Virtual Reality and Anxiety Disorders Treatment: Evolution and Future Perspectives

Berenice Serrano-Zárate, Ph.D.¹, Cristina Botella, Ph.D.^{1,4}, Brenda K. Wiederhold, Ph.D. MBA, BCB, BCN^{2,5}, and Rosa M. Baños, Ph.D.^{3,4}

¹Universitat Jaume I, Castellón, Spain ²Virtual Reality Medical Center, San Diego, CA, USA ³Universitat de Valencia, Valencia, Spain

⁴CIBER Fisiopatología, Obesidad y Nutrición, Instituto Salud Carlos III, Girona, Spain ⁵Virtual Reality Medical Institute, Brussels, Belgium

Abstract

Virtual reality (VR) is a technology that allows the simulation of different real-life situations on a tridimensional computer-generated environment where the user can interact with the environment as if he/she were the real world. VR has potential as an exposure technique for treating anxiety disorders because VR and real objects have similar characteristics, which creates the illusion that the user is immersed and engaged with objects in the real world. Regarding the efficacy of using virtual reality exposure-based therapy (VR-EBT), for more than two decades, there has been sufficient empirical evidence regarding VR-EBT for treating anxiety disorders. Finally, this chapter ends with some directions and perspectives for future VR-EBT developments and treatments protocols.

1. Introduction

Anxiety is a natural response and a necessary warning adaptation in people. Anxiety can become a pathologic disorder when it is excessive and uncontrollable, requires no specific external stimulus, and manifests with a wide range of physical and affective symptoms as well as changes in behavior and cognition. The last version of the DSM (American Psychiatric Association, 2013) introduced several changes in the classification and diagnostic criteria for anxiety disorders, specifically on specific phobias, social anxiety disorder, and agoraphobia. APA defines anxiety disorders as "Disorders that share features of excessive fear and anxiety and related behavioral disturbances. The anxiety disorders differ from one another in the types of objects or situations that induce fear, anxiety, or avoidance behavior, and the associated cognitive ideation." The new classification of DSM-5 for anxiety disorders includes separation anxiety disorder, selective mutism, specific phobias (animal, natural environment, bloodinjection-injury, situational), social anxiety disorder (SAD), panic disorder, agoraphobia, generalized anxiety disorder (GAD), anxiety disorder due to another medical condition, other specified anxiety disorder, and unspecified anxiety disorder. In this chapter, we will focus on anxiety disorders in which there is empirical evidence regarding the use of VR-EBT in its treatment. This new classification for anxiety disorders no longer includes obsessive-compulsive disorder or posttraumatic stress disorder and acute stress disorder, and for this reason, they are not included in this chapter.

1.1. Virtual reality in the treatment of anxiety disorders

Virtual Reality (VR) is a technology that allows the simulation of different real-life situations in a tridimensional computer-generated environment where the user can interact with the environment as if he/she were in the real world. VR has potential as an exposure technique for treating anxiety disorders because VR and real objects have similar characteristics, which creates the illusion that the user is immersed and engaged with objects in the real world. Since its emergence, several studies have proved the usefulness of virtual reality exposure-based therapy (VR-EBT) for treating several psychological disorders, many of them focusing on anxiety disorders. These studies highlight the usefulness of VR-EBT in particular because it allows the patient to confront the different stimuli and significant elements associated with the anxiety disorder (Botella, Quero, Baños, Perpiñá, & García-Palacios, 2004b). Since the first VR systems emerged in the 90s, these have now become less costly, more widely available, and generally more usable; however, it is necessary that future researches report uniform and detailed information regarding presence, immersion, anxiety duration, and demographics (Parsons & Rizzo, 2008).

Another technology, which has also started to be explored for treating specific phobias, is augmented reality (AR). Which is considered as a variant of VR technology because it combines real world objects with virtual objects, using computer graphics that are blended into the real world and in real time. The user sees the real world "augmented" by virtual objects, that is, AR tries to complement or improve the reality, not to replace it. A core aspect of AR is that virtual objects add relevant and helpful information to the physical details of the real world (Azuma, 1997). Milgram and Kishino (1994) analyze the qualities of VR and AR systems along a continuum from real to virtual environments. In VR systems, the user is completely immersed in synthetic contexts, whereas in AR the user sees an image comprising both the real world and virtual objects. The review of Baus and Bouchard (2014) emphasizes that augmented reality exposure-based therapy (AR-EBT) has proven itself to be a tool where people suffering from specific phobias can be exposed safely to the fear objects, without the costs associated with programming complete VR environments.

Regarding the use of VR-EBT and AR-EBT in treating anxiety disorders, to date several studies have made important contributions to guide the study of the application of VR-EBT for treating anxiety disorders. These studies have shown promising results for generalizing the effectiveness of VR-EBT in the treatment of anxiety disorders.

A meta-analysis (Powers & Emmelkamp, 2008) compared controlled studies using VR-EBT with in vivo exposure therapy and a control group. This work was focused on the study of VR-EBT as a stand-alone treatment and excluded other studies combining VR-EBT with cognitive behavior therapy (CBT). The authors concluded that compared with in vivo exposure, VR-EBT was equally effective, however the small number of controlled studies based on a standalone VR-EBT, does not allow the generalization of these results to all anxiety disorders.

The results of a later meta-analysis (Opriş et al., 2012) which compared VR-EBT with evidence-based interventions, revealed several interesting conclusions regarding the use of VR-EBT on the treatment of anxiety disorders: (1) VR-EBT does far better than a waiting-list group. (2) The post-treatment results showed similar efficacy between the behavioral and the cognitive behavioral interventions incorporating a VR-EBT and evidence-based intervention with non-VR-EBT. (3) VR-EBT has a powerful real-life impact, similar to that of the classical evidence-based treatments. (4) VR-EBT has good stability of results over time, similar to that of the evidencebased treatments. (5) There is a dose–response relationship for VR-EBT. (6) There is no difference in the dropout rate between VR-EBT and in vivo exposure.

Likewise, literature reports VR-EBT presents several advantages in the treatment of anxiety disorders, for example:

- The main advantage of using VR-EBT is the *high degree of control* that the therapist has over the anxiogenic objects or situations; this control may encourage patients to begin exposure treatment, as it can prevent the occurrence of unpredictable events, which sometimes happens with in vivo exposure. The highest rated benefit was the ability to expose the patient to stimuli and places that would otherwise be difficult to access (e.g. an airplane, a high building, etc.).
- VR-EBT is an *effective treatment* for anxiety disorders.
- VR-EBT can be used to *maximize the benefits* of in vivo exposure.
- VR-EBT provides an *alternative* for those persons who consider that in vivo exposure is aversive.
- VR-EBT offers a more *confidential* setting than in vivo exposure; the patient's exposure task takes place within the discreet confines of the therapist's office.
- Using VR-EBT is *attractive* because of the cost-efficiency and simplicity relative to in vivo exposure.
- VR-EBT is a *flexible tool* that has allowed replicating different physical environments for treating several anxiety disorders.

VR-EBT research is *expanding* in different parts of the world with research carried out in the United States, Spain, Canada, Italy, Netherlands, United Kingdom, Germany, Australia, France, Belgium, South Korea, Switzerland, Israel, Luxembourg, Austria, Brazil, Mexico, South Africa, Chile, Sweden, Hungary, India, Portugal, Romania, Singapore among others. Although it has demonstrated its efficacy and numerous advantages, the use of VR-EBT in psychological treatments still has some limitations, years ago, was mainly noted the high costs or the limited accessibility to VR-EBT to therapists. However, as stated before (Parsons & Rizzo, 2008) in the last decade the costs have been reduced significantly, and therapists have access to more specific training regarding the application of VR-EBT in psychological treatments; this has facilitated its implementation throughout the world.

1.2 Virtual reality software developments

Several universities around the world have been studying for almost two decades, the possible insertion of VR-EBT in psychological treatments. Today this is a reality, and several mental health centers offer treatments based on VR-EBT to the general population. Some VR environments are commercially available for use in the treatment of several psychological disorders. These VR environments have demonstrated efficacy in the evidence-based treatment of different anxiety disorders. PreviSL (http://www.previsl.com) has available VR environments validated in the Hispanic population for treating claustrophobia, fear of flying, agoraphobia, and acrophobia. VRMC: Virtual Reality Medical Center (http://www.vrphobia.com) and Virtual Reality Medical Institute (http://www.vrphobia.eu) have available VR environments validated in English-speaking, and German-speaking populations for treating posttraumatic stress disorder (PTSD), chronic and acute pain, fear of flying, fear of heights, fear of spiders, and other specific phobias. Virtually Better (http://www.virtuallybetter.com) has available VR environments validated in English-speaking population for treating acrophobia, storm phobia, social anxiety disorder (SAD), fear of public speaking, and fear of flying. These centers also

provide support services for installation, training, and problem solving. CleVR (<u>http://clevr.net</u>) offers VR environments for treating fear of flying and fear of heights. Cliniques and Development in Virtuo (<u>www.invirtuo.com</u>) provides VR environments for treating specific phobias, GAD, SAD, obsessive compulsive disorder (OCD) and PTSD.

A few VR environments are also freely available on the condition of having a legal license of the programs necessary for its proper functioning, and these do not have support services for installation, training, or problem solving. The Cyberpsychology Lab at Université du Québec en Outaouais (http://w3.uqo.ca/cyberpsy/en/index_en.htm), freely shares three VR environments designed for treating arachnophobia, acrophobia, and claustrophobia. NeuroVR (http://www.neurovr.org), is a cost-free VR platform based on open-source software that offers a number of VR scenes which are configurable (office, class, apartment, scale, swimming pool, restaurant, lake, campfire, mountain, park, valley, waterfall, beach, desert, gazebo, island, waves, supermarket, auditorium, cinema, square, campfire, beach, lake and desert with oasis, hospital, station).

However, most VR environments remain commercially unavailable; this aspect continues limiting its imminent implementation in public and private mental health services, both industrialized and developing countries. Despite the limitations, more and more mental healthcare providers are approaching the empirically validated treatments using VR-EBT to the general population in different places in the world. Table 1 contains the main mental health centers that offer VR-EBT.

