) was found in veterans suffering with PTSD and/or mild traumatic brain injury (mTBI) (Roy 2008, The ViRTICo Trial: Virtual Reality Therapy and Imaging in Combat Veterans with PTSD and Blast Injury [study in progress]). More research in this field needs to be done to confirm the neurological components of PTSD, and therefore more effectively treat this condition.

3.7 VR/fMRI to assess and treat drug and alcohol addiction

While it has been shown that VR is effective with CET to decrease the desire to drink alcohol and to smoke (Lee et al. 2003, 2007), the physical changes that can be seen in the brain as a result of this decreased desire have gone long undiscovered. In a study by Lee et al. (2005), eight adolescent smokers were recruited from a smoking cessation program in high school. Each of the eight participants reported smoking at least ten cigarettes per day. Participants were shown either a 2D or a 3D (VR) environment of neutral and smoking-related cues. Results showed that while the group mean of participants' brain activity in the 2D condition showed increased activity in participants' prefrontal cortex (PFC), left anterior cingulated gyrus, left SMA, right inferior temporal gyrus, right lingual gyrus, and right precuneus. In the VR condition, however, the PFC, the superior frontal gyrus, the superior temporal gyrus, the inferior occipital gyrus, and the cerebellum were also activated. These results suggest that the use of VR as opposed to 2D images not only activates participants' desire to smoke, but actually activates many of the components of attention, visual balance, and coordinating movement (Lee et al. 2005). This study both proves the effectiveness of the VR environment to elicit the desire to smoke and confirms that brain-related activity associated with smoking cues can be studied with the use of fMRI.

4 Future directions

4.1 VR and fMRI as a tool to assess, treat, and study the brain

In these pioneering studies that combine the ability of VR to assess and treat conditions with the ability of fMRI to find and confirm the neural correlates of such conditions, a new direction for cognitive research has truly been established. Through the use of VR to bring participants into a virtual world, and the use of fMRI to then study that world, a wealth of new information on the various diseases and disorders that science struggles with finding a cure for can truly be reached. Not only are the VR methods proven effective as a form of treatment, they improve upon existing methods of anxiety and phobia treatment, pain distraction, rehabilitation, and drug and alcohol addiction treatment to further the ability of medical science to understand and correct these disorders. While previous research has often relied on 2-dimension images to study and treat what occurs in the real world, VR allows for a midpoint between the endless possibilities of the real world and the strictly controlled environment of the clinic by bringing the real world inside. The use of VR in conjunction with fMRI allows for a way to study the complexities of the brain while still maintaining the control necessary to run an accurate experiment. These fMRI studies serve a dual purpose by also confirming, through the neural correlates fMRI can record, that VR does in fact work at the neurological level to create a near real-world environment that can distract participants from their pain, cure them of their phobia or addiction, and even help them rehabilitate portions of their brains.

4.2 Where to go from here

The use of VR in conjunction with fMRI is truly a unique tool that can resolve common clinical problems. In the past decade, VR has gone from using simple virtual worlds seen through huge, bulky devices, to complex virtual worlds that can be seen on devices no more intrusive than a pair of glasses. The advent of the fMRI-safe VR HMD has allowed patients to experience VR while their neural activity is being recorded in an MRI machine. Since VR is truly the closest thing to the real world that can be utilized in a laboratory environment, it will result in the most accurate data science has been able to obtain thus far about the living brain in action, and, as the emergence of new brain imaging technologies that are less bulky, more accurate, and less intrusive than fMRI continues, VR will become a necessary tool in the clinical, psychiatric, and research communities.

