Pers Ubiquit Comput (2013) 17:253–260
DOI 10.1007/s00779-011-0467-0

ORIGINAL ARTICLE

Virtual reality and mobile phones in the treatment of generalized anxiety disorders: a phase-2 clinical trial

Claudia Repetto · Andrea Gaggioli · Federica Pallavicini · Pietro Cipresso · Simona Raspelli · Giuseppe Riva

Received: 22 January 2011 / Accepted: 20 June 2011 / Published online: 2 October 2011

Abstract Several studies have demonstrated that exposure therapy—in which the patient is exposed to specific feared situations or objects that trigger anxiety—is an effective way to treat anxiety disorders. However, to overcome a number of limitations inherent in this approach—lack of full control of the situation, costs and time required, etc.—some therapists have started to add virtual reality (VR) to the in vivo exposure-based therapy, providing in-office, controlled exposure therapy. Compared to the in vivo exposure, VR Exposure Therapy (VRET) is completely controlled: the quality, the intensity and the frequency of the exposure are decided by the therapist, and the therapy can be stopped at any time if the patient does not tolerate it. Moreover, the flexibility of a virtual experience allows the patient to experience situations that are often much worse and more exaggerated than those that are likely to be encountered in real life. However, a critical issue underlying the use of VRET in the treatment of anxiety-related disorders is the lack of a virtual reality system in the patient's real-life context. In this paper, we present a clinical protocol for the treatment of Generalized Anxiety Disorders (GAD) based on the ubiquitous use of a biofeedback-enhanced VR system. The protocol includes the use of a mobile exposure system allowing patients to perform the virtual experience in an outpatient setting. A between-subjects study, involving 25 GAD patients, was carried out to verify the efficacy of the proposed approach. The clinical data in this pilot study seemed to support the efficacy of the ubiquitous approach.

Keywords Virtual reality · Mobile phones · Generalized anxiety disorders · Clinical trial · Ubiquitous computing

1 Introduction

Anxiety is a typical human emotion that people experience when some crucial personal goals (i.e. safety, self esteem, approval, etc.) are challenged and the subject forecasts an oncoming bust [1]. In most cases, anxiety can be considered as a normal reaction to a demanding emotional context: in such cases, people are able to deal with this emotional activation spontaneously by applying strategies that allow a cognitive resizing of the source of worry and a consequent positive management of the situation.

However, a level of anxiety which is so high as to prevent people from leading a normal life constitutes an anxiety disorder. Anxiety disorders are very common worldwide [2, 3] and have a considerable impact on personal and professional life: usual activities become very stressful and this leads people to avoid the feared situation or to undertake rumination activities. Avoidance behaviours tend to worsen with time and start a vicious circle: in terms of conditioning paradigms, avoidance behaviours are negative reinforcements since they prevent an aversive symptom (anxiety); however, they also maintain the link

C. Repetto (✉) · G. Riva
Department of Psychology, Università Cattolica del Sacro Cuore, Largo Gemelli 1, 20123 Milan, Italy
e-mail: claudia.repetto@unicatt.it

A. Gaggioli · F. Pallavicini · P. Cipresso · S. Raspelli · G. Riva
Applied Technology for Neuro-Psychology Lab, Istituto Auxologico Italiano, Milan, Italy

A. Gaggioli
ICE-NET Lab, Università Cattolica del Sacro Cuore, Milan, Italy

F. Pallavicini · S. Raspelli
Centre for Studies in Communication Sciences, University of Milan-Bicocca, Milan, Italy

between conditioned and unconditioned stimuli, preventing the extinction phenomenon. Furthermore, rumination triggers a vicious circle in which the source of worry is increasingly present in the subjects' mind and becomes an intrusive and persecutory thought. People suffering from anxiety disorders usually do not recover spontaneously and have to undergo a specific treatment. Many different treatments are now available for anxiety disorders: behavioural treatments, cognitive psychotherapy, medication and biofeedback are among the most used. Several studies investigating the effectiveness of the various treatments have demonstrated that exposure-based therapies are more suitable and effective than others [4–12].

