Pharmacology, Biochemistry and Behavior 91 (2009) 393–397

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

journal homepage: www.elsevier.com/locate/pharmbiochembeh

Quantitative electroencephalographic (qEEG) correlates of craving during virtual reality therapy in alcohol-dependent patients

Sang Hoon Lee [a], Doug Hyun Han [b,*], Seman Oh [a], In Kyoon Lyoo [c], Young Sik Lee [b], Perry F. Renshaw [d], Scott E. Lukas [e]

[a] Eun Hye Hospital, Incheon, South Korea
[b] Department of Psychiatry, Chung Ang University College of Medicine, Seoul, South Korea
[c] Department of Psychiatry, Seoul National University College of Medicine, Seoul, South Korea
[d] Brain Institute, University of Utah, Salt lake City, UT, United States
[e] Behavioral Psychopharmacology Research Laboratory and Sleep Research Program, McLean Hospital, Department of Psychiatry, Harvard Medical School, Belmont, MA, United States

ARTICLE INFO

Article history:
Received 15 June 2008
Received in revised form 5 August 2008
Accepted 9 August 2008
Available online 17 August 2008

Keywords:
Virtual reality
Alcohol dependence
Craving
EEG
Frontal cortex

ABSTRACT

Virtual reality (VR) is an evolving technology that is being applied to treat a wide range of medical and psychiatric diseases. A virtual reality therapy (VRT) with multisensory stimulation has been applied to patients with alcohol dependence (ADP). We hypothesized that the VRTP for alcohol dependence would reduce the craving for alcohol and increase alpha wave activity in frontal areas of individuals with ADP. Twenty ADP and eighteen ADP were exposed to a series of 10 VRTP sessions (VRTP-ADP) and cognitive behavioral therapy (nVRTP-ADP), respectively. Fifteen healthy controls were exposed to VRTP for comparing the changes of craving and EEG during all three phases of VRTP. The VRTP-ADP exhibited a greater decrease in craving after the 10th VRTP session, when compared to the nVRTP-ADP. Compared to the healthy control subjects, VRTP-ADP group showed higher magnitude of the change in craving throughout VRTP sessions. These results suggest that VRTP may be useful as an adjunct to treating alcohol dependence but may also serve as an evaluation tool to identify high-risk patients.

1. Introduction

Virtual reality (VR) was originally defined as I^3 for "Immersion–Interaction–Imagination" (Burdea and Coiffet, 1994). This distinction was made because the construct of VR requires that sensory systems are integrated with computerized models of the individual's environment. To effectively accomplish a true VR experience, it is felt that multiple sensory systems such as visual, auditory, tactic, smell and taste, should be included (Burdea, 1996).

Virtual reality is an evolving technology that has been applied to treat and study a variety of medical and psychiatric disorders (Cosman et al., 2002). It has been most successful in treating a spectrum of anxiety disorders, specifically certain phobias (North et al., 1998). The VR program for treating phobias (e.g., acrophobia, fear of flying, fear of public speaking) has consistently been reported to have an excellent outcome in relieving symptoms of anxiety and preventing relapse (Anderson et al., 2005; Jang et al., 2002; Klinger et al., 2004; North et al., 1998; Rothbaum et al., 2001).

A limited number of laboratories have reported that VR is a valuable tool for evoking cue reactivity to drug-related stimuli in an attempt to treat drug addiction. In a smoking cue-related virtual environment, evoked craving for tobacco has been more effective than traditionally used methods to reduce tobacco smoking (Baumann and Sayette, 2006; Lee et al., 2005). Lee et al. (2005) used functional MRI to demonstrate that cue-induced craving for tobacco in a virtual environment activated prefrontal cortex (PFC) including the superior frontal gyrus as well as the superior temporal gyrus, inferior occipital gyrus and cerebellum.

Multisensory integration involves using at least three of the senses (e.g., visual, vestibular, and somatosensory) to generate the VR environment. With this approach, Viaud-Delmon et al. (2006) found that subjects with high levels of anxiety were able to efficiently integrate vestibular and visual information in order to resolve internal conflicts about their phobias. Recently, Yong et al. (2007) reported that multisensory cues were strongly associated with stimulation, perception and translation.

Craving, an important element in the pathophysiology of alcoholism, has been known to play a role in controlled drinking (Robinson and Berridge, 1993; Wise, 1988), relapse (Anton, 1996; Ludwig et al., 1974), and prognosis of treatment (Littleton, 1995; Volpicelli et al., 1992). Because of its multidimensional construct (Myrick et al., 2004), a single aspect of craving is not adequate to define it. Currently, due to the use of various modalities for evaluation and treatment of alcohol dependence, the understanding of craving in alcohol dependence has been progressed (Myrick et al., 2004).