New Research into fMRI and Virtual Reality			
Navigation			
Astur, St Germain, Baker, Calhoun, Pearlson, Constable	VR version of radial arm maze task during fMRI may be used to assess integrity of hippocampus	"fMRI hippocampal activity during a virtual reality arm maze"	Applied Psychophysiology and Biofeedback, 30(3), 307–317, 2005
Parslow, Morris, Fleminger, Rahman, Abrahams, Recce	Study of 1 pt implicates rt hippocampal formation in spatial memory functioning using controlled VR	"Allocentric spatial memory in humans with hippocampal lesions"	Acta Psychologica, 118, 123–147, 2005
Slobounov, Wu, Hallett, Shibasaki, Slobounov, Newell	Activation of specific brain structures as subjects experienced egomotion & reported vection in VR moving room	"Neural underpinnings of postural responses to visual field motion"	Biological Psychology, 72, 188–197, 2006
Pain distraction			
Hoffman, Richards, Coda, Richards, Sharar	Strong sense of presence in VR despite fMRI distracting elements (loud noises)	"The illusion of presence in immersive virtual reality during an fMRI brain scan."	CyberPsychology & Behavior, 6(2), 127–131, 2003
Hoffman, Richards, Coda, Bills, Blough, Richards, Sharar	fMRI shows that VR reduces pain-related brain activity in five areas of the brain	"Modulation of thermal pain-related brain activity with virtual reality: Evidence from fMRI."	NeuroReport, 15(8), 1245–1248, 2004
Gold, Kim, Kant, Joseph, Rizzo	MR/CT scans show decreased pain during acute venipuncture procedure in children playing VR video game vs. controls	"Effectiveness of virtual reality for pediatric pain distraction during IV placement."	CyberPsychology & Behavior, 9(2), 207–212, 2006
Anxiety and PTSD			
Garcia-Palacios, Hoffman, Richards, Sharar	VR (vs. music) reduced anxiety from nine (0–10 scale) to three in single participant previously unable to complete MR scan	"Use of virtual reality to reduce claustrophobia during MRI scans"	Presented at CyberTherapy 11, Gatineau, Quebec, Canada, June 12–15, 2006
Roy, Francis, Banks-Williams, Friedlander, Taylor, Tarpley, Vythilingam, Blair, Grillon, McLellan, Lande, Difede, Rothbaum, Rizzo	Study in progress: Mild decreases in CAPS scores in both VR group ($n = 3$) & PE group ($n = 2$) in vets w/ & w/o PTSD &/or mTBI (four groups $\times$ 22n)	"The ViRTICo trial: Virtual reality therapy & imaging in combat veterans"	Presented at CyberTherapy 13, San Diego, CA, June 23–25, 2008
Rehabilitation sudies			
Ku, Mraz, Baker, Zakzanis, Lee, Kim, Kim, Graham	fMRI shows tactile feedback from fMRI-safe data glove w/vibratory stimulus enhances VR experience	"A data glove with tactile feedback for fMRI of virtual reality experiments"	CyberPsychology & Behavior, 6(5), 508, 2003
You, Jang, Kim, Hallett, Ahn, Kwon, Kim, Lee	After physical rehab w/VR IREX, fMRI shows cortical reorganization of locomotor functions in brains of patients with stroke	"Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke: an experimenter-blind randomized study"	Stroke, 36, 1166–1171, 2005
You, Jang, Kim, Kwon, Barrow, Hallett	After physical rehab w/VR IREX, fMRI shows cortical reorganization of locomotor functions in a brain of a child with cerebral palsy	"Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy"	Developmental Medicine & Child Neurology, 47, 628–635, 2005

Table continued

New Research into fMRI and Virtual Reality			
Alcohol and smoking studies			
Calhoun, Carvalho, Astur, Pearlson	Lower blood alcohol content (0.04) participants performed slightly better than higher (0.08) in VR driving test w/fMRI	"Using virtual reality to study alcohol intoxication effects on the neural correlates of simulated driving"	Applied Psychophysiology & Biofeedback, 30(3), 285–306, 2005
Young-chul Jung, M.D.,	Five sessions of VR cue exposure therapy/skill training over 2 wks decreased brain activation related to craving in 2 alcoholics (M, F)	"Functional Imaging data before and after VR based cue exposure therapy"	Personal communication, July 9, 2008
Moon, Graham, Lee	Six sessions of VR cue exposure therapy decreased brain activation related to craving in 8 M smokers	"The efficacy of cue exposure treatment for nicotine craving in a virtual environment"	Annual Review of CyberTherapy & Telemedicine, vol 5. San Diego, CA: IMI, 2007, 237–238
Lee, Lim, Wiederhold, Graham	fMRI shows that smoking cues in VR can evoke strong cravings more effectively than traditional methods	"A functional magnetic imaging (fMRI) study of cue-induced smoking craving in virtual environments"	Applied Psychophysiology & Biofeedback, 30(5), 195–204, 2005

References

Astur RS, St Germain SA, Baker EK, Calhoun V, Pearlson GD, Constable RT (2005) fMRI Hippocampal activity during a virtual radial arm maze. Appl Psychophysiol Biofeedback 30(3):307–317