The exposure process involves the patient's progressive exposure to the situation that causes anxiety. Exposure alone, without relaxation training, has proved effective to treat a number of anxiety disorders and phobias, such as panic disorders, agoraphobia [6], social phobia [13] and obsessive–compulsive disorders [9]. However, in the case of systematic desensitization [14], exposure is used in combination with relaxation, an emotional and physiological state considered incompatible with anxiety [15]. In these protocols, the patient learns how to manage the symptoms of anxiety by replacing emotional maladaptive activation with relaxation. Since patients have the opportunity to monitor their thoughts and beliefs with the therapist while experiencing anxiety, they can reduce their cognitive attributions. Exposure may be achieved by different means: in vivo, through direct contact with the stimulus, by imagery, and more recently using virtual reality (VRET). However, despite their effectiveness, the first two types of exposure present some limitations: some patients report difficulties to imagine the feared situation because of poor abilities in creating mental images and in getting inside a specific situation. In vivo exposure poses other critical issues: first of all, many patients are rather unwilling to expose themselves to the real situation since it is considered too frightening; second, the therapist is not fully in control of the real situation; third, the costs and time requirements are considerable since the therapist and the patient usually meet each other outside the therapist's office to work together on the stimulus target. For all these reasons, VRET has take root in the treatment of anxiety disorders in the last few decades.

As a matter of fact, VRET presents several advantages when compared with the traditional treatments using both in vivo and imagination techniques. First of all, the stimulus is under the full control of the therapist, who has the opportunity to select an emotional intensity suitable to each patient as well as the hierarchical order of the stimuli that trigger anxiety; furthermore, during the VRET, the session can be stopped in case of excessive emotional activation (which is, however, extremely rare). In this way, the patient feels less uncomfortable about the treatment and his/her motivation increases. Compared to imagination, VRET offers the possibility to visualize a realistic environment and to interact with it, without making any imaginative effort.

Another field of application that could take advantage from the above mentioned use of virtual reality for the treatment of anxiety disorders is the Stress Inoculation Training (SIT) [16]. SIT has been employed to prevent the disorder and to treat individuals who have experienced stress responses. The purpose of the treatment is to help patients to cope with various form of stress and sources of worry [16–18]. After this kind of intervention, patients should be able to bolster their coping repertoire (intra- and interpersonal skills) and should become more confident in their own abilities to apply coping strategies in a flexible way depending on the context.

Furthermore, VR lends itself to be associated with biofeedback training, especially if aimed at relaxation. Biofeedback is a coaching and training technique that helps people learn how to change physiological response patterns, in order to improve their mental and emotional functioning. Being connected to psychophysiological biosensors, the person uses the information provided as feedback to increase awareness or consciousness of the changes in the body/mind function. The feedback could be delivered by visual or acoustic signals. Virtual environments are known to facilitate relaxation, reducing stress and improving positive emotional states [19, 20]; moreover, the sense of presence and the immersive visual cue make the virtual environments a privileged place where visual and highly significant feedback could be provided.

1.1 The mobile dimension as a tool for ubiquitous treatment

It should be noticed that a critical issue related to the use of virtual exposure in the treatment of anxiety disorders is the lack of availability of VR systems in the patient's real-life context: both the cost and the setting of the system limit its use to the health care centre/hospital/therapist's office. The possibility to do the exercises trained with the therapist in the real life has at least two functions: first of all, cognitive-behavioural exercises are very powerful techniques but need to be learned and repeated over time in order to be correctly applied and to be effective. In this perspective, the availability of VR outside the therapist's office is critical to speed up the learning process and achieve quickly clinical results. Second, the patient experiences the emotions of anxiety and fear spontaneously in everyday life due to the natural exposure to events that cause such emotional activations; for this reason, the support of VR as a portable device is required to deal with the stressful situations (i.e. doing a relaxation exercise).