-Insert Table 1-

2. Virtual reality and specific phobias

According to the DSM-5, individuals with specific phobias are fearful or anxious, or avoidant of circumscribed objects or situations. A specific cognitive ideation is not featured in this disorder, as it is in other anxiety disorders. The fear, anxiety, or avoidance is almost always immediately induced by the phobic situation, to a degree that is persistent and out of proportion to the actual risk posed. There are various types of specific phobias: animal; natural environment; blood-injection-injury; situational; and other situations. It is common for individuals to have multiple specific phobias. The average individual with specific phobia fears three objects or situations, and approximately 75% of individuals with specific phobia fear more than one situation or object. In the United States, the 12-month community prevalence estimate for specific phobia is approximately 7% - 9%. Prevalence rates in European countries are largely similar to those in the United States (e.g., about 6%), but rates are generally lower in Asian, African, and Latin American countries (2% - 4%). Prevalence rates are approximately 5% in children and are approximately 16% in 13- to 17-year-olds. Prevalence rates are lower in older individuals (about 3% - 5%), possibly reflecting diminishing severity to subclinical levels (American Psychiatric Association, 2013).

2.1 Efficacy of virtual reality in specific phobias treatment

The use of VR environments for treating specific phobias has been the field most studied with regard to psychological treatments. Literature reports since the year 1995 to 2017 more of 80 studies that demonstrate its effectiveness, advantages, and limitations. The variety of specific phobias in which the usefulness and effectiveness of VR-EBT has been studied are numerous, among which are the fear of flying, arachnophobia, claustrophobia, acrophobia, driving phobia, storm phobia, school phobia, cockroaches phobia, blood-injection phobia and small-animal phobia. Treatments have been carried out from a single session to an average of 12 sessions.

The first case study, which explored the utility of VR-EBT for specific phobias in acrophobia, was carried out by Rothbaum et al. (1995). This study was one of the starting points to perform other studies and thus to study the usefulness and effectiveness of VR-EBT in the treatment of specific phobias. Most studies have found positive results, demonstrating the effectiveness of VR-EBT for treating specific phobias.

2.1.1 Acrophobia treatment using VR-EBT

Acrophobia is characterized by a marked anxiety upon exposure to heights, avoidance of heights, and a resulting interference in functioning of the individual. VR-EBT technology has been used in the psychological treatment of acrophobia since the first randomized clinical trial (RCT) published in 1995 (Rothbaum et al., 1995) which evaluated the *efficacy* of a VR-EBT in a sample of 20 participants. The only treatment condition was carried out on 8-weekly sessions, demonstrating its effectiveness. It was found significant differences between the VR-EBT and a waiting-list group. The authors conclude that treatment with VR-EBT was successful in reducing fear of heights.

The *efficacy* of another RCT with two treatment conditions (VR-EBT and in vivo exposure treatment) has been proved with a sample of 33 acrophobic participants (Emmelkamp et al., 2002). The treatment conditions were carried out on three sessions. Results showed that VR-EBT was as effective as in vivo exposure treatment, reducing the acrophobia symptoms; in addition, the results were maintained up to 6-month follow-up.

These positive results were also found in another study conducted by Coelho, Silva, Santos, Tichon, and Wallis (2008) showing significant progress on anxiety and avoidance behavior when participants were confronted with real height circumstances, participants keep these results in the one-year follow-up.

The *role of cognitive self-statements* on VR-EBT has been explored in a study with a sample of 26 participants (Krijn, Emmelkamp, Ólafsson, Schuemie, & Van Der Mast, 2007b). The authors hypothesized that coping self-statements would enhance the effectiveness of VR-EBT. Results showed improvements regardless of the addition of coping self-statements. Specifically, VR-EBT with coping self-statements decreased anxiety of heights, decreased avoidance of height situations, and improved attitudes towards heights. However, these positive results were not maintained in the 6-month follow-up.

Many research groups have realized the importance of including objective physiological measures in VR treatment protocols. Wilhelm et al. (2005) immersed 20 non-phobic participants in a virtual elevator while monitoring heart rate and skin conductance to determine if VR was able to activate both the behavioral activation (BA) and the behavioral inhibition (BI) systems. Analysis of high-anxiety and low-anxiety groups revealed no statistically significant difference in heart rate (BA) but did reveal a difference in skin conductance (BI). When individuals are exposed in vivo, both systems are activated. As VR systems progress in power and believability, the activation of both systems could leader to more powerful VR-EBT.

In addition to peripheral physiology, it is important to begin to understand the neurophysiological processes involved in VR-EBT. A group of researchers studied the impact of glucocorticoids in 40 patients suffering from acrophobia (De Quervain et al., 2011). Subjects were given either cortisol or a placebo one hour prior to each of three sessions of VR-EBT. Among other measures, the Acrophobia Questionnaire was administered pre- and post-treatment

(3-5 days after the last exposure) and at 1 month follow-up. Results showed that acrophobics receiving VR-EBT combined with cortisol showed greater fear reduction at post-treatment and follow-up compared to subjects in the placebo condition.

In literature are also described different VR-EBT and AR-EBT systems, with different immersion levels and characteristics. These systems have demonstrated its ability to generate sense of presence and immersion; they also showed its potential usefulness in the treatment of acrophobia (Ibrahim et al., 2008; Jang et al., 2002; Juan et al., 2006). A study evaluated *differences in sense of presence using an HMD or a CAVE system* (Krijn et al., 2004). VR-EBT for treating acrophobia showed to be effective in the post-treatment and at 6-month follow-up, but no differences were found in effectiveness between VR-EBT outcomes using an HMD or a CAVE.

Subsequent studies have been able to replicate the mentioned results, thus revealing the effectiveness of the use of VR in the treatment of this specific phobia (Coelho, Silvério, Da Silva, & Santos, 2014; Levy, Leboucher, Rautureau, & Jouvent, 2015)

Beyond these studies, it is also important to point out that VR has been transitioned successfully from the laboratory to the private clinical setting. As an example, at the Virtual Reality Medical Centers in California, Belgium and China, the success rate of VR-EBT for specific phobias is estimated at 92%. At these clinics, the treatment is set up much like many of the studies above however; the VR-EBT can be combined with other forms of therapy to create a more individualized approach for clients to improve the chance of a successful treatment outcome.

2.1.2 Arachnophobia treatment using VR-EBT

Arachnophobia is a persistent fear of spiders, an immediate anxiety response on exposure to spiders, and avoids spiders. These symptoms can interfere with the patient normal social routines, activities, and interpersonal relationships and can produce distress about having the fear. The person typically recognizes that his or her fear is excessive or unreasonable.

The first case study regarding the use of a VR-EBT for arachnophobia treatment (Carlin, Hoffman, & Weghorst, 1997) demonstrated the efficacy of a VR-EBT combined with mixed reality (touching real objects which participant also saw on VR-EBT). Treatment was conducted in 12 sessions. The authors described that each session consisted of five, 5-min trials with a 2 or 3-min break between trials. The participant was sometimes encouraged to pick up the spider and/or web with her cyber-hand and place it in orientations that were most anxiety provoking. Spiders were placed in a cupboard with a web, made to jump unpredictably upon being touched, made to climb or drop in incremental jumps between the ceiling and the virtual kitchen floor, and they were touched, held and manipulated by the participant. Results suggest that VR-EBT was effective in reducing anxiety and avoidance of real spiders. A RCT with one treatment condition compared the efficacy of a VR-EBT versus a waiting-list group (García-Palacios, Hoffman, Carlin, Furness, & Botella, 2002) with a sample of 23 participants, who received four sessions of treatment. The authors report that to have completed treatment participants must be able to achieve a final exposure goal, holding a big virtual spider with tactile feedback while reporting low levels of anxiety. Then as the participants reached out with their cyber-hand to explore the virtual spider, their real hand explored a toy spider. Results showed that VR-EBT was effective for treating arachnophobia; the authors

suggest that using VR-EBT with tactile augmentation significantly reduced fear and avoidance of spiders. A later RCT confirmed the hypothesis that *tactile augmentation improves the outcome of immersive VR-EBT* because it adds a physical texture and force feedback cues to VR-EBT (Hoffman, García-Palacios, Carlin, Furness, & Botella, 2003). Tactile augmentation is defined as a simple, safe, and inexpensive interaction technique for adding physical texture and force-feedback cues to virtual objects. The purpose of this study was to give participants the illusion of physically touching a virtual spider and evaluated that this increases treatment effectiveness. Eight participants with arachnophobia were assigned to a no treatment group, a VR-EBT, or a VR-EBT with tactile augmentation group; in this last, a physically "touchable" virtual spider (a toy spider) was used. Treatment was carried out in three sessions. Results showed that the VR-EBT with tactile augmentation had the greatest progress on behavioral avoidance and subjective fear ratings.

A less expensive alternative VR-EBT system for treating arachnophobia has been tested in an open trial conducted by Bouchard, Côté, St-Jacques, Robillard, and Renaud (2006). The VR-EBT system was developed using modified 3D games to offer graduals hierarchies of fearful stimuli. It was tested in 10 participants who received a five session of treatment. Results showed significant improvement in avoidance, beliefs, and perceived self-efficacy after the treatment. The authors suggest that this results using VR-EBT by a modified computer game are promising and useful in the treatment of arachnophobia. A later RCT with two treatment conditions and 3month follow-up (Michaliszyn, Marchand, Bouchard, Martel, & Poirier-Bisson, 2010) compared the efficacy of VR-EBT and in vivo exposure with a waiting-list group. A total of 32 participants took part in the study; participants received eight treatment sessions. Clinical and statistically significant improvements were found both VR-EBT and in vivo exposure groups; no significant differences between both groups were found. The authors suggest that both in vivo exposure and VR-EBT are efficient methods of treating arachnophobia.