Calhoun VD, Altschul D, McGinty V, Shih RA, Scott D, Pearlson GD (2004a) Alcohol intoxication effects on visual perception: an FMRI study. NeuroImage 21:15–26

Calhoun VD, Pekar JJ, Pearlson GD (2004b) Alcohol intoxication effects on simulated driving: exploring alcohol-dose effects on brain activation using functional MRI. Neuropsychopharmacology 29:2097–2107

Calhoun VD, Carvalho K, Astur R, Pearlson GD (2005) Using virtual reality to study intoxication effects on the neural correlates of simulated driving. Appl Psychophysiol Biofeedback 30(3):285–306

Difede J, Hoffman HG (2002) Virtual reality exposure therapy for world trade center post-traumatic stress disorder: a case report. Cyberpsychol Behav 5(6):529–535

Evers SR (1999) Anxiety of MR patients extends beyond claustrophobia. Diagn Imaging 21(7):41–43, 45, 48

Garcia-Palacios A, Hoffman HG, Richards TR, Seibel EJ, Sharar SR (2007) Use of a virtual reality distraction to reduce claustrophobia symptoms during a mock magnetic resonance imaging brain scan: a case report. CyberPsychol Behav 10(3):485–488

Glantz K, Rizzo AA, Graap K (2003) Virtual reality for psychotherapy: current reality and future possibilities. Psychother Theory Res Pract Train 40(1/2):55–67

Grealy MA, Johnson DA, Rushton SK (1999) Improving cognitive function after brain injury: the use of exercise and virtual reality. Arch Phys Med Rehabil 80(6):661–667

Grey SJ, Price G, Mathews A (2000) Reduction of anxiety during MR imaging: a controlled trial. Magn Reson Imaging 18(3):351–355

Hoffman HG (2004) Virtual reality therapy. Sci Am 291(2):58–65

Hoffman HG, Patterson DR, Carrougher GJ (2000) Use of virtual reality for adjunctive treatment of adult burn pain during physical therapy: a controlled study. Clin J Pain 16(3):244–250

Hoge CW, Messer SC, McGurk D, Cotting DI, Koffman RL (2004) Combat duty in Iraq and Afghanistan, mental health problems and barriers to care. N Engl J Med 351(1):13–22

Jang DP, Ku JH, Choi YH, Wiederhold BK, Nam SW, Kim IY, Kim SI (2002) The development of virtual reality therapy (VRT) system for the treatment of acrophobia and therapeutic case. IEEE Trans Inf Technol Biomed 6(3):213–217

Ku J, Mraz R, Baker N, Zakzanis KK, Lee JH, Kim IY, Kim SI, Graham SJ (2003) A data glove with tactile feedback from fMRI of virtual reality experiments. CyberPsychol Behav 6(5):497–508

Lee DN, Aronson E (1974) Visual proprioceptive control of standing in human infants. Percept Psychophys 15:529–532

Lee JH, Ku JH, Kim KU, Kim BN, Kim IY, Yang BH (2003) Experimental application of virtual reality for nicotine craving through cue exposure. CyberPsychol Behav 6(3):275–280

Lee JH, Lim Y, Wiederhold BK, Graham SJ (2005) A functional magnetic resonance imaging (fMRI) study of cue-induced smoking craving in virtual environments. Appl Psychophysiol Biofeedback 30(3):195–204

Lee JH, Kwon H, Choi J, Yang BH (2007) Cue-exposure therapy to decrease alcohol craving in virtual environment. CyberPsychol Behav 10(5):617–623

Mosso JL, Rizzo S, Wiederhold B, Lara V, Flores J, Espiritusanto E, Minor A, Santander A, Avila O, Balice O, Benavides B (2007) Cybertherapy: new applications for discomfort reductions. Med Meets Virtual Real 15:334–336

Mülhberger A, Wieser MJ, Kenntner-Mabiala R, Pauli P, Wiederhold BK (2007) Pain modulation during drives through cold and hot environments. CyberPsychol Behav 10(4):516–522

Murphy KJ, Brunberg JA (1997) Adult claustrophobia, anxiety and sedation in MRI. Magn Reson Imaging 15(1):51–54

Oyama H (1998) Virtual reality for palliative medicine. Stud Health Technol Inform 58:140–150