A promising tool that, from a technological point of view, already meets the requirements needed to support VR environments and, at the same time, is portable and easily available is the mobile phone. The role of mobile phones as a tool for responding to a variety of clinical needs has been recently investigated [21]. The interest for this device is motivated by its wide diffusion: the penetration of mobile phones in the world population has rapidly increased in the last few decades, also thanks to its decreasing price. Furthermore, the advanced technology now available makes mobile phones something more than a calling device: new generation mobile phones are able to achieve broader communication capabilities, supporting 3D graphics, pictures, sounds and software. Preziosa et al. (ibidem) discussed the results of two studies based on the use of mobile phones for anxiety management. In the first experiment, a Stress Inoculation Training was used to reduce examination stress: The data supported the hypothesis that the combination of video and audio narratives administered via UMTS induced more relaxation when compared with the other experimental conditions (either video or narratives administered with alternative means, such as CD and MP3 players). In the second study, mobile phones were used to train the ability to relax in a group of stressed patients by administering mobile narratives. The outcome of this research, together with other experimental studies on mobile phones, suggests that this technology is promising in the treatment of anxiety disorders, since it offers the opportunity to bridge the gap between inpatient and outpatient sessions.

In this paper, we present a clinical protocol for the treatment of Generalized Anxiety Disorders (GAD) based on the ubiquitous use of a biofeedback-enhanced virtual reality (VR) system. The paper also describes the results of a phase-2 controlled trial (NCT00602212) involving 24 GAD patients.

1.2 The treatment of generalized anxiety disorders: a ubiquitous approach

Generalized Anxiety Disorder (GAD) is a psychiatric disease characterized by long-lasting anxiety that is not focused on a specific object or situation. According to the DSM-IV-TR (APA, 2000), the essential feature of GAD is at least 6 months of "excessive anxiety and worry" about a variety of events and situations. Anxiety and worry are often accompanied by a variety of physical symptoms like restlessness, being easily fatigued, difficulty in concentrating, irritability, muscle tension and disturbed sleep. The high prevalence of GAD in the general population and the severe limitations it causes point out the necessity to find new strategies to treat it in a more efficient way. Within the treatment of GAD, physical (relaxation and controlled breathing), behavioural (visualization and controlled exposure) and cognitive control strategies (challenging negative thoughts) represent a key part of the treatment, even if they are hard to learn. Given the features of this disease and its pervasive effect on patients' personal, professional and affective life, we thought it could benefit from a ubiquitous treatment. Therefore, we suggested to improve the treatment of GAD through the use of a biofeedback-enhanced virtual reality (VR) system used for relaxation, controlled exposure [22, 23] and SIT. The use of SIT in the context of GAD is motivated by the acknowledgment that sometimes stressors cannot be avoided or altered [24] and then patients cannot apply strategies focused on finding solutions. In these cases, the coping effort should be directed to an emotionally palliative set of responses such as acceptance, reframing and perspective thinking. All these cognitive changes are facilitated if relaxation is induced at the same time. The treatment involves two virtual reality components (see Fig. 1): (1) an immersive virtual reality system experienced in the therapist's office; (2) a mobile exposure system allowing patients to perform the virtual experience in an outpatient setting. The role of the mobile exposure system is the following:

- To present and structure emotionally relevant contents in a ubiquitous context.
- To verify the patient's compliance and, if necessary, alert the patient/therapist;
- To track the emotional level of the patient in real time and record it for later assessment by the therapist;
- To provide feedback to the patients to help them cope with the contents;