Kleim et al. (2013) have studied the *enhancement of memory consolidation with sleep*: eighty subjects were recruited and fifty (who met inclusion criteria) were given one-session of VR-EBT. The protocol was similar to that used for an acrophobia study done by this group (De Quervain et al., 2011). After exposure, participants were randomly assigned to a wake condition (watching a neutral movie) or were allowed to nap. All participants then completed a behavior avoidance test (BAT) and after 1 week returned for a second BAT. Those in the sleep condition had a greater reduction in anxiety. This approach could allow for a more effective VR-EBT for those patients who do not initially receive benefit from exposure or who suffer from relapse (Craske & Mystkowski, 2006).

2.1.3 Claustrophobia treatment using VR-EBT

Botella's team (Botella et al., 1998) has developed and validated the first VR-EBT for treating claustrophobia. This first case study involving this VR-EBT showed improvement in claustrophobia symptoms and these were maintained at one-month follow-up. A later case study (Botella, Villa, Baños, Perpiñá, & García-Palacios, 1999) suggested that this same VR-EBT had an effect over other specific symptoms which were not treated. The authors concluded that VR-EBT was effective in reducing fear in closed spaces, in increasing self-efficacy in claustrophobic situations, and in improving other problems not specifically treated. Moreover, changes in participants were maintained at 3-month follow-up. A later open trial with a 3-month follow-up has proved the *effectiveness of this VR-EBT in* the treatment of claustrophobia (Botella, Baños, Villa, Perpiñá, & García-Palacios, 2000). Four participants took part in the study. Treatment

consisted of eight sessions. VR-EBT lasted approximately 35 to 45 minutes each session; the therapist's instructions in the VR-EBT sessions were similar to those used in regular in vivo exposures. The therapist encouraged the participant to interact with the VR-EBT environments long enough for his or her anxiety to decrease. Results supported the effectiveness of the VR-EBT for treating claustrophobia; moreover, changes were maintained at 3-month follow-up. The authors suggest that VR-EBT was effective in reducing fear and avoidance in closed spaces and for increasing self-efficacy in claustrophobic situations. A later case study (Botella et al., 2002) again found these positive findings.

2.1.4 Fear of flying treatment using VR-EBT

Fear of flying is a specific situational phobia. It is characterized by an excessive, irrational fear of airplanes or any related situations, which are avoided or endured with great anxiety. Several studies using VR-EBT have demonstrated its effectiveness for treating this specific phobia.

Wiederhold and cols., carried out the first RCT to explore the *efficacy of VR-EBT and physiological monitoring* for treating people with specific phobia (Wiederhold, Gevirtz, & Wiederhold, 1998). A case study was first done to evaluated the physiological symptoms that a person with fear of flying versus a person without fear of flying manifest. Heart rate, peripheral skin temperature, respiration rate, sweat gland activity, and brain wave activity were measured during a 5-min eyes closed baseline period, a 20-min virtual flight, and a 5-min eyes closed recovery period. Differences were found between the two participants' physiological responses. The authors suggest that physiological monitoring appears to be helpful when working with persons in VR-EBT environments and provides objective data that desensitization is occurring. A

later RCT (Wiederhold et al., 2002) evaluated the efficacy of a VR-EBT compared with an *imagination exposure treatment*. A sample of 30 participants was randomized into three groups (VR-EBT with or without physiological feedback, and imagination exposure); treatment was carried out in 6 exposure sessions done once per week. Each group showed improvements in selfreport measures, and participants in the VR-EBT groups were able to fly without medication during a post-treatment follow-up period (VR-EBT with physiological feedback, 100%; VR-EBT alone 80%). Moreover, the analysis of physiological responses showed that both VR-EBT groups became much more physiologically aroused than did the exposure with imagination group. The authors suggest that VR-EBT may help in the habituation process. One-year later, the authors presented the data of the 3-year follow-up treatment (Wiederhold & Wiederhold, 2003). Results showed all participants in the VR-EBT with physiological feedback maintained their ability to fly after three years post-treatment whereas there was some relapse in those receiving only VR-EBT. The authors suggest that the addition of teaching self-control via visual feedback of physiological signals may serve to enhance treatment success initially and may help to maintain treatment gains in long-term follow-up.

Rothbaum and cols., have also studied the *efficacy of VR-EBT* for treating this specific phobia. In their first work (Rothbaum, Hodges, Smith, Lee, & Price, 2000) conducted a RCT with a 6-month follow-up using a VR-EBT environment described in a previous study (Hodges, Watson, Kessler, Rothbaum, & Opdyke, 1996). A sample of 49 participants was randomly assigned to VR-EBT, traditional in vivo exposure therapy, or to a waiting-list group. Treatment was completed in eight sessions. Results indicated that VR-EBT and traditional exposure therapy were both superior to waiting list group, with no differences between VR-EBT and traditional in vivo exposure therapy; in addition, the gains observed in the treatment were maintained *at 6-month follow-up*. A later study (Rothbaum, Hodges, Anderson, Price, & Smith, 2002) reported

the *12-month follow-up data*. At 12-month follow-up participants maintained their treatment gains, and 92% of VR-EBT participants and 91% of traditional in vivo exposure therapy participants had traveled by airplane. A later RCT (Rothbaum et al., 2006) with a larger sample (83 participants) tested a VR-EBT with a six and 12-month follow-up and compared it with a traditional in vivo exposure therapy and a waiting-list group. The treatment consisted of eight sessions of anxiety management training followed either by exposure to a virtual airplane or a real airplane at the airport. Results indicated that VR-EBT was superior to waiting-list group. Nevertheless, they found no significant differences between VR-EBT and in vivo exposure therapy. Follow-up assessments at six and 12 months indicated that treatment gains were maintained.

Another RCT (Tortella-Feliu et al., 2011) analyzed the efficacy of *three computer-based exposure treatments* for fear of flying: a VR-EBT, a computer-aided exposure with a therapist's assistance, and a self-administered computer-aided exposure (without therapist's assistance). A sample of 60 participants with fear of flying was randomly assigned to each group. Results showed that the three treatments were effective in reducing fear of flying at post-treatment and at one-year follow-up. Large within-group effect sizes were found for all three treatments conditions at both post-treatment and at follow-up. The authors suggest that therapist involvement might be minimized during computer-based treatments, and that a self-administered computer-aided exposure with or without therapist's assistance can be as effective as VR-EBT in reducing fear of flying.

The RCT conducted by Rus-Calafell, Gutiérrez-Maldonado, Botella, and Baños (2013) compared the effectiveness of a *VR-EBT with an exposure treatment with imagination*; a sample of 15 participants with fear of flying were randomly assigned to either VR-EBT or exposure treatment with imagination; treatments consisted of six exposure sessions. Results showed no

differences between the two treatments in relation to reduced clinical symptomatology associated with fear of flying, although participants in the VR-EBT experienced less anxiety during the real flight after the treatment. Furthermore, at 6-month follow-up, danger expectations and flight anxiety continued to decrease in participants who had received the VR-EBT, and some participants took at least one more flight. Results were consistent with those found by Wiederhold et al. (2002) who also evaluated the effectiveness of a VR-EBT compared to a treatment with imaginal exposure.

Botella and cols., have also carried out several studies which have demonstrated the efficacy of VR-EBT in the treatment of this specific phobia. First, a case study (Baños, Botella, Perpiná, & Quero, 2001) and a case series study with four participants (Baños et al., 2002) demonstrated its effectiveness. In a later open trial with one-year follow-up (Botella, Osma, García-Palacios, Quero, & Banõs, 2004a) the short and long term efficacy of VR-EBT was evaluated. The study was carried out with a sample of nine participants using a multiple baseline design (one, two, and three weeks). The treatment included one session of education about anxiety, flying, and exposure, and six sessions of VR-EBT. Results obtained, at post-treatment and one-year follow-up, support the efficacy of VR-EBT in the treatment of fear of flying; after the treatment, all participants flew. This study supported the hypothesis that VR-EBT can be considered as a unique therapeutic component for fear of flying treatment. A cross-cultural validation of this VR-EBT was carried out in a Mexican population (Cárdenas et al., 2009). Five participants took part in the study. Results showed that VR-EBT was effective for treating fear of flying in Mexican population. Participants achieved improvement regarding their avoidance and fear; they were able to control their anxiety levels; and all were able to fly into the three months after the treatment. In addition, results offer evidence regarding the convenience to crosscultural validation for treatment protocols, it showed a high percentage average of agreement

between judges in the dimensions of cultural pertinence, language, and theoretical validity, in the dimension of wording the average scores above 90%. The authors suggest that the emotional perception of the problems as well as the idiomatic expressions have to be adapted to the cultural and social context of the target population.

Another open trial was carried out in a collaborative effort between Bouchard's clinic in Québec (Canada) and Wiederhold's clinics in California (USA) (Robillard, Wiederhold, Wiederhold, Larouche, & Bouchard, 2004). A total of 53 aviophobics received 8 to 10 VR-EBT sessions with therapists who varied in their experience with VR. Results showed a statistically significant reduction in the scores on two questionnaires: Fear of Flying and Attitudes towards Flying, with large effect sizes (>.60).

Other aspects such as the *treatment time and efficacy of treatment components* have also been studied. The efficacy of a 1-session of VR-EBT with a 6-month follow-up was evaluated in a sample of 45 participants (Mühlberger, Wiedemann, & Pauli, 2003). The VR-EBT environment was validated in a previous study (Mühlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001) demonstrating its effectiveness as a tool for treating fear of flying. Participants were randomly assigned to a VR-EBT with motion simulation, a VR-EBT, or a cognitive treatment alone. Results revealed reduced fear of flying only in the VR groups' treatment. Regarding the dismantling of treatment components in VR-EBT with motion simulation, results also revealed that visual and acoustic stimuli were the main active components of VR-EBT; motion simulation as part of VR-EBT exposure does not seem to further enhance treatment effects.

The comparative efficacy of *VR-EBT with CBT and bibliotherapy* (without therapist contact) has been evaluated in an open trial (Krijn et al., 2007a) with a sample of 86 participants who took part in the study. VR-EBT was carried out in four weekly sessions. Results showed that the treatment with VR-EBT or CBT was more effective than bibliotherapy; statistically

significant differences were not found between VR-EBT and traditional CBT. Regarding effectiveness, VR-EBT as a sole treatment component was not sufficiently effective in reducing phobic symptoms. The authors suggest that VR-EBT or CBT hold promise as treatment for fear of flying; in this study it was the addition of cognitive training with an in vivo exposure component that showed the largest decrease in participants' anxiety, therefore, they suggest the combination of CBT with exposure techniques.