* Corresponding author. 140-757, Department of Psychiatry, Chung Ang University College of Medicine, Han Gang Ro 2Ga, Yong San Gu, Seoul, South Korea. Tel.: +82 2 748 98057; fax: +82 2 6381 9972.
E-mail address: hduk@yahoo.com (D.H. Han).

0091-3057/$ – see front matter.
doi:10.1016/j.pbb.2008.08.014

While the etiology of craving is not completely understood, it is presumed to be related to a dysfunction of the orbitofrontal cortex (OFC) and its subcortical connectivity to the limbic system that mediates reward processes. These areas (e.g., nucleus accumbens, amygdala) have been reported to be activated during craving using several different neuroimaging techniques such as SPECT, PET and fMRI (George et al., 2001; Modell and Mountz, 1995; Myrick et al., 2004). The OFC has been known to contribute to a variety of behavioral states and functions, including the processing of reward, emotion and decision-making, all of which are essential components of motivational-directed behavior (Bechara et al., 2000; Rolls, 2000; Schultz et al., 2000).

Electrocecephalography has been used to help localize the acute effects of drugs and drug-related cues on brain function. Lukas and colleagues (Lukas et al. 1986; Lukas and Mendelson, 1988; Lukas et al., 1990, 1995) have consistently reported the increased alpha EEG activity during euphoria after acute ethanol, cocaine and marihuana administration. Conversely, Bauer and Kranzler (1994) found that drug-related cues produce a diffuse decrease in EEG power and Liu et al. (1998) reported that cocaine-related cues increased EEG arousal (desynchronization) with the evidence of sharp decline in EEG power in the alpha1 band when compared to the neutral test session. Kim et al. (2003) showed that EEG changes were induced by alcohol cue exposure in alcohol-dependent patients.

Based on the literature to date, we hypothesized that VRTP would reduce craving for alcohol in patients with alcohol dependence, compared to general alcohol treatment (education and cognitive treatment). Furthermore, the reduction of craving would be associated with an increase of alpha EEG activity over frontal areas. To the best of our knowledge, this is the first multisensory stimulation virtual reality therapy for patients with alcohol dependence.

2. Material and methods

2.1. Participants

A total of twenty alcohol-dependent male inpatients (age 38.6±5.9, range 30–51 years), consuming 1744.5±446.6 ml/day of alcohol (Korean Sake (Soju)) agreed to participate in this study. A psychiatrist (Lee, S.H.) evaluated and diagnosed patients using DSM-IV. The other groups of 18 alcohol-dependent males with general treatment (education and cognitive treatment) (nVRTP-ADP) were age- (37.5± 4.6 yr), education- (9.3±1.7 yr) and alcohol consumption- (1683.0± 502.9 ml/day of alcohol) matched to the alcohol-dependent inpatients with VRTP (VRTP-ADP). There was no significant difference in age, education, alcohol consumption, smoking status, and craving for alcohol at baseline between VRTP-ADP and nVRTP-ADP (Table 1). Both VRTP-ADP and nVRTP-ADP groups had completed an inpatient alcohol detoxification program 7 days before being enrolled in this study. The treatment in which the nVRTP group received included 45-minute general treatment of cognitive behavioral therapy (6 sessions) and education (2 sessions). This has been performed 2 times/week for 5 weeks by two psychiatrists (S.M. Oh and S.H. Lee). During the study period, all patients with alcohol dependence were medication-free except for occasional small doses of a short-acting benzodiazepine for insomnia. There was no difference in cumulative dose and total frequency of consumption of lorazepam between VRTP-ADP and nVRTP-ADP throughout the period (Table 1). If patients took prn drug of benzodiazepine, the craving and EEG were assessed 48 h after drug administration. For the comparison of EEG pattern change, a group of 15 healthy adult males were age- (38.6±4.6 yr) and education-matched to the alcohol-dependent inpatients. The average alcohol consumption by the healthy controls was 32.39±21.2 ml/day. In all three groups, participants with a history of Axis I psychiatric disorder, head trauma, other drug abuse, mental retardation, visual and auditory impairment, or medical illness were excluded from the study. Written informed consent was obtained from all participants. All aspects of the clinical protocol were reviewed and approved by Institutional Review Boards in Eun-Hye Incheon state Hospital.