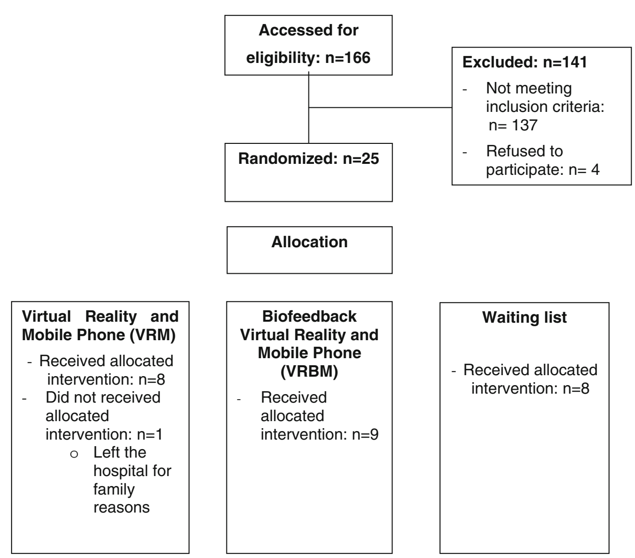

Fig. 1 Consort flowchart for randomized trial

- To contact the therapist automatically if the emotional level is higher than a preset cut-off value defined by the therapist.

The critical features of the mobile system in a real clinical context are:

- *Cost effectiveness*: even with the creation of PC-based VR, the cost of a VR system is still too expensive for the typical patient (2,000/3,000 € for a non-immersive system). Our goal was to develop a system with a price <1,000 €.
- *Usability*: the mobile system has to be simple enough to be used by an unsupervised patient after some training sessions.
- *Use of easily available technology:* the mobile system has to be based as much as possible on off-the-shelf components and protocols.
- *Emotional response:* the mobile system has to be emotionally connected with the contents of the VR sessions experienced in the health care centre/hospital/therapist's office. This can be achieved by presenting on the mobile system a non-navigable version of the same virtual reality environment experienced during the therapy. Some features of the experience—speed, contents, etc.—were driven by the emotional status of the patient.

For these reasons, the technology used in the protocol is the following:

- A wireless (Bluetooth) multi-sensor module (GSR/HR Sensor Module including finger sensors that simultaneously measure heart rate and electrodermal activity, GSR).
- The Virtual Reality control unit: Asus G2S portable computer with Intel® Core™2 Extreme Processor X7800, Nvidia GeForce 8600 GT 256 MB DDR3 graphic card, Bluetooth support.
- A head-mounted display: Vuzix iWear VR920 with twin high-resolution 640 × 480 (920,000 pixels) LCD displays, iWear® 3D compliant.
- The therapist's netbook, (EEPC 100H-BK039X) used to control in real time the features of the virtual environment and to assess physiological parameters.
- A joypad (Xbox Controller)
- A Smartphone (HTC Touch Pro T7272) for relaxation homework. The Smartphone uses the Windows Mobile® 6.1 Professional operating system. It also includes a 2.8-inch TFT-LCD flat touch-sensitive screen with VGA resolution

2 Testing the approach: a phase-2 controlled trial

2.1 The sample

One hundred and sixty-six consecutive patients seeking treatment in a public health care institute in Italy were seen for screening interviews for admission to the study. Criteria for participation in the study included: (1) Diagnosis of GAD according to DSM-IV-TR criteria; (2) Age between 18 and 50 years; (3) No psychotherapy received for GAD; (4) In case of pharmacotherapy, the kind and amount of medication should not have varied during the experimental period; (5) No history of neurological diseases, mental retardation, psychosis, alcohol or drug addiction; (6) No migraine, headache or vestibular abnormalities; (7) Women who were pregnant or breastfeeding were also excluded.

Of these, 141 either did not fulfil the inclusion criteria or were excluded for other reasons (e.g. time constraints, involvement in other treatments, refusal to participate). All the 25 patients who met the inclusion criteria (16 women and 9 men) entered the treatment phase. The majority of them (65%) had graduated from upper secondary school, were employed at the time of the study and were married.

The study was approved by the Ethical Committee of the Istituto Auxologico Italiano and was recorded in the Clinicaltrials.gov database with the official trial number "NCT00602212".

2.2 Assessment tools

A semi-structured interview was used to identify relevant DSM-IV-TR diagnostic criteria for GAD in the sample.