Since 1998, studies support the efficacy of VR-EBT in the treatment of fear of flying. Table 2 shows a comparative of the components for fear of flying treatments included in some VR-EBT protocol treatments. Recent studies have replicated the mentioned results, thus revealing the effectiveness of the use of VR in the treatment of this phobia (Boyd & Hart, 2016; Czerniak et al., 2016; Ferrand, Ruffault, Tytelman, Flahault, & Négovanska, 2015).

-Insert Table 2-

2.1.5 Driving phobia treatment using VR-EBT

Driving phobia is defined as a specific phobia. It is considered as a situational phobia, and is one of five types of specific phobias that also include animal, natural environment, bloodinjection-injury, and others. Driving phobia has been less studied compared to other specific phobias (e.g., fear of flying, spider phobia, or claustrophobia). In literature there are few preliminary results regarding the efficacy of VR-EBT for treating driving phobia. A case study (Wald & Taylor, 2000) evaluated its efficacy in a long-standing driving phobia; the participant was treated with a VR-EBT with a design including a 7-day baseline phase followed by three treatment sessions using a standardized treatment protocol. Results showed that phobic symptoms decreased from the pre-treatment assessment, and gains were maintained at 1 and 7-month follow-up assessments.

The effectiveness of the *combination of two technologies involving computer-generated environments* (a driving game and a VR-EBT) for treating driving phobia has been evaluated (Walshe, Lewis, Kim, O'Sullivan, & Wiederhold, 2003). The open trial was carried out with a sample of 14 participants diagnosed with driving phobia after a motor vehicle accident. The treatment was carried out a maximum of 12 sessions. In addition to the exposure component, the treatment included self-monitoring, cognitive reappraisal, physiological feedback, and diaphragmatic breathing. Measures included physiological response, subjective ratings of distress, and severity of driving phobia, post-traumatic stress, depression, and achievement of target behaviors. Findings at post-treatment supported the utility of VR-EBT and computer games in the treatment of driving phobia even when co-morbid conditions such as post-traumatic stress disorder and depression were present.

The *efficacy of VR-EBT* in the treatment of driving phobia has also been demonstrated in another open trial with one-year follow-up (Wald, 2004). The VR-EBT was applied during 8weekly sessions in a sample of five participants. Results showed significant reductions in fear and avoidance symptoms in three of five participants that were maintained at one-year follow-up. However, VR-EBT did not result in an increase in driving frequency for any of the participants. The author suggests that VR-EBT might be most useful as a preparatory intervention or as an adjunct for in vivo exposure rather than as a stand-alone intervention.

These studies regarding the use of VR-EBT for treating driving phobia are preliminary but they offer promising findings; however, we need studies for exploring the efficacy of VR-EBT in this specific phobia. The main potential advantages of VR-EBT for treating driving phobia lie in its ability to provide safe, controlled, and standardized driving practice. It may be a more acceptable and less-threatening treatment medium than in vivo exposure for some people. However, there is relatively little controlled treatment outcome research on driving phobia and no controlled studies to date have examined the efficacy of VR-EBT for this type of phobia (Wald, 2004).

Additionally, the systematic environments offered by VR can also be used for testing driving abilities. A study conducted at VRMC in San Diego in 2002 tested the effects of antihistamines (fexofenadine, loratidine, and cetirizine) on cognitive abilities (Wiederhold & Wiederhold, 2013).

2.1.6 Cockroaches phobia and arachnophobia treatment using AR-EBT

The first study offering a detailed description of a system for AR-EBT (Botella et al., 2005) used only *one-session* for the treatment of cockroaches phobia. Results of this study were very encouraging, and indicated that the AR-EBT system was capable of generating anxiety in participants; furthermore, their levels of anxiety and avoidance decreased. Other studies (Juan et al., 2005; Juan et al., 2006; Juan et al., 2004) confirm the efficacy of VR-EBT in the treatment of cockroaches phobia and arachnophobia using AR-EBT and offer data concerning the ability of the AR-EBT system to activate anxiety in participants suffering cockroach phobia or arachnophobia.

An open trial carried out with six participants diagnosed with cockroach phobia (Bretón-López et al., 2010) validated the stimuli included into an AR-EBT system depending on the capacity of the elements to activate the fear structure. The main aim of the study was to explore whether the various stimuli included into the AR-EBT system can induce anxiety in participants. Results supported the adequacy of AR-EBT system in inducing anxiety in all participants. The authors confirmed the results obtained in previous studies (Botella et al., 2005; Juan et al., 2005) regarding the capacity of the AR-EBT system to elicit sense of presence and reality judgment. The efficacy of this system in AR-EBT for cockroach phobia was demonstrated in a later open trial (Botella, Bretón-López, Quero, Baños, & García-Palacios, 2010). The AR-EBT was applied using a one-session treatment and in addition, includes modeling, reinforced practice, and cognitive challenge. Results showed that AR-EBT was effective for treating cockroach phobia. All participants improved significantly in all outcome measures after the treatment; furthermore, the treatment gains were maintained at 3, 6, and 12-month follow-up assessment.

The only system reported in the literature using a *serious game by mobile phone* as tool for treating cockroaches phobia



Figure 1) based in an *AR-EBT* has been tested in a case study (Botella et al., 2011). This system follows a series of clinical indications according to the existing knowledge of exposure therapy: (1) it includes different levels regarding the feared stimuli in order to make it possible to develop a hierarchy that would enable systematic and graduated exposure; (2) it allows users to gradually advance in the game, enhancing the sense of mastery and self-efficacy regarding being able to stay in a place where cockroaches are present; (3) it uses a neutral context; (4) it does not include any reference to dirt so that the user can overcome irrational thoughts associated with

this; (5) it includes elements related to game and challenge; (6) it includes some kind of reward. Results showed that the use of the mobile phone serious game reduced the level of fear and avoidance. The participant found very helpful the use of the serious game and she was willing to use it after AR-EBT session as a homework assignment. The authors suggest that although the results of the case study are preliminary, serious game could be an emerging subject of research with high interest for treating specific phobias.



-Insert

Figure 1-

Another interesting tool is the *interactive projection-based AR-EBT system* for treating cockroach phobia and arachnophobia named *"Therapeutic Lamp"* (Wrzesien et al., 2013). This is a tabletop system that integrates the user's hands, a coffee mug, a cardboard box, a flyswatter, a finger and object detection, and a tracking over a flat surface (a table or a floor). For the small animal stimuli application, were modeled from small size to medium-size stimuli, in addition to a tarantula (for arachnophobia). The system was tested with a subclinical population sample. The

results indicated that this system seems an effective, well-adapted tool for cockroach phobia and arachnophobia treatments.

2.1.7 Storm phobia treatment using VR-EBT

A versatile VR-EBT system without HMD has been used for treating storm phobia (Botella et al., 2006b). A case study showed the efficacy of this system for reducing phobic symptoms. The treatment was applied in two phases: in vivo exposure and VR-EBT simulating storms, rain, thunders, and lightings. For VR-EBT, was used a virtual meadow in which was included a storm with lightings, thunders of different intensity, and it was varied the time of day (from morning until night). The treatment consisted of a total of 7-sessions: two psychoeducation sessions, three in vivo exposure sessions, and two intensive VR-EBT sessions. Results showed positive changes in the phobic symptoms; at the end of the treatment, the participant was able to confront the situations related to storms; results were maintained at 6-month follow-up. In addition, the participant reported a high sense of presence. The authors suggest a high potential of VR-EBT for treating storm phobia.

;Error! No se encuentra el origen de la referencia.Figure 2 shows some examples of VR-EBT environments used for treating specific phobias.

-Insert Figure 2–

Finally to mention that studies regarding the uses of VR-EBT in the treatment of specific phobias have been mainly focused in the treatment of adult population. In the last years, it has also begun to study more specifically, the use of VR-EBT for treating *specific phobias in children*, for example for treating small-animal phobia or arachnophobia (Botella, Baños, &

Fabregat, 2006a; Bouchard, 2011; Bouchard, St-Jacques, Robillard, & Renaud, 2007; Quero et al., 2014a; St-Jacques, Bouchard, & Bélanger, 2010) or for treating school phobia (Gutiérrez-Maldonado, Magallón-Neri, Rus-Calafell, & Peñaloza-Salazar, 2009). Considering the high prevalence of specific phobias in children, this is a field of study, which should be paid more attention.

3. Social anxiety disorder

According to the DSM-5, the individual with social anxiety disorder (SAD) is fearful or anxious or avoidant of social interactions and situations that involve the possibility of being scrutinized. These include social interactions such as meeting unfamiliar people, situations in which the individual may be observed eating or drinking, and situations in which the individual performs in front of others. The cognitive ideation is of being negatively evaluated by others, by being embarrassed, humiliated, or rejected, or offending others. The 12-month prevalence estimate of SAD for the USA is approximately 7%. Lower 12-month prevalence estimates are seen in much of the world using the same diagnostic instrument, clustering around 0.5%-2.0%; median prevalence in Europe is 2.3%. The 12-month prevalence for older adults ranges from 2% to 5%. Prevalence in the USA is higher in American Indians and lower in persons of Asian, Latino, African American, and Afro-Caribbean descent compared with non-Hispanic whites. SAD is associated with elevated rates of school dropout and with decreased well-being, employment, workplace productivity, socioeconomic status, and quality of life. SAD is also associated with being single, unmarried or divorced, and with not having children, particularly among men (American Psychiatric Association, 2013).