Rizzo A, Pair J, Graap K, Manson B, McNerney PJ, Wiederhold B, Wiederhold M, Spira J (2006) A virtual reality exposure therapy application for Iraq war military personnel with post traumatic stress disorder: from training to toy to treatment. Novel approaches to the diagnosis and treatment of posttraumatic stress disorder, vol 1. IOS Press, Amsterdam, pp 235–247

Rothbaum BO, Hodges L, Alarcon R, Ready D, Shahar F, Graap K, Pair J, Hebert P, Gotz D, Wills B, Baltzell D (1999) Virtual reality exposure therapy for PTSD Vietnam veterans: a case study. J Trauma Stress 12(2):263–271

Roy M (2008) The ViRTICo trial: virtual reality therapy and imaging in combat veterans. Presented at CyberTherapy 13, San Diego (in press)

Slobounov S, Wu T, Hallett M, Shibasaki H, Slobounov E, Newell K (2005) Neural underpinnings to postural responses to visual field motion. Biol Psychol 72:188–197

Tanielian T, Jaycox LH (eds) (2008) Invisible wounds of war: psychological and cognitive injuries, their consequences, and services to assist recovery. RAND Corporation, Santa Monica, 492pp

Vincelli F, Choi H, Molinari E, Wiederhold BK, Bouchard S, Riva G (2002) Virtual reality assisted cognitive behavioral therapy for the treatment of panic disorders with agoraphobia. Stud Health Technol Inform 85:552–559

Volkow ND, Fowler JS, Wang GJ, Baler R, Telang F (2008) Imaging dopamine's role in drug abuse and addiction. Neuropharmacology [Epub ahead of print]

Walshe DG, Lewis EJ, Kim SI, O'Sullivan K, Wiederhold BK (2003) Exploring the use of computer games and virtual reality in exposure therapy for fear of driving following a motor vehicle accident. CyberPsychol Behav 6(3):329–334

Wiederhold BK, Wiederhold MD (2000) Lessons learned from 600 virtual reality sessions. CyberPsychol Behav 3(3):393–400

Wiederhold BK, Wiederhold BK, Wiederhold MD (2004) Virtual reality therapy for anxiety disorders. American Psychological Association Press, Washington, D.C

Wiederhold BK, Wiederhold MD (2006) From SIT to PTSD: developing a continuum of care for the warfighter. Annu Rev CyberTher Telemed 4:13–18

Wiederhold BK, Wiederhold MD (2008) Virtual reality for posttraumatic stress disorder and stress inoculation training. J CyberTher Rehabil 1(1):23–35

Wiederhold BK, Gevirtz R, Wiederhold MD (1998a) Fear of flying: a case report using virtual reality therapy with physiological monitoring. CyberPsychol Behav 1(2):97–103

Wiederhold BK, Rizzo AA, Wiederhold MD (1998b) The use of virtual reality in psychology. Calif Psychol XXXI(6):25

Wiederhold BK, Gevirtz RN, Spira JL (2001a) Virtual reality exposure therapy vs. imagery desensitization therapy in the treatment of flying phobia. Towards CyberPsychology: mind, cognitions and society in the Internet age. IOS Press, Amsterdam

Wiederhold BK, Jang D, Kim S, Wiederhold MD (2001b) Using advanced technologies to treat fear of driving. Proceedings of the 9th Annual Medicine Meets Virtual Reality Conference. January 24–27, 2001, Newport Beach, California

Wiederhold BK, Jang DP, Gervitz RG, Kim SI, Kim IY, Wiederhold MD (2002) The treatment of fear of flying: a controlled study of imaginal and virtual reality graded exposure therapy. IEEE Trans Inf Technol Biomed 6(3):218–223

Wood DP, Murphy JA, Center KB, Russ C, McClay RN, Reeves D, Pyne J, Shilling R, Hagan J, Wiederhold BK (2008) Combat related post-traumatic stress disorder: a multiple case report using virtual reality graded exposure therapy with physiological monitoring. Med Meets Virtual Real 16:556–561

You SH, Jang SH, Kim YH, Hallett M, Ahn SH, Kwon YH, Kim JH, Lee MY (2005a) Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke. Stroke 36:1166–1171

You SH, Jang SH, Kim YH, Kwon YH, Barrow I, Hallett M (2005b) Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy. Dev Med Child Neurol 47:628–635