The following psychometric questionnaires were also administered to each patient at pre-treatment and upon completion of the Beck Anxiety Inventory (BAI, [25]), a 21-item scale measuring cognitive, behavioural and physiological symptoms of anxiety.

- State-Trait Anxiety Inventory Form Y-2 (STAI-Y [26]), a 2-scale questionnaire including 20 items each, that measures anxiety in adults. The STAI clearly differentiates between the temporary condition of "state anxiety" (STAY-Y1) and the more general and long-standing quality of "trait anxiety" (STAY-Y2).
- Hamilton Anxiety Rating Scale (HAM-A [27]). The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety).

2.3 Protocol

The patients were randomly assigned to the following groups (see Fig. 1—Consort Flow Chart—for detail): (1) the VR and Mobile group (VRMB) including a biofeedback-assisted relaxation program—7 subjects; (2) the VR and Mobile group (VRM) without biofeedback—9 subjects; (3) the waiting list (WL) group—8 subjects:

1. *Virtual reality + mobile phone without biofeedback condition (VRM).* In this experimental condition, patients received an eight-session VR-based treatment including both relaxation and exposure techniques. In sessions 1–6, the patients explored a beautiful VR tropical island (experienced with a head-mounted display and head-tracking) following a predefined path leading to different relaxing areas: Campfire, Beach and Waterfall. In these areas, the patients started to relax by observing the flickering campfire, watching waves lapping gently on a shore or looking to the waterfall and fish pond. Each experience was supported by an audio narrative based on progressive muscle relaxation and/or autogenic techniques. All the environments were developed by the ESIEA INTREPID team (J. L. Dautin, J. Ardouin, F. Crison and M. Le Renard—www.esiea.fr) using the 3DVIA 4.1 Virtools toolkit by Dassault Systèmes—www.virtools.com. To improve the efficacy of the training and to increase the effects of relaxation, patients could access a non-navigable version of the same virtual reality environment experienced during the therapy also from home using a mobile phone. The patient was asked to train relaxation abilities at least once a day for the entire duration of the treatment according to the plan provided by the therapist. In sessions 7 and 8, the patients explored the island again and reached a gazebo in which they were exposed to pre-selected words or images related to their personal stressful events. The patients were then asked to use the relaxation techniques they had learned to cope with them.
2. *Virtual reality + mobile phone with biofeedback condition (VRMB*). The patients followed the same protocol described above with biofeedback support (see Figs. 2, 3). During the sessions, the therapist used HR variations [28–31] to modify specific features of the virtual environment:

   (a) *Campfire (sessions 1–2).* HR controls the fire intensity: a reduction in the patient's physiological activation reduces the intensity of the fire until it disappears;

   (b) *Beach (sessions 3–4).* HR controls the movement of the waves: a reduction in the patient's physiological activation reduces the movement of the waves until the ocean becomes completely calm;

   (c) *Waterfall (sessions 5–6):* HR controls the movement of the water: a reduction in the patient's physiological activation reduces the movement of the water until the water flow becomes completely still;

   (d) *Gazebo (sessions 7–8*): HR controls the size of a stressful image or video: a reduction in the patient's physiological activation reduces the size of the stimulus until it disappears. This exercise is designed following the procedure of SIT.

Fig. 2 A screenshot from the VR environment experienced by the VRM Group. The figure illustrates a campfire, one of the relaxing environments showed to the patients during the treatment

Fig. 3 A screenshot from the VR Biofeedback experienced by the VRMB Group. A *bar* placed on the right and showing the patients' physiological parameters allows them to monitor their emotional state through in vivo measures during the relaxation exercise

3. *Waiting list condition (WL).* This was a control condition, in which patients were included in a waiting list and did not receive any kind of relaxation training.

The randomization scheme was generated using the website www.randomization.com. After the randomization, a patient in the VRM group refused to participate in the study and abandoned the trial for family and work reasons.