3.1 Efficacy of virtual reality in social anxiety disorder and fear of public speaking treatments

Some studies have been published regarding the efficacy of VR-EBT in the treatment of people suffering SAD or fear of public speaking (FPS) and the few controlled studies that have been conducted also suggest that VR-EBT is effective in its treatment. However, research on the application of VR-EBT in this disorder remains limited. In most studies, the VR-EBT environments were scenes with an audience facing which participants had to talk (Anderson, Zimand, Hodges, & Rothbaum, 2005; Harris, Kemmerling, & North, 2002; Pertaub, Slater, & Barker, 2002). These audiences were characterized by showing different attitudes towards the person in order to generate anxiety. The mean number of sessions was around four and five, in a range from one to 12 sessions. Frequency was weekly or intensive sessions (Anderson, Rothbaum, & Hodges, 2003). Other studies have tested other scenarios as being in a subway, a bar, a coffee shop, or a job interview, in order to expose participants to other typical anxiogenic states to work the lack of assertiveness, interaction, intimacy, or evaluation by the others (Grillon, Riquier, Herbelin, & Thalmann, 2006; James, Lin, Steed, Swapp, & Slater, 2003; Klinger et al., 2005; Roy et al., 2003; Wallach, Safir, & Bar-Zvi, 2009).

The first study that investigated the usefulness of VR-EBT in the treatment of FPS (North, M., & Coble, 1998) compared a VR-EBT environment with social anxiogenic scenes with another VR-EBT environment without social anxiogenic scenes. The treatment was carried out in 5-weekly sessions. In the study collaborated 16 participants. Results show significant differences, the group with VR-EBT and social anxiogenic scenes showed significant improvement.

Another early study that evaluated the usefulness of VR-EBT for FPS treatment (Slater, Pertaub, & Steed, 1999) measured the emotional response when participants were exposure to a virtual audience seems attentive and interested, or when audience seems hostile and disinterested. Their main finding was that participants responded appropriately to negative or positive audiences; negative audiences evoked high anxiety levels, even when these are virtuals. These results were confirmed in a subsequent study (Pertaub et al., 2002) with a sample of 40 participants. A later study evaluated the response of persons with social anxiety regarding to a VR-EBT environment (Slater, Pertaub, Barker, & Clark, 2006). The main contribution of these studies was to demonstrate the utility of VR-EBT in the treatment of FPS and the VR-EBT environment capability for generating sense of presence.

The RCT conducted by Harris et al. (2002) compared the efficacy of a VR-EBT treatment for FPS with a waiting-list group. The sample was composed of 14 participants how received four individual exposure sessions of approximately 15 min. Results suggested that four VR-EBT sessions were effective for reducing the symptoms of FPS.

One year later, a case study with two participants (Anderson et al., 2003) evaluated the efficacy of a VR-EBT when this was applying on 10-weekly sessions or six intensive sessions (during three days). Participants met criteria for SAD and FPS, and they were exposed to a virtual audience. The VR-EBT environments consisted of videos embedded within a virtual classroom, these proved its effectiveness for reducing social anxiety symptoms. In both case studies, scores on all measures of FPS decreased. Results from these two case studies suggested that VR-EBT may be a useful tool for SAD and FPS treatments. In a later study, a VR-EBT was evaluated in a sample of 10 participants diagnosed with FPS; treatment was carried out in eight sessions. Results suggested that 80% of participants were significantly improved after VR-EBT, and 75% of them maintained treatment gains at 3-month follow-up.

The first RCT that used VR-EBT for treating SAD (Roy et al., 2003) demonstrated its efficacy compared with a traditional CBT and a waiting-list group. The VR-EBT was evaluated in a sample of 10 participants suffering SAD. Participants were exposed to four VR-EBT environments that evoked performance, intimacy, scrutiny, and assertiveness. Each participant attends 12 sessions of VR-EBT. In a later RCT with a large sample of 36 participants diagnosed with SAD was compared a VR-EBT with a CBT (Klinger et al., 2005). Results showed statistically and clinically significant improvement in both treatments; these were highly effective to reduce social anxiety and social avoidance. The differences in efficacy between VR-EBT and CBT were not significant. In both studies the VR environments used for VR-EBT included situations that target fears other than fear of public speaking.

The efficacy of a VR-EBT was studied in another RCT with a sample of 88 participants with FPS (Wallach et al., 2009). The VR-EBT was compared with a traditional CBT and a waiting-list group. Treatment was carried out in 12 sessions. Results showed a large effect sizes for anxiety reduction following treatment both VR-EBT and CBT; therefore, the authors concluded that both VR-EBT and CBT are useful treatments for FPS. In addition, they found a lower dropout rate from VR-EBT in relation to the CBT; VR-EBT was found most attractive to participants. A later study including a one-year follow-up (Safir, Wallach, & Bar-Zvi, 2012) found that the positive VR-EBT treatment effects were maintained on anxiety symptoms. However, the authors note that treatment helped to reduce avoidance to a non-clinical level and that fear level had not yet been reduced to a non-clinical level; therefore, they suggest that perhaps fear reduction requires more than a 12-session program.

The RCT conducted by Anderson et al. (2013) with a 12-month follow-up, evaluated the efficacy of a VR-EBT compared with an in vivo exposure therapy and a waiting-list group. In the study took part 97 participants diagnosed with SAD. The treatment was carried out in eight

sessions. Results showed that participants from VR-EBT and in vivo exposure group therapy significantly improved on all but one measure (length of speech for the exposure group therapy and self-reported fear of negative evaluation for VR-EBT). At 12-month follow-up, people showed significant improvement from pre-treatment on all measures. There were no differences between both exposure treatments. The authors suggest that VR-EBT is equally effective as in vivo exposure group therapy.

In a recent RCT to address the broad spectrum of social fears of people suffering from SAD, Bouchard et al. (2017) recruited 59 adults receiving a diagnosis of SAD that were randomly assigned to CBT with traditional in vivo exposure, VR-EBT and a waiting list. Participants in the active treatment conditions received 14 individual weekly CBT sessions with exposure sessions performed either only in vivo or only in virtuo. Treatment integrity was maintained by reliance on a treatment manual adapted from Clark (2001) and assessment included anxiety scales and self-report questionnaires (e.g. LSAS, Social Anxiety Disorder Scale, Fear of Negative Evaluation, Beck Depression Inventory-II) and a BAT. Two sets of analyses were performed: (a) classical statistical inferences tests to find differences between the two active treatments, and (b) non-inferiority tests to document with statistical tests the lack of difference between the two active treatments. Results with the final sample and the follow-up data confirmed that both treatments were more effective than the no-treatment condition and as effective to each other. This finding is already interesting. But Bouchard et al. (2017) also documented the efforts required by therapists to conduct the exposure sessions and found important advantages of conducting exposure in virtuo, which was significantly less cumbersome and costly to conduct than in vivo ones, in terms of having access to relevant stimuli to induce ridicule, duration, preparation, worries about confidentiality, costs of gathering staff members to attend at public speaking exercises.

Table 3;Error! No se encuentra el origen de la referencia.;Error! No se encuentra el origen de la referencia. show a summary of the treatment protocols, used in some of these RCT.

-Insert Table 3-; Error! No se encuentra el origen de la referencia.

Other specific factor in SAD, is the *eye contact avoidance*, which has been studied by using an eye-tracking system (Grillon et al., 2006). The treatment was carried out using a VR-EBT in a sample of eight participants with SAD. Results suggested a significant improvement after the treatment and a positive correlation between the decrease of anxiety and the decrease of eye contact avoidance; eye-contact avoidance diminished after the treatment.

In addition to the above, also mention that in SAD treatment using VR-EBT some issues has been little studied. For example, *free speech dialogues* with avatars is an issue poorly studied because most of studies have focused mainly on recreating a social setting (e.g., a bar, a shop, a dinner), or non-verbal language of avatars (e.g., attentive, boring, or tired). The work of Brinkman et al. (2012) evaluated a VR-EBT based on speech dialogues; therapists can select from a limited set of avatar's reply sentences, or they can speak live through a microphone to create the avatar's voice, this allow participants to be exposed to free speech dialogues with different avatars. The authors also suggest that a system with these characteristics could be used in a remote setting, where therapist and participants are located at different locations. This system used a remote VR-EBT platform that supports remote treatment, using the Internet to connect the therapist and the patient computer.

Another issue poorly studied is the *interaction in real time with avatars* into VR-EBT environments. The study conducted by Powers et al. (2013) explored the possibility that virtual avatars interact and converse with the patient in real time. This technology allowing to therapist directly control the avatar (including speaking) during VR-EBT. Results showed that

conversation in VR-EBT environment elevated fear ratings; however, in vivo conversation was rated as more realistic than the conversation in VR-EBT environment. The authors suggest that real time interaction or conversation in VR-EBT environment may prove useful for treating SAD in future studies.

Another recent studies have been able to replicate all these results, but also have found interesting findings that make the use of RV be much more effective in the treatment of this disorder (Anderson, Edwards, & Goodnight, 2017; Kim et al., 2017; Parrish, Oxhandler, Duron, Swank, & Bordnick, 2016).

4. Panic disorder and agoraphobia

The latest edition of DSM has separated panic disorder and agoraphobia. From this perspective, the person with panic disorder, experiences recurrent unexpected panic attacks and is persistently concerned or worried about having more panic attacks or changes in his or her behavior in maladaptive ways because of panic attacks. Panic attacks are abrupt surges of intense fear or intense discomfort that reach a peak within minutes, accompanied by physical and cognitive symptoms. Panic attacks may be expected, such as on response to a typically feared object or situation, or meaning that the panic attack occurs for no apparent reason. In the general population, the 12-month prevalence estimate for panic disorder across the USA and several European countries is about 2%-3% in adults and adolescents. In the USA, significantly, lower rates of panic disorder are reported among Latinos, African Americans, Caribbean blacks, and Asian Americans, compared with non-Latino whites; American Indians, by contrast, have significantly higher rates. Lower estimates have been reported for Asian, African, and Latin American countries, ranging from 0.1% to 0.8%. Panic disorder is associated with high levels of

social, occupational, and physical disability; considerable economic costs; and the highest number of medical visits among anxiety disorders, although the effects are strongest with the presence of agoraphobia. Individuals with panic disorder may be frequently absent from work or school for doctor and emergency room visits, which can lead to unemployment or dropping out of school (American Psychiatric Association, 2013).