Table 1
Demographic characteristics

	VRTP-ADP (20)	nVRTP-ADP (18)	z/χ^2, p
Age (years)	38.6±5.9	39.1±5.8	−0.38, 0.70
Education (years)	9.1±1.7	9.3±1.6	−0.47, 0.65
Alcohol (years)	14.9±5.3	13.1±4.5	1.15, 0.25
Alcohol amt. (ml/day)	1744.5±446.6	1726.1±525.4	−0.08, 0.94
Craving	6.8±1.9	6.7±1.5	0.37, 0.71
Lorazepam			
Dose (mg)	4.5±2.1	4.7±1.8	0.24, 0.81
Freq (n)	6.0±3.4	6.1±2.9	0.06, 0.95
Smoker/non-smoker	15/5	13/5	0.04, 0.85

VRTP-ADP: Alcohol dependence patient with virtual reality alcohol treatment program (VRTP), nVRTP-ADP: alcohol dependence patient without VRTP, Education: number of years of education, Alcohol: mean lifetime duration of alcohol dependence, Alcohol amt.: consuming alcohol amount/day, craving: craving for alcohol, Dose: mean dose of lorazepam during research period. Freq: total number of lorazepam consuming during research period.

2.2. Virtual reality therapy (VRT)

The virtual reality therapy (VRT) consisted of a series of scenes that were associated with relaxation, simulating a high-risk situation (virtual alcohol cues) and then an aversive stimulation. The VR system includes two projectors, a silver-coated screen for stereoscopic display, VR goggles for the participant to view the images, a separate monitor for the experimenter/controller, a joystick input and a computer platform. This custom-made VRTP program allows the participants to select a type of alcoholic beverage and drinking situation to view during the high-risk situation. The therapist used the joystick to move the subject through the scenes and also change the subject's perspective of the drinking situation so that their environment was more realistic and craving experience was maximized for that situation. The VRTP was designed to be switched to the next stage when the participant experienced craving for 10 min, the high-risk situation or to the relaxation scenario when dysphoria emerged during the 10 min of the aversive scenario.

2.3. VRTP preparations

One psychiatrist and one nurse were present for every treatment session. The psychiatrist managed all treatment procedures as follows: 1) communicating with the participant via microphone or bell signal in the operating room; 2) operating the virtual reality computer system using a joystick and keyboard; 3) assessing craving with visual analog scale (VAS) during treatment and real time EEG monitoring; 4) closely observing the subjects for reactions such as sweating, nausea and vomiting when the participants were exposed to the aversive stimulation. In addition, we prepared medications including injection of short-acting benzodiazepine (lorazepam) for the unexpected emergent anxiety or behavioral outbursts. Subjects' psychological and medical conditions were constantly monitored before and after treatment.

2.4. Treatment room setting

The VRTP was delivered in a two-room environment with one room for the participant and the other for controlling the VR system. A glass wall separated the two rooms so that the participants could be monitored throughout the experiment. The EEG electrode array was set up in the room for the participants and the main EEG computer system was in a control room. A fiber-optic cable connected the two rooms to minimize electromagnetic interference artifact. The screen for image projection was located in front of the participants and a surround-sound speaker system was used to deliver the auditory

stimuli. An emergency bell was located on the participants' seat, which was connected to the control room, and was used to signal the experimental team if the participant wanted to stop the study.

2.5. Treatment procedures

The VRTP was offered to alcohol-dependent patients only after they had completed a 7-day inpatient alcohol detoxification period. Each session was run between 7:00 and 8:00pm, 2 times/week, for a total of 10 sessions. During that period, participants did not have any prescription medications except lorazepam (2–8 mg/day) for the prevention of withdrawal symptoms. After any alcohol withdrawal symptoms abated, a baseline EEG was collected with eyes closed in a light- and sound-attenuated room without any stimulation for 5 min. Each of the three treatment sessions (relaxation (5 min); high-risk situation (10 min); aversive stimulation (10 min)) was presented in succession. Visual analog scales, used to measure craving for alcohol, were completed by participants after each scenario.

2.5.1. Relaxation

The participant chose one of five different landscapes with which they were most comfortable. The therapist then asked the participant to recollect a happy situation while the landscape was projected on the screen. The participant was instructed to activate the bell when he experienced a sense of well-being and felt very relaxed. Thereafter, the therapist reviewed the visual analogue scales of craving, mood and anxiety and recorded the EEG activity while the participant kept his eyes closed.