2.4 Statistical analysis

A power calculation was made to evaluate the possibility of detecting statistically significant differences both between (independent measures) and within the groups (repeated measures). Given the low statistical power due to the relatively small number of participants, the non-normality of several distributions and the unbalanced groups, we decided to use the exact methods with Monte Carlo approximation, a series of non-parametric statistical algorithms that enable researchers to make reliable inferences when data are sparse, heavily tied or unbalanced, not normally distributed, or fail to meet any of the underlying assumptions necessary to obtain reliable results using the standard asymptotic method. The exact methods with Monte Carlo approximation used for the comparisons are the Kruskal–Wallis test with post hoc analysis [32] for independent measures, the Wilcoxon rank-sum test for repeated measures and the Chi-square for categorical variables, with $\alpha = 0.5$, two tailed.

2.5 Results

Non-parametric tests indicated that there were no significant differences in the age and years of education of the subjects (Table 1). Similarly, no significant differences were found in their clinical characteristics (Table 2).

2.5.1 Before/after session analysis

The GSR and the HR, as well as the STAI-Y1 were recorded at the beginning and at the end of each training session in the VRMB and in the VRM groups. Both groups were able to obtain a significant reduction (5/10% of the initial level) in both physiological (HR only) and self-assessed measures of anxiety (STAI-Y1) at the end of the different sessions (Table 1). In particular, the ability of the subjects to attenuate HR responses during a behavioural challenge is very interesting because these situations are particularly relevant to real-life events. However, no significant differences were found between the groups.

2.5.2 Before/after treatment analysis

To evaluate the overall effect of the treatment, we analysed the treatment effects (pre- vs. post-treatment) on the psychometric variables within the 3 groups. The results (Table 3) showed:

- *VRMB group*: a significant decrease in the BAI ($Z = -1.826$; $p < .05$) and STAI-Y2 ($Z = -1.826$; $p < .05$) scores;
- *VRM group*: a significant decrease in the BAI ($Z = -2.383$; $p < .05$) scores
- *WL group*: no significant changes.

Non-parametric K-Independent Tests were also used to analyse the differences between the subjects in the pre- and post-treatment anxiety questionnaires. Given the limited statistical power, no significant differences were found for $p < .05$.

3 Discussion

Different VR applications for the understanding, assessment and treatment of mental health problems have been developed over the last 15 years [33, 34].

Even if VR offers several advantages when compared with traditional cognitive-behavioural procedures, the fact that VR tools are confined to the therapist's office has been recognized as a limitation, especially for the treatment of anxiety disorders. This experiment evaluated the possibility to use a ubiquitous approach, based on a virtual environment uploaded on a mobile phone, for the treatment of GAD. Even if the small sample leads us to consider the study as a pilot one, it achieved two interesting results. On the one hand, it confirmed the possibility of using VR in the treatment of GAD. Both experimental groups had better clinical outcomes at the end of the treatment. On the other hand, it supported the clinical use of a mobile phone to re-

Table 1 Anxiety differences in pre- and post-sessions

	Group	Mean	SD
Mean of HR differences (pre–post, all sessions)	VRMB	5.71	2.34
	VRM	3.83	1.19
Mean of STAI-Y1 differences (pre–post, all sessions)	VRMB	6.59	2.71
	VR	5.11	3.26

Table 2 Psychometric questionnaires: pre-treatment and post-treatment scores

Variables	Group			*F*	*p*
	VRMB Mean (SD)	VRM	WL		
BAI Pre	26.65 (20.3)	29.4 (11.059)	27.50 (13.204)	0.012	.988
Post	14.50 (10.733)	19.25 (9.7)	19.75 (6.946)		
p	.05	.05	.11		
HAM-A Pre	25.00 (8.679)	19.50 (3.697)	25.00 (7.439)	0.838	.464
Post	15.00 (4.802)	18.75 (9.743)	16.25 (6.702)		
p	.11	.42	.11		
STAI-Y2 Pre	54.15 (2.630)	50.65 (4.573)	59.50 (9.434)	0.471	.539
Post	45.50 (8.396)	46.25 (9.912)	58.00 (5.831)		
p	.05	.11	.54		