DSM-5 agoraphobia conceptualization, describes people who are fearful and anxious about two or more of the following situations: using public transportation; being in open spaces; being in enclosed places; standing in line or being in a crowd; or being outside of the home alone in other situations. The individual fears these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms. Every year approximately 1.7% of adolescents and adults have a diagnosis of agoraphobia. Agoraphobia is associated with considerable impairment and disability in terms of role functioning, work productivity, and disability days. Agoraphobia severity is a strong determinant of the degree of disability, irrespective of the presence of comorbid panic disorder, panic attacks, and other comorbid conditions. More than one-third of people with agoraphobia are completely homebound and unable to work (American Psychiatric Association, 2013).

4.1 Efficacy of virtual reality in panic disorder and/or agoraphobia treatments

Panic disorder and agoraphobia have received quite attention from the scientific community in the field of cyberpsychology. Since 1996, several studies have proved the efficacy of VR-EBT in the treatment of these disorders.

One of the first studies focused on the evaluation of the potential uses of VR-EBT in panic disorder and agoraphobia treatment (Moore, Wiederhold, Wiederhold, & Riva, 2002) reported that the VR-EBT environment activated anxiety in non-phobic people. The study explored the *physiological responses of non-phobics* when placed in a VR-EBT environment. People without a diagnosis of panic disorder and/or agoraphobia, were exposed to four VR-EBT environments (elevator, supermarket, town square, and beach).

The first RCT (Vincelli et al., 2003) to evaluate the *efficacy of VR-EBT in panic disorder and agoraphobia treatment* compared the efficacy of VR-EBT, CBT, and a waiting-list group in a sample of 12 participants diagnosed with panic disorder and/or agoraphobia. The treatment protocol was carried out in eight sessions for VR-EBT group and 12 sessions for CBT group; in addition, several support sessions were required. The results showed that both CBT and VR-EBT could significantly reduce the number of panic attacks. However, VR-EBT procured these results using 33% fewer sessions than CBT; this datum suggest the authors, reflects that VR-EBT could be better than CBT in relation to the *cost-benefit of the treatment*, justifying the added use of VR-EBT equipment in the treatment of panic disorder.

In another RCT conducted by Botella et al. (2007b) with a larger sample and a 12-month follow-up with a larger sample and a 12-month follow-up, the *efficacy of VR-EBT in panic disorder and agoraphobia treatment* was also evaluated. The study compared VR-EBT and traditional CBT with a waiting-list group in a sample of 37 participants diagnosed with panic disorder and/or agoraphobia. The VR-EBT environments include some anticipatory anxiety objects (e.g., an answering machine with a message, a radio were shopping center are announced, or an anxiogenic conversations). They include anxiety modulators that can be adjusted by the therapist (e.g., the number of people, simulating unexpected events, the trip duration). Also they included interoceptive elements that can be conducted simultaneously to provoke bodily sensations (e.g., fast heartbeat, accelerated breathing, tunnel vision, blurred vision, and double vision). This study is the only study, which aimed to distinguish interoceptive exposure in

traditional CBT from that in VR-EBT The VR environments (see



Figure 3) designed by Botella's team (Botella et al., 2004c) include the ability to deliver VR-interoceptive exposure simultaneously with VR-EBT. While participants were exposed to virtual agoraphobic situations (e.g., living room), they were also exposed to heightened bodily sensations by means of VR-interoceptive exposure (e.g., fast heartbeat); or by means of traditional interoceptive exposure (e.g., hyperventilation triggered through exposure to the VR-EBT environments). This study also demonstrated the efficacy of VR-EBT in the panic disorder and agoraphobia treatment and showed that a multi-component CBT using a VR-EBT environment for the exposure to aversive objects or situations was superior to a waiting-list group and as efficacious as a traditional multi-component CBT with in vivo exposure. Furthermore, significantly therapeutic outcomes were maintained at 12-month follow-up; in addition, participants showed a high level of satisfaction with the VR-EBT component.

Few research studies have focused on the study of VR-*EBT effects in individuals with only a diagnosis of agoraphobia.* A RCT conducted by Peñate, Pitti, Bethencourt, de la Fuente, and Gracía (2008) found that using VR-EBT is as effective as traditional CBT for people with agoraphobia. The study evaluated the efficacy of VR-EBT compared with a traditional CBT. The study was carried out in a sample of 28 participants with chronic agoraphobia (with two or more years under psychoactive drug treatment). The treatment protocol included 11-weekly sessions. Results showed a significant improvement in cognition, body sensation, anxiety level, and depression symptoms in both treatment groups; this improvement remained in the 3-month follow-up. The authors reported that participants in the VR-EBT condition showed a slight amelioration of symptoms compared with the CBT participants group. In addition, changes regarding the use of pharmacological treatment were found from the end of the treatment until 3-month follow-up: 23.10% of CBT and 40% of VR-EBT patients discontinued drug use. The main limitation of this study was that participants had a combined pharmacological treatment, limiting confirms the real effect of VR-EBT or CBT on their improvement.

The RCT directed by Meyerbroeker, Morina, Kerkhof, and Emmelkamp (2013) has also evaluated the *effects of* VR-EBT *in agoraphobic symptoms* in a sample of 55 participants, all of them diagnosed with panic disorder and agoraphobia. It was compared a VR-EBT and a traditional CBT with a waiting-list group. The treatment components were four sessions of cognitive techniques and six sessions with virtual or in vivo exposure. For agoraphobia symptoms, results did not show differences between VR-EBT and CBT; both were effective compared to no treatment. For panic symptoms was found that CBT was more effective than VR-EBT. The authors hypothesized that initial changes in agoraphobic cognitions during the cognitive phase predicted later changes in agoraphobic avoidance behavior. In addition, they found that VR-EBT or CBT tending to have larger effect sizes than the other treatment components.

Several studies have focused on different aspects involved in the treatment of these disorders. Two works studied the possibility of using *VR-interoceptive exposure* in the treatment of panic disorder and agoraphobia finding that using VR-interoceptive is as effective as traditional interoceptive exposure; in addition, VR-interoceptive was well accepted, and expectation and satisfaction of the participants were very positive. The first study (Pérez-Ara et al., 2010) evaluated the differential *efficacy of VR-interoceptive exposure* versus traditional interoceptive exposure in order to clarify its effects versus traditional interoceptive exposure. A sample of 29 participants diagnosed with panic disorder and/or agoraphobia received VR-interoceptive exposure to be exposed to visual and audio effects (fast

heartbeat, accelerated breathing, tunnel vision, blurred vision, or double vision), simultaneously they were

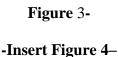


exposed to VR environments (

Figure 3) validated in previous studies (Botella et al., 2007b; Botella et al., 2004c). In contrast, participants who received traditional interoceptive exposure were first exposed to the VR environments and then were exposed to traditional interoceptive activities (e.g., physical exercises, hyperventilation, or spinning) in order to elicit bodily sensations. Figure 4 shows an example of VR and traditional interoceptive stimuli. Results showed no significant differences between VR-interoceptive and traditional interoceptive exposure; both treatment conditions were equally effective for reducing relevant symptoms related to panic disorder and agoraphobia; results were maintained at 3-month follow-up assessment. However, the authors report that VRinteroceptive exposure provides some advantages versus traditional interoceptive exposure, for example, to control and provoke at any time some bodily sensations such as tunnel vision, blurred vision, or double vision, which are difficult to provoke with traditional interoceptive exposure. In a later study (Quero et al., 2014b) was examined the VR-interoceptive exposure acceptability versus traditional exposure. In addition, was explored the relationship between participants' treatment expectation and satisfaction, and clinically significant change. Results showed that VR-interoceptive exposure (fast heartbeat, accelerated breathing, tunnel vision, blurred vision, or double vision) and traditional interoceptive exposure (e.g., hyperventilation, running, spinning, breathing through a narrow straw, shaking one's head rapidly) were well accepted by participants. Expectation and satisfaction were evaluated as very positive in both

interoceptive exposure conditions before and after the treatment, and in the 3-month follow-up. They also showed that VR-interoceptive exposure might create a more intense interoceptive experience overall by combining simultaneously with traditional interoceptive exposure (e.g., hyperventilation).





The *influence of different displays (HMD or CAVE) in the treatment outcomes and sense of presence* was evaluated in a study (Meyerbröker, Morina, Kerkhof, & Emmelkamp, 2011) including a sample of 11 participants diagnosed with panic disorder and/or agoraphobia who were assigned to an HMD or a CAVE treatment group, they were evaluated versus a waiting-list group. Participants received a VR-EBT which included 10 sessions focused on psychoeducation, cognitive restructuring, interoceptive exposure, and VR-EBT. Results revealed that VR-EBT was more effective than no treatment. Results also indicated that there was no relationship between the level of presence and treatment outcomes; no differences in effectiveness were found between using an HMD or a CAVE system. A later study (Meyerbroeker et al., 2013) again demonstrated the effectiveness of a VR-EBT in agoraphobia and panic disorder treatment.

The effectiveness of using *VR-EBT with or without cognitive restructuring* has been evaluated in an open trial conducted by Malbos, Rapee, and Kavakli (2013) with a sample of 18 agoraphobic participants. The treatment protocol included 10-weekly sessions lasting 90-minutes. The results reported that adding cognitive therapy did not provide significant additional benefit for agoraphobia treatment. The impact of the VR-EBT without cognitive restructuring was maintained across the 3-month follow-up; the authors suggest that adding cognitive therapy did not provide significant longer-term improvements. In a previous study (Malbos, Rapee, & Kavakli, 2011), the authors found similar results with a sample of 10 agoraphobic participants.

These studies, which have explored the use of VR-EBT for panic disorder and/or agoraphobia treatment, have demonstrated that using a VR-EBT is as effective as using a traditional CBT in the treatment of these disorders; they have also identified some advantages over traditional treatments and that results are maintained in the long term. **;Error! No se encuentra el origen de la referencia.** Lists de measures included in assessment protocol of some controlled studies, **;Error! No se encuentra el origen de la referencia.** shows the treatment sessions of Vincelli's and Botellas's protocols **;Error! No se encuentra el origen de la referencia.** for panic disorder and agoraphobia.