2.5.2. High-risk situation (HRS: VR cue exposure)

The virtual drinking situations could stimulate multiple sensory functions, which included the following: visual, auditory and olfactory. Visual stimulations including four kinds of alcoholic beverage (beer, soju, whiskey, and wine) and snacks, and 4 drinking environments (beer garden, whiskey house, restaurant, and pub). The subject could select an alcoholic beverage and environment in line with his preference (tailor-made virtual alcohol cues). While the therapist created the drinking situation via the computer system in the operating room, the patient enjoyed the situation with the scene that he made. An alcohol-dipped cotton tissue using their beverage of choice was provided to the subject to provide olfactory stimulation. When the cue-induced craving increased to the maximum level with the sign of bell, the therapist checked the VAS for craving, anxiety, mood and EEG changes.

2.5.3. Aversive situation (AVS)

The aversive stimulations also included visual, auditory and olfactory stimuli. The aversive stimulation involved viewing a short movie depicting an alcohol-dependent patient who was vomiting. While the patient watched the movie, he drank a small amount of kefir. Kefir is a fermented milk drink, a gelatinous substance which includes bacteria and yeasts yielding a tart taste. This taste has been equated to being similar to that of vomitus. Therefore, the ingestion of a small amount of kefir, while seeing a vomiting-movie, encouraged patients to recollect unpleasant memories associated with frequent vomiting after excessive alcohol consumption. The auditory stimulation consisted of the sound of vomiting. When the patient was unable to tolerate aversive stimuli, he could press the bell located at the side of patient's seat. At this time, the therapist checked the visual analogue scale and EEG with eyes closed. When checking the EEG, the patient imagined the aversive scene and past experience with vomiting.

2.6. Assessment

The assessment was divided into two parts. First, we compared the effect on craving and EEG activity between VRTP and nVRTP group. Second, we also measured the changes in the craving and EEG activity between alcoholic patients and healthy control subjects for showing the effect of each stimulation during VRTP.

2.6.1. Craving scale

Alcohol craving was measured both before and after the VR treatment sessions throughout all three stages (Relaxation, HRS, and AVS). Alcohol craving was assessed using 10 point visual analog scale (VAS), similar to that used by Modell and Mountz (1995) and Kim et al. (2003). The subjects responded on a scale of 0 to 10, with "0" indicating "not at all" and "10" indicating "extremely".

2.6.2. EEG recording

The EEG in participants with alcohol dependence was assessed for significant change both before and after the VRTP.

For each phase of the treatment (Relaxation, HRS and AVS), 30 epochs (1 s each, for total of 30 s) of artifact-free data was collected from 5 min of continuous EEG during "eyes closed" condition. These EEG epochs were subjected to power spectral analysis using Fast Fourier Transformation (FFT). Frequency bands were defined as follows: delta (1.0 to 3.5 Hz), theta (4 to 7.5 Hz), alpha (7.5–12.5 Hz), and beta (12.5–25 Hz).

EEG acquisition was collected from the 19 monopolar electrode sites (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2) of the international 10/20 system referenced to linked earlobes. The electrophysiological data was acquired with a 32-channel Alpha-trace TC 32 EEG system (B.E.S.T medical systems, Wien, Austria) set with a 10 μV/mm sensitivity, a bandpass of 0.3–70 Hz, with a 60 Hz notch filter. Samples were digitized at a rate of 256 Hz.

2.7. Statistical analysis

The changes in craving for alcohol and absolute EEG power between VRTP-ADP and nVRTP-ADP after 10 sessions of VRTP and general treatment were compared using repeated measure ANOVA. Statistical analyses were also performed using repeated measure ANOVA to compare the craving scale and changes in absolute EEG power during first session between VRTP-ADP and healthy control groups. Post-hoc repeated measures ANOVA was used to analyze the data from the three stages (Relaxation, HRS, and AV). The relationship between the changes