Table 3 Demographic details of the sample

Variables	Group			*p*
	VRMB Mean (SD)	VRM	WL	
Age	45.25 (14.24)	48.5 (12.662)	49.25 (9.845)	.702
Years of education	13.25 (2.1)	12.75 (4.787)	11.25 (4.594)	.455

experience and anchor the contents of the VR sessions at home. When interviewed about the usefulness of mobile phones, most of the patients (91%) answered that they were very satisfied because they helped them consolidate the relaxation training in the absence of the therapist. Moreover, portable devices are useful instruments that can be used whenever the patient needs them, not only at home, but also in every real-life situations in which he/she needs help to relax. This could solve the problem of the lack of availability of a VR system in the patient's real-life context.

The study also suggested a possible added value offered by the use of biofeedback: only in the VRMB group, we found a significant reduction in two different anxiety scores (BAI and STAI) after the treatment. As regards the patients' physiological responses, we found a tendency indicating a decrease in HR and GSR between the pre- and post-session measurements in the VRMB group, higher than in the VRM group.

In conclusion, this study showed that (1) VR can be used also in the treatment of GAD; (2) in a VR treatment, patients could take advantage of a mobile device that was not only well tolerated but also appreciated by the patients. Despite the need for further analysis, the study also suggested that, with these patients, the effectiveness of an immersive virtual relaxing environment may be improved by using physiological data to modify specific features of the virtual environment in real time.

Acknowledgments The present work was supported by the European Union IST Programme (Project "INTREPID—A Virtual Reality Intelligent Multi-sensor Wearable System for Phobias' Treatment"—IST-2002-507464). The virtual environments used in the study were developed by the ESIEA INTREPID team (J.L. Dautin, J. Ardouin, F. Crison and M. Le Renard—http://www.esiea.fr) using 3DVIA Virtools 4.1.

References

1. Sassaroli S, Lorenzini R, Ruggiero GM (2006) Psicoterapia Cognitiva dell'Ansia—Rimuginio, controllo ed evitamento. Raffaello Cortina Editore, Milano
2. Michael T, Zetsche U, Margraf J (2007) Epidemiology of anxiety disorders. Psychiatry 6(4):136–142
3. Pull CB (2008) Recent trends in the study of specific phobias. Curr Opin Psychiatr 21(1):43–50
4. Asukai N, Saito A, Tsuruta N, Kishimoto J, Nishikawa T (2010) Efficacy of exposure therapy for Japanese patients with posttraumatic stress disorder due to mixed traumatic events: a randomized controlled study. J Trauma Stress 23(6):744–750. doi:10.1002/jts.20589
5. Barlow JH, Ellard DR, Hainsworth JM, Jones FR, Fisher A (2005) A review of self-management interventions for panic disorders, phobias and obsessive-compulsive disorders. Acta Psychiatr Scand 111(4):272–285. doi:10.1111/j.1600-0447.2005.00499.x
6. Craske M, Barlow D (2007) Panic disorder and agoraphobia. In: Barlow DH (ed) Clinical handbook of psychological disorders: a step-by-step treatment manual, 4th edn. Guilford, New York, pp 1–64
7. Deacon BJ, Abramowitz JS (2004) Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. J Clin Psychol 60(4):429–441