-Insert ¡Error! No se encuentra el origen de la referencia.-

As was noted in this section, evidence has demonstrated the effectiveness of VR-EBT in the treatment of panic disorder and agoraphobia. Nevertheless, it is necessary to carry out more controlled studies to evaluate the role of each treatment component, the exclusion, or inclusion of some treatment component, or the necessary number of sessions for treatments. For example, in relation to characteristics of VR environments, it is suggested that one aspect that is very important to pay attention in VR environment is the role of avatars because in agoraphobics, the interaction with other persons in different context produces anxiety responses; thus, the presence of avatars is necessary to create situations that are more realistic (Peñate et al., 2008). It has also been suggested that it is necessary to determine the efficacy of each treatment component in the specific case of people with agoraphobia (Malbos et al., 2011, 2013; Meyerbroeker et al., 2013; Meyerbröker et al., 2011; Peñate et al., 2008).

The most recent studies (Breuninger, Sláma, Krämer, Schmitz, & Tuschen-Caffier, 2017; Pitti et al., 2015; Quero et al., 2014b) continue to replicate these great results, thus reaffirming the effectiveness of this technology for the treatment of these two disorders.

5. Generalized anxiety disorder

DSM-5 describes generalized anxiety disorder (GAD) as persistent and excessive anxiety and worry about various domains, including work and school performance that the person finds difficult to control. In addition, the person experiences physical symptoms, including restlessness or feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; and sleep disturbance. Excessive worrying impairs the individual's capacity to do things quickly and efficiently, whether at home or work. The worrying takes time and energy; the associated symptoms of muscle tension and feeling keyed up or on edge, tiredness, difficulty concentrating, and disturbed sleep contribute to the impairment. Importantly the excessive worrying may impair the ability of individuals with GAD to encourage confidence in their children. The 12-month prevalence of GAD is 0.9% among adolescents and 2.9% among adults in the general community of the USA. The 12-month prevalence for the disorder in other countries ranges from 0.4% to 3.6%. GAD accounts for 110 million disability days per annum in the USA citizens (American Psychiatric Association, 2013).

5.1 Efficacy of virtual reality in generalized anxiety disorder treatment

Very few studies have addressed the usefulness and effectiveness of VR in the treatment of GAD (Gorini & Riva, 2008; Pallavicini, Algeri, Repetto, Gorini, & Riva, 2009; Repetto et al., 2013); databases only contain some jobs since 2008.

In a first approximation, a treatment protocol has been presented (Gorini & Riva, 2008). This proposed the use *of VR to facilitate the relaxation process* by visually presenting key relaxing images in order to master anxiety management skills. The treatment protocol is based on 14 treatment sessions. The authors suggest that the visual presentation of a VR calm scenario can facilitate participants' practice and mastery of relaxation, making the experience more vivid and real than the one that most participants can create using their own imagination and memory, and triggering a broad empowerment process within the experience induced by a high sense of presence. **;Error! No se encuentra el origen de la referencia.**

An open trial with a sample of 12 participants proposed improvement of treatment for GAD *using a biofeedback VR system* which was used to master anxiety management skills (Pallavicini et al., 2009). This system was tested in a mobile phone for allowing participants perform the VR experience in an out-participant setting. Participants were assigned to a VR intervention with biofeedback were the physiological data controlled the movement of the waves, for example, a reduction of the participants' physiological activation reduced the movement of the waves (until the ocean becomes completely calm); the other treatment was carried out without biofeedback and both treatments were compared with a waiting-list group. Participants who received the VR intervention with biofeedback reported a higher decrease in anxiety scores after the treatment. Regarding the participants' physiological responses in VR intervention with

biofeedback, they found a decrease tendency in HR and GSR. Results showed that biofeedback used in combination with VR, increased its effect helping participants to better control their physiological responses and to gauge their success in a more efficient way. On the other hand, the authors suggest that using mobile phones could solve the problem of using VR in psychological treatments regarding the impossibility of using a VR system in the real life context of the patient. In other open trial with a large sample (25 participants), these results were confirmed (Repetto et al., 2013). Results suggest the possibility of using VR as a component of GAD treatment, and advocate the clinical use of VR supported by mobile phone to practice session contents at home. About the usefulness of mobile phone in the treatment, participants considered it helped them consolidate the relaxation training in the absence of the therapist. The authors consider that a critical issue related to the use of VR in the treatment of anxiety disorders, is the lack of availability of VR systems in the patient's real-life context to practice what was learned in sessions. In this perspective, add the authors, the availability of VR systems outside the therapist's office is critical to speed up the learning process and achieve quickly clinical results.

In summary, the very limited number of studies regarding the use of VR in GAD treatment reveals the need for further studies to explore the effectiveness of using this technology in the treatment of this psychopathology. It is also important to study other potential uses of VR in other GAD treatment components in addition to relaxation training and mastering anxiety management skills. Therefore, in order to generalize the effects of VR in GAD treatment, more controlled studies with larger samples and follow-up assessment are needed.

6. Conclusions and future directions of virtual reality in the treatment of anxiety disorders

Regarding the efficacy of using VR-EBT in the treatment of anxiety disorders, during the last 20 years there has been sufficient empirical evidence regarding VR-EBT: data reveal the effectiveness of using VR-EBT with or without cognitive techniques for the treatment of anxiety disorders. Also nowadays, there are data regarding the effect of specific treatment components such as VR-interoceptive exposure for panic disorder and agoraphobia treatment, the acceptability, the differential efficacy between treatment components, or combining VR-EBT with other technologies like mobiles phones. In addition, combining VR with pharmaceuticals has proven successful in several studies (Rothbaum, 2009; Wiederhold & Wiederhold, 2013).

So far, it has been demonstrated that VR-EBT is effective in treating anxiety disorders and represents several advantages over traditional CBT, which converts VR-EBT into a powerful tool by which treatments are less aversive and more accessible. Most of studies have found no significant differences between the effectiveness of VR-EBT and traditional CBT; about this some authors hypothesize that with larger samples sizes and the use of more robust anxiety measures it could be possible to find those differences in favor of VR-EBT (Klinger et al., 2005).

6.1 Future directions to virtual reality treatments

Botella et al. (2007a) suggest that technology will evolve to support the knowledge society of the 21st Century and it will be rooted in the following areas: *Environmental intelligence* that allows through the development of networking technologies and intelligent

sensors that capture physiological, psychological, and context information of the user. *Persuasive computing* that enable contents generation in order to change or reinforce users behaviors. *Ubiquitous computing* that enables the user to access to the system anywhere, anytime, and under multiple ICT supports and therapy systems including VR or AR technology and natural interfaces. However, more efforts are required to make the use of RV be more routinely by clinicians; because in as much complex and expensive is the technology, the probability that the user accept and incorporate it into their daily work is lower (Botella, García-Palacios, Quero, Baños, & Bretón-López, 2006c).

For future development of VR systems, VR-EBT treatment protocols, and researches, it would be desirable to keep and strengthen the following issues that summarize the main conclusions regarding the use of VR in psychological treatments:

- 1) The measure of *physiological variables* can provide an objective measurement of improvement over the course of VR-EBT, in addition to self-report measures. Therefore, in the future it could be useful to promote the inclusion of standardized physiological measures in most assessment protocols; for example, heart rate variability, breathing rate, skin conductance, or blood pressure in order to further understand the process that occurs in people suffering an anxiety disorder (Wiederhold & Wiederhold, 2003). It is also suggested to use routinely *BAT* in the assessment protocols before and after VR-EBT.
- 2) Currently there are good evidence regarding the effectiveness of VR-EBT in psychological treatment protocols; however, its usefulness and integration *in assessment protocols* (Rothbaum, 2009) has been little studied (Mühlberger, Sperber, Wieser, & Pauli, 2008; Wald, Liu, & Reil, 2000). Likewise, it has been analyzed the inclusion of other assessment methods such as the magnetic resonance (Clemente et al., 2013; Clemente et al., 2010).

- 3) Exploring the possibilities of *integrating VR-EBT into Internet* (Rothbaum, 2009) in order to provide psychological treatment to more people in more places, at any time (for example, people with chronic agoraphobia who have difficulty leaving home would benefit especially). In this way, a pilot study (Yuen et al., 2013) has investigated the efficacy and feasibility of implementing an online VR treatment for SAD through Second Life. Analyses showed significant pre-treatment to follow-up improvements in social anxiety symptoms. Participants and therapists rated the treatment program as acceptable and feasible, despite frequently encountered technical difficulties.
- 4) Psychological treatments are evolving, and new guidelines begin to take hold regarding the *application of evidence-based CBT and VR-EBT or other technologies* (e.g., augmented reality or mobile systems). For example, AR-EBT systems or Serious Games have been used for treating cockroach phobia (Botella et al., 2010; Bretón-López et al., 2010; Wrzesien et al., 2013).
- 5) Mobile devices have demonstrated its usefulness in facilitating exposure therapy for treating cockroach phobia (Botella et al., 2011) and GAD (Pallavicini et al., 2009; Repetto et al., 2013). Nevertheless, there are few studies focused in these possibilities; therefore, this is an issue that should continue to be studied as well as the inclusion of *VR-EBT in other mobile technologies*.
- 6) Developing *open and flexible VR environments* that can be provide feedback to the patient (e.g., adding pictures, videos, audio-recorder, music, or specific sounds) and for adapting them to the nature and needs of each patient.
- 7) It is important to research on the *cost-benefit ratio* existing between the therapeutic procedure (e.g., money, time, emotional involvement) and VR-EBT outcomes.