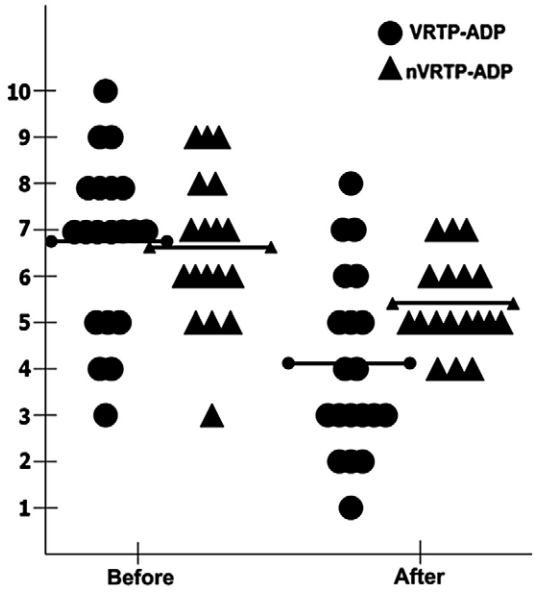

Fig. 1. Changes in craving for alcohol in VRTP-ADP and nVRTP-ADP before and after 10 session treatment. —: Mean, Wicoxon-signed rank test: VRTP-ADP (z=3.88, p<0.01) and nVRTP-ADP (z=3.17, p<0.01), Repeated measure ANOVA between VRTP-ADP and nVRTP-ADP, F=8.73, p=0.01, VRTP-ADP: alcohol-dependent patient with virtual reality therapy for alcohol, nVRTP-ADP: alcohol-dependent patient without VRTP, Before: craving before treatment; After: craving after treatment.

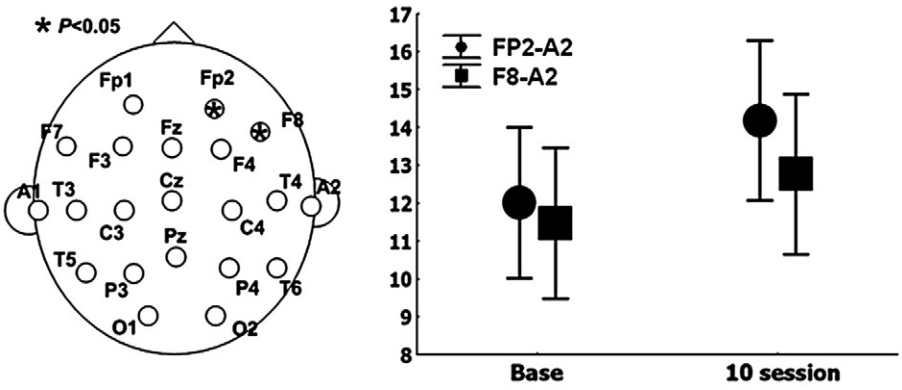

Fig. 2. Changes in craving for alcohol in VRTP-ADP before and after 10 session treatment. Wicoxon-signed rank test: VRTP-ADP ($z=2.91$, $p<0.01$) and nVRTP-ADP ($z=3.80$, $p<0.01$), VRTP-ADP: alcohol-dependent patient with virtual reality therapy, nVRTP-ADP: alcohol-dependent patient without VRTP.

in craving and EEG activity was analyzed by Pearson correlation analysis. All statistical analyses were performed using Statistica 6.0 (StatSoft®, Tulsa, Oklahoma).

3. Results

3.1. The change of craving and EEG between VRTP-ADP and nVRTP-ADP after the 10th VRTP and general treatment sessions

The craving changed in both VRTP-ADP ($z=3.88$, $p<0.01$) and nVRTP-ADP ($z=3.17$, $p<0.01$). However, the VRTP-ADP exhibited a greater decrease in craving after the 10th VRTP session, when compared to the nVRTP-ADP after the 10th general treatment ($F=8.73$, $p=0.01$) (Fig. 1). When the before and after treatment of the VRTP-ADP were compared, the absolute EEG alpha power in Fp2-A2 ($z=2.91$, $p<0.01$) and F8-A2 ($z=3.80$, $p<0.01$) increased after the 10th session of VRTP (Fig. 2). However, there was no difference in the pattern of the change of 16 EEG leads in nVRTP-ADP.

3.2. The changes in craving between alcohol-dependent patients with VRTP (VRTP-ADP) and healthy comparisons

During three VRTP session, the magnitude of induced craving was significantly higher in the alcohol-dependent patients as compared to the healthy controls ($F=17.44$, $p<0.01$). In the post-hoc analysis, the VRTP-ADP reported greater magnitude of increased craving for alcohol from the relaxation to high-risk situation (HRS) compared to healthy comparisons ($F=13.8$, $p=0.01$). A greater magnitude of decreased craving for alcohol from HRS to AVS was observed in VRTP-ADP, compared to healthy comparisons ($F=26.6$, $p<0.01$) (Fig. 3).