8. Emmelkamp PM (2003) Behavior therapy in adults. In: Handbook of psychotherapy and behavior change. Wiley, New York. pp 393–446
9. Franklin M, Foa E (2007) Obsessive compulsive disorder. In: Barlow DH (ed) Clinical handbook of psychological disorders: a step-by-step treatment manual, 4th edn. Guilford, New York, pp 164–215
10. Landon TM, Barlow DH (2004) Cognitive-behavioral treatment for panic disorder: current status. J Psychiatr Pract 10(4):211–226
11. Olatunji BO, Cisler JM, Deacon BJ (2010) Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. Psychiatr Clin North Am 33(3):557–577. doi: 10.1016/j.psc.2010.04.002
12. Rothbaum BO, Schwartz AC (2002) Exposure therapy for posttraumatic stress disorder. Am J Psychother 56(1):59–75
13. Heimberg R, Dodge C, Hope D, Kennedy C, Zollo L, Becker R (1990) Cognitive behavioural group treatment for social phobia: comparison with a credible placebo control. Cogn Ther Res 14:1–23
14. Wolpe J (1958) Psychotherapy by reciprocal inhibition. Standford University Press, Standford
15. Hazlett-Stevens H, Craske M (2008) Live (in vivo) exposure. In: O'Donohue W, Fisher J (eds) Cognitive behavior therapy—applying empirically supported techniques in your practice, 2nd edn. Wiley, New York
16. Meichenbaum D (1985) Stress inoculation training. Pergamon Press, Elmsford
17. Meichenbaum D, Jaremko ME (eds) (1993) Stress reduction and prevention. Plenum Press, New York
18. Meichenbaum D (2007) Stress inoculation training: a preventative and treatment approach. In: Woolfolk RL, Lehrer PM (eds) Principles and practice of stress management. Guilford, New York, pp 497–518
19. Villani D, Lucchetta M, Preziosa A, Riva G (2009) The role of interactive media features on the affective response: a virtual reality study. Int J Human Comput Interact 1(5):35–55
20. Villani D, Riva F, Riva G (2007) New technologies for relaxation: the role of presence. Int J Stress Manag 14(3):260
21. Preziosa A, Grassi A, Gaggioli A, Riva G (2009) Therapeutic applications of the mobile phone. Br J Guid Couns 37(3):313–325
22. Repetto C, Gorini A, Algeri D, Vigna C, Gaggioli A, Riva G (2009) The use of biofeedback in clinical virtual reality: the intrepid project. Stud Health Technol Info 144:128–132
23. Repetto C, Gorini A, Vigna C, Algeri D, Pallavicini F, Riva G (2009) The use of biofeedback in clinical virtual reality: the INTREPID project. J Vis Exp JoVE (33):2–3
24. Meichenbaum D (2006) Trauma and suicide. In: Ellis T (ed) Cognition and suicide: theory, research and practice. American Psychological Association, Washington, DC
25. Steer RA, Rissmiller DJ, Ranieri WF, Beck AT (1993) Structure of the computer-assisted Beck anxiety inventory with psychiatric inpatients. J Pers Assess 60(3):532–542
26. Spielberger CD, Gorsuch RL, Lushene RE (1970) STAI manual for the state-trait anxiety inventory (self-evaluation questionnaire). Consulting Psychologists, Palo Alto
27. Hamilton M (1959) The assessment of anxiety states by rating. Br J Med Psychol 32(1):50–55
28. Achmon J, Granek M, Golomb M, Hart J (1989) Behavioral treatment of essential hypertension: a comparison between cognitive therapy and biofeedback of heart rate. Psychosom Med 51(2):152–164
29. Benson H, Shapiro D, Tursky B, Schwartz GE (1971) Decreased systolic blood pressure through operant conditioning techniques in patients with essential hypertension. Science 173(3998):740
30. Blanchard EB, Young LD, Haynes MR (1975) A simple feedback system for the treatment of elevated blood pressure. Behav Ther 6(2):241–245
31. Elder ST, Eustis NK (1975) Instrumental blood pressure conditioning in out-patient hypertensives. Behav Res Ther 13(2–3):185–188
32. Siegel S, Castellan NJ (1992) Nonparametric statistics for the behavioral sciences. McGraw-Hill, Milano
33. Repetto C, Riva G (2011) From virtual reality to interreality in the treatment of anxiety disorders. Neuropsychiatry 1(1):31–43
34. Riva G (2005) Virtual reality in psychotherapy: review. Cyberpsychol Behav 8:220–230