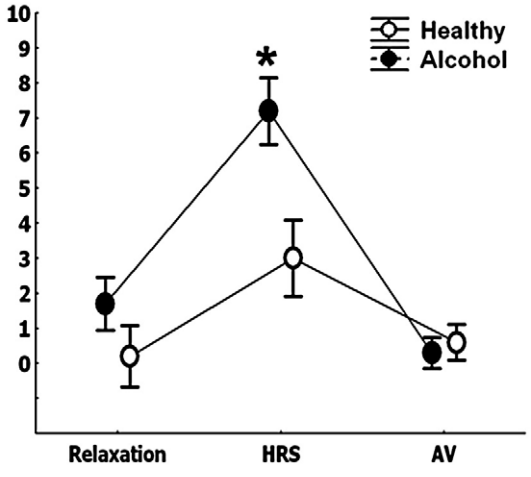

Fig. 3. The change in craving for alcohol in patients with alcohol dependence versus healthy controls during first VRTP session. VRTP-ADP: alcohol dependence patients with virtual reality therapy for alcohol, Health: healthy comparison subjects, Relaxation: craving for alcohol during relaxation, HRS: craving for alcohol during exposure to the high-risk situation, AV: craving for alcohol during aversive stimulation. Repeated measure ANOVA, Relaxation-AV: $F=17.44$, $p<0.01$, Relaxation-HRS: $F=13.8$, $p=0.01$, HRS-AV: $F=26.6$, $p<0.01$, Values are means±95% C.I. *: significant difference of HRS between patients and controls, in dependent test: $t=6.64$, $p<0.01$.

4. Discussion

The present study demonstrated that VRTP was more effective in decreasing the craving for alcohol than cognitive therapy in patients with alcohol dependence. In addition, the degree of alcohol craving during each step of virtual reality therapy (VRT) was different between patients with alcohol dependence and healthy comparison subjects.

Compared to patients with 10 sessions of cognitive therapy (nVRTP-ADP), the VRTP-ADP experienced a greater reduction in craving for alcohol. We posit that this difference may be due to using individualized, tailor-made scenes with multisensory modes of stimulation. While several studies have reported that abstinence is effective in treating some alcohol-dependent persons (Elkins, 1991; Howard and Jenson, 1990; Smith and Frawley, 1990), the addition of an aversive therapy session was found to maintain higher rates of abstinence rate during individual and group counseling. Elkins (1991) andSmith and Frawley (1990) reported high abstinence rates, but the magnitude of the aversive electrical and chemical stimuli can only be moderate (and so limits its efficacy) as it would be unethical to increase the intensity of the stimuli. Recently, Mihai et al. (2007) used a graphic videotape without chemical or electrical stimulation and reported that a new aversive method of having the participants view a scene of a person experiencing delirium tremens was very effective in maintaining abstinence. The results from the present study are consistent with these findings as the sound of vomiting and Kefir (sour yogurt) was added for multisensorial integration as an aversive stimulation in our VRTP. However, the use of a noxious liquid (Kefir), that is paired with an equally disturbing video, can be considered as a type of classical behavioral therapy.

While the nVRTP-ADP showed no change in EEG after 10 sessions of cognitive treatment, the VRTP-ADP reported a decrease in craving for alcohol with a corresponding increase in frontal alpha activity after the 10th session of VRTP. These EEG findings are similar to those reported by Liu et al. (1998) and Kim et al. (2003). Liu et al. (1998) reported that cocaine-related cue exposure increased EEG arousal resulting in decreased power in the alpha band. Kim et al. (2003) noted that EEG changes induced by alcohol cues are prominent in the frontal cortex. Interestingly, this appears to be a “threshold” phenomenon as there was no difference in the EEG patterns or craving through the first 5 sessions of treatment. Thus, it appears that multiple sessions are required to produce the desired effects. The longitudinal brain change of patients with alcohol dependence in fMRI has been

noted by Schneider et al. (2001). Activation of subcortical-limbic region in patients before treatment was changed to the activation of superior temporal gyrus after drug treatment, suggesting that brain activity could be a marker for particular states in alcohol-dependent patients (Schneider et al., 2001). Therefore, we cautiously suggest that the altered EEG patterns observed in the alcohol-dependent patients in the present study may be another biological marker of cue-reactive "state" in these individuals. The extent to which this information relates to ultimate treatment success or ability to remain abstinent remains an area of further research.

The VRTP used in the present study consisted of three stages: relaxation, exposure to a high-risk situation, and aversive stimulation. Alcohol-dependent persons differed from healthy control subjects during all three of the stages. The patients experienced a more abrupt increase in craving during the high-risk situation (alcohol cue) and a more immediate decrease in craving after aversive stimulation. Patients with alcohol dependence were reported to be more sensitive to situations when alcohol was present without actually consuming alcohol (Lee et al., 2006). The expectancy for alcohol effects due to its ready availability and the strength of association of alcohol cues to memories of previous drinking episodes in patients with alcohol dependence appear to be correlated with alcohol use and abuse (Stacy and Newcomb, 1998). Alcohol expectancies have been known to serve as powerful predictors of drinking in a variety of studies involving different patient populations and methodologies (Christiansen et al., 1989). Lambrey and Berthoz (2003) reported that the expectancy for alcohol was associated with highly individualized responses. Comprehensively, we cautiously suggest that alcohol patients would respond to stimuli in the manner of large magnitude of craving. VRTP would decrease the craving in response to alcohol stimuli.

There are several limitations in our study. First, the sample size was small and there were a large number of variables that were analyzed over time. Considering the risk of a Type I error, particularly regarding the EEG data, generalizing other types of drinkers may not be possible at this time and the interpretation of results should cautiously be done. Second, the follow up period was relatively short and so the "persistence" of the beneficial effects of VRTP after treatment has ceased is not known. Third, the Kefir that was used in the Aversive Situation (AVS) usually contains 1% alcohol, which may have a minor effect on craving and EEG responses in alcohol-dependent or control subjects.

In conclusion, virtual reality therapy (VRT) with the three steps of relaxation, exposure to a high-risk situation and exposure to aversive stimuli has better treatment efficacy than general cognitive therapy. Moreover, these VRTP-induced changes in desire for alcohol have a neurobiological basis as revealed by the changes in EEG activity.

Acknowledgements

We are thankful for the technical help of Blue Media Technology Co., Ltd., Korea. This research was supported by a Research Grant for alcohol treatment by Grants from Seo Cheon foundation 2006, Korea and NIDA Grants DA015116 and DA003H3.

Disclosure/conflict of interestI declare that, except for income received from my primary employer, no financial support or compensation has been received from any individual or corporate entity over the past 3 years for research or professional service and there are no personal financial holdings that could be perceived as constituting a potential conflict of interest.

References

Anderson PL, Zimand E, Hodges LF, Rothbaum BO. Cognitive behavioral therapy for public-speaking anxiety using virtual reality for exposure. Depress Anxiety 2005;22: 156–8.
Anton RF. New methodologies for pharmacological treatment trials for alcohol dependence. Alcohol Clin Exp Res 1996;20:3A–9A.
Bauer LO, Kranzler HR. Electroencephalographic activity and mood in cocaine-dependent outpatients: effects of cocaine cue exposure. Biol Psychiatry 1994;36: 189–97.
Baumann SB, Sayette MA. Smoking cues in a virtual world provoke craving in cigarette smokers. Psychol Addict Behav 2006;20:484–9.
Bechara A, Damasio H, Damasio AR. Emotion, decision making and the orbitofrontal cortex. Cereb Cortex 2000;10:295–307.
Burdea G. Force and Touch Feedback for Virtual Reality. New York: John Wiley & Sons; 1996.
Burdea G, Coiffet P. Virtual Reality Technology. New York: John Wiley & Sons; 1994.
Christiansen BA, Smith GT, Roehling PV, Goldman MS. Using alcohol expectancies to predict adolescent drinking behavior after one year. J Consult Clin Psychol 1989;57: 93–9.
Cosman PH, Cregan PC, Martin CJ, Cartmill JA. Virtual reality simulators: current status in acquisition and assessment of surgical skills. ANZ J Surg 2002;72:30–4.
Elkins RL. An appraisal of chemical aversion (emetic therapy) approaches to alcoholism treatment. Behav Res Ther 1991;29:387–413.
George MS, Anton RF, Bloomer C, Teneback C, Drobes DJ, Lorberbaum JP, et al. Activation of prefrontal cortex and anterior thalamus in alcoholic subjects on exposure to alcohol-specific cues. Arch Gen Psychiatry 2001;58:345–52.
Howard MO, Jenson JM. Chemical aversion treatment of alcohol dependence. II. Future research directions for the '90s. Int J Addict 1990;25:1403–14.
Jang DP, Ku JH, Choi YH, Wiederhold BK, Nam SW, Kim IY, et al. The development of virtual reality therapy (VRT) system for the treatment of acrophobia and therapeutic case. IEEE Trans Inf Technol Biomed 2002;6:213–7.
Kim DJ, Jeong J, Kim KS, Chae JH, Jin SH, Ahn KJ, et al. Complexity changes of the EEG induced by alcohol cue exposure in alcoholics and social drinkers. Alcohol Clin Exp Res 2003;27:1955–61.
Klinger E, Legeron P, Roy S, Chemin I, Lauer F, Nugues P. Virtual reality exposure in the treatment of social phobia. Stud Health Technol Inform 2004;99:91-119.
Lambrey S, Berthoz A. Combination of conflicting visual and non-visual information for estimating actively performed body turns in virtual reality. Int J Psychophysiol 2003;50:101–15.
Lee JH, Lim Y, Wiederhold BK, Graham SJ. A functional magnetic resonance imaging (FMRI) study of cue-induced smoking craving in virtual environments. Appl Psychophysiol Biofeedback 2005;30:195–204.
Lee E, Namkoong K, Lee CH, An SK, Lee BO. Differences of photographs inducing craving between alcoholics and non-alcoholics. Yonsei Med J 2006;47:491–7.
Littleton J. Acamprosate in alcohol dependence: how does it work? Addiction 1995;90: 1179–88.
Liu X, Vaupel DB, Grant S, London ED. Effect of cocaine-related environmental stimuli on the spontaneous electroencephalogram in polydrug abusers. Neuropsychopharmacology 1998;19:10–7.
Ludwig AM, Wikler A, Stark LH. The first drink: psychobiological aspects of craving. Arch Gen Psychiatry 1974;30:539–47.
Lukas SE, Mendelson JH. Electroencephalographic activity and plasma ACTH during ethanol-induced euphoria. Biol Psychiatry 1988;23:141–8.
Lukas SE, Mendelson JH, Benedikt RA, Jones B. EEG alpha activity increases during transient episodes of ethanol-induced euphoria. Pharmacol Biochem Behav 1986;25: 889–95.
Lukas SE, Mendelson JH, Kouri E, Bolduc M, Amass L. Ethanol-induced alterations in EEG alpha activity and apparent source of the auditory P300 evoked response potential. Alcohol 1990;7:471–7.
Lukas SE, Mendelson JH, Benedikt R. Electroencephalographic correlates of marihuana-induced euphoria. Drug Alcohol Depend 1995;37:131–40.
Mihai A, Damsa C, Allen M, Baleydier B, Lazignac C, Heinz A. Viewing videotape of themselves while experiencing delirium tremens could reduce the relapse rate in alcohol-dependent patients. Addiction 2007;102:226–31.
Modell JG, Mountz JM. Focal cerebral blood flow change during craving for alcohol measured by SPECT. J Neuropsychiatry Clin Neurosci 1995;7:15–22.
Myrick H, Anton RF, Li X, Henderson S, Drobes D, Voronin K, George MS. Differential brain activity in alcoholics and social drinkers to alcohol cues: relationship to craving. Neuropsychopharmacology 2004;29:393–402.
North MM, North SM, Coble JR. Virtual reality therapy: an effective treatment for phobias. Stud Health Technol Inform 1998;58:112–9.
Robinson TE, Berridge KC. The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain Res Brain Res Rev 1993;18:247–91.
Rolls ET. The orbitofrontal cortex and reward. Cereb Cortex 2000;10:284–94.
Rothbaum BO, Hodges LF, Ready D, Graap K, Alarcon RD. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. J Clin Psychiatry 2001;62:617–22.
Schneider F, Habel U, Wagner M, Franke P, Salloum JB, Shah NJ, et al. Subcortical correlates of craving in recently abstinent alcoholic patients. Am J Psychiatry 2001;158:1075–83.
Schultz W, Tremblay L, Hollerman JR. Reward processing in primate orbitofrontal cortex and basal ganglia. Cereb Cortex 2000;10:272–84.
Smith JW, Frawley PJ. Long-term abstinence from alcohol in patients receiving aversion therapy as part of a multimodal inpatient program. J Subst Abuse Treat 1990;7: 77–82.
Stacy AW, Newcomb MD. Memory association and personality as predictors of alcohol use: mediation and moderator effects. Exp Clin Psychopharmacol 1998;6:280–91.
Viaud-Delmon I, Warusfel O, Seguelas A, Rio E, Jouvent R. High sensitivity to multisensory conflicts in agoraphobia exhibited by virtual reality. Eur Psychiatry 2006;21:501–8.
Volpicelli JR, Alterman AI, Hayashida M, O'Brien CP. Naltrexone in the treatment of alcohol dependence. Arch Gen Psychiatry 1992;49:876–80.
Wise RA. The neurobiology of craving: implications for the understanding and treatment of addiction. J Abnorm Psychol 1988;97:118–32.
Yong NA, Paige GD, Seidman SH. Multiple sensory cues underlying the perception of translation and path. J Neurophysiol 2007;97:1100–13.