- 8) More cross-cultural studies are needed in order to facilitate the generalization of treatment outcomes; for example, some VR environments used in the treatment of Spanish population have been used in Mexican population demonstrating its effectiveness (Cárdenas et al., 2009). A study (Wallach et al., 2009) suggests that VR environments culturally adapted could increase sense of presence and thus VR-EBT effectiveness.
- **9)** In the process of research, it is important that the clinical experiences carried out in VR environments related to *real experiences*, within a flexible context that combines cultural, physical and cognitive aspects and in so doing, reach a high degree of sense of presence and reality judgment (Carvalho, Freire, & Nardi, 2010).
- 10) Although there have been some studies, is not conclusive the relationship between the level of sense of presence, the level of fear/anxiety and the treatment outcomes. Therefore, this issue should be explored further.
- **11**) In order to assess the maintenance of the results of VR-EBT, more *studies with long term follow-up* (e.g., 6 or 12-month) are needed.
- 12) It has been widely demonstrated that VR-EBT is effective in the treatment of various anxiety disorders; however, the studies have been conducted mainly in adult samples. Very few studies have evaluated the *efficacy of VR-EBT in the treatment of children* with anxiety disorders, and these have focused primarily on the treatment of specific phobias (Botella et al., 2006a; Bouchard et al., 2007; Gutiérrez-Maldonado et al., 2009; Miller, Silva, Bouchard, Bélanger, & Taucer-Samson, 2012; Quero et al., 2014a; St-Jacques et al., 2010). Bouchard (2011) stated that the use of VR-EBT with children suffering from more complex anxiety disorders, such as obsessive–compulsive disorder and post-traumatic stress disorder (López-Soler, Castro, Alcántara, & Botella, 2011) must be studied. Therefore, this issue should be explored further.

On the other hand, it has been found that VR is well accepted as exposure technique in the treatment of specific phobias (García-Palacios, Botella, Hoffman, & Fabregat, 2007), it can be used to support empirically validated treatment programs in order to increase its efficiency or to enhance its efficiency and acceptance. Likewise, several authors suggest other fields of application and further research of VR to improve the psychological treatments and in order to promote the health and people's quality of life. Riva et al. (2009) propose that VR can be more than a tool to provide exposure and desensitization, and it can be a clinical tool for *personal* empowerment. Botella, García-Palacios, Baños, and Quero (2009) emphasize that unique feature of VR is very relevant for its use in clinical psychology. At the same time, it can raise several ethical issues and it is important to investigate the possible effects of blurring the distinction between real and virtual worlds in vulnerable populations. Carvalho et al. (2010) suggest that despite the great advance of VR use in psychotherapy, a great deal of its potential is still unknown, therefore requiring the creation of new VR environments so that controlled studies regarding its clinical application can be conducted. Throughout the process of elaboration and investigation, clinical experiences in VR environments must be related to real experiences in a flexible context that combines relevant cultural, physical, and cognitive aspects. These authors note that it is important the rapid results dissemination in order to help improve the development of VR environments and the speed at which they occur, thus preventing several researchers do trial and error as they develop similar work.

Based on all presented in this chapter, there are still several research questions to explore regarding the use of VR-EBT in anxiety disorders, for example:

-Is it necessary to generate higher levels of sense of presence to get better treatment outcomes? -Fully immersive systems like CAVE. Do they necessarily generate higher levels of sense of presence? In addition, does this improve the treatment outcomes? - Is the use of VR-EBT via Internet as effective as the use with HMD or similar devices? -Stimulating other senses in addition to sight and hearing (e.g., smell, taste, and/or touch), or including elements of augmented virtuality within VR-EBT. Could this improve or facilitate the conduct of therapy or treatment outcomes?

-Can VR facilitate or improve the assessment process for anxiety disorders?

-*Can VR-EBT be adapted to mobile devices, entertainment systems (e.g., smart phones, tables, serious games by video game consoles), or to future mobile technologies?*

References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (*DSM-5*) (Fifth ed.). Arlington, VA: American Psychiatric Association.
- Anderson, P., Rothbaum, B. O., & Hodges, L. F. (2003). Virtual reality exposure in the treatment of social anxiety. *Cognitive and Behavioral Practice*, 10(3), 240-247. doi: 10.1016/s1077-7229(03)80036-6
- Anderson, P. L., Edwards, S. M., & Goodnight, J. R. (2017). Virtual Reality and Exposure Group Therapy for Social Anxiety Disorder: Results from a 4–6 Year Follow-Up. *Cognitive Therapy and Research*, 41(2), 230-236. doi: 10.1007/s10608-016-9820-y
- Anderson, P. L., Price, M., Edwards, S. M., Obasaju, M. A., Schmertz, S. K., Zimand, E., & Calamaras, M. R. (2013). Virtual reality exposure therapy for social anxiety disorder: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, *81*(5), 751-760. doi: 10.1037/a0033559

- Anderson, P. L., Zimand, E., Hodges, L. F., & Rothbaum, B. O. (2005). Cognitive behavioral therapy for public-speaking anxiety using virtual reality for exposure. *Depression and Anxiety*, 22(3), 156-158. doi: 10.1002/da.20090
- Azuma, R. T. (1997). A survey of augmented reality. *Presence: Teleoperators and Virtual Environments*, 6, 355–385.
- Baños, R. M., Botella, C., Perpiná, C., & Quero, S. (2001). Tratamiento mediante realidad virtual para la fobia a volar: Un estudio de caso. *Clinica y Salud*, 12(3), 391-404.
- Baños, R. M., Botella, C., Perpiñá, C., Alcañiz, M., Lozano, J. A., Osma, J., & Gallardo, M.
 (2002). Virtual reality treatment of flying phobia. *IEEE Transactions on Information Technology in Biomedicine*, 6(3 SPEC.), 206-212.
- Baus, O., & Bouchard, S. (2014). Moving from virtual reality exposure-based therapy to augmented reality exposure-based therapy: A review. *Frontiers in Human Neuroscience*, 8. doi: 10.3389/fnhum.2014.00112
- Botella, C., Baños, R. M., & Fabregat, S. (2006a). Tratamiento del miedo a los animales pequeños por medio de realidad virtual. In X. Méndez, J. P. Espada & M. Orgiles (Eds.), *Terapia psicológica con niños y adolescentes: Estudio de casos clínicos* (pp. 49-65). Madrid: Pirámide.
- Botella, C., Baños, R. M., García-Palacios, A., Quero, S., Guillén, V., & Marco, H. (2007a). La utilización de las nuevas tecnologías de la información y la comunicación en psicología clínica. UOC Papers, 4, 32-41.
- Botella, C., Baños, R. M., Guerrero, B., García-Palacios, A., Quero, S., & Alcañíz, M. (2006b).
 Using a flexible virtual environment for treating a storm phobia. *PsychNology Journal*, 4(2), 12-144.

- Botella, C., Baños, R. M., Perpiñá, C., Quero, S., Villa, H., García-Palacios, A., & Fabregat, S.
 (2002). El tratamiento de la claustrofobia por medio de realidad virtual. *Analisis y Modificacion de Conducta*, 28(117), 109-127.
- Botella, C., Baños, R. M., Perpiñá, C., Villa, H., Alcañiz, M., & Rey, A. (1998). Virtual reality treatment of claustrophobia: A case report. *Behaviour Research and Therapy*, 36(2), 239-246.
- Botella, C., Baños, R. M., Villa, H., Perpiñá, C., & García-Palacios, A. (2000). Virtual reality in the treatment of claustrophobic fear: A controlled, multiple-baseline design. *Behavior Therapy*, 31(3), 583-595.
- Botella, C., Bretón-López, J., Quero, S., Baños, R., & García-Palacios, A. (2010). Treating cockroach phobia with augmented reality. *Behavior Therapy*, *41*(3), 401-413.
- Botella, C., Breton-López, J., Quero, S., Baños, R. M., García-Palacios, A., Zaragoza, I., &
 Alcaniz, M. (2011). Treating cockroach phobia using a serious game on a mobile phone and augmented reality exposure: A single case study. *Computers in Human Behavior*, 27(1), 217-227.
- Botella, C., García-Palacios, A., Baños, R. M., & Quero, S. (2009). Cybertherapy: Advantages, limitations, and ethical issues *PsychNology Journal*, *7*(1), 77-100.
- Botella, C., García-Palacios, A., Quero, S., Baños, R. M., & Bretón-López, J. M. (2006c). Virtual reality and psychological treatments: A review. *Behavioral Psychology*, 14(3), 491-509.

Botella, C., Gracía-Palacios, A., Villa, H., Baños, R. M., Quero, S., Alcañiz, M., & Riva, G.
(2007b). Virtual reality exposure in the treatment of panic disorder and agoraphobia: A controlled study. *Clinical Psychology and Psychotherapy*, *14*(3), 164-175. doi: 10.1002/cpp.524

- Botella, C., Osma, J., García-Palacios, A., Quero, S., & Banõs, R. M. (2004a). Treatment of flying phobia using virtual reality: Data from a 1-year follow-up using a multiple baseline design. *Clinical Psychology and Psychotherapy*, 11(5), 311-323.
- Botella, C., Quero, S., Baños, R. M., Perpiñá, C., & García-Palacios, A. (2004b). Virtual reality and psychotherapy. In G. Riva, C. Botella, P. Légeron & G. Optale (Eds.), *Cybertherapy* (Vol. 99, pp. 37-52). Amsterdam: IOS Press.
- Botella, C., Villa, H., Baños, R., Perpiñá, C., & García-Palacios, A. (1999). The treatment of claustrophobia with virtual reality: Changes in other phobic behaviors not specifically treated. *Cyberpsychology and Behavior*, 2(2), 135-141.
- Botella, C., Villa, H., García-Palacios, A., Baños, R. M., Perpiñá, C., & Alcañiz, M. (2004c).
 Clinically significant virtual environments for the treatment of panic disorder and agoraphobia. *Cyberpsychology and Behavior*, 7(5), 527-535. doi: 10.1089/cpb.2004.7.527
- Botella, C. M., Juan, M. C., Baños, R. M., Alcañiz, M., Guillén, V., & Rey, B. (2005). Mixing realities? An application of augmented reality for the treatment of cockroach phobia. *CyberPsychology and Behavior*, 8(2), 162-171.
- Bouchard, S. (2011). Could virtual reality be effective in treating children with phobias? *Expert Review of Neurotherapeutics*, 11(2), 207-213. doi: 10.1586/ern.10.196
- Bouchard, S., Côté, S., St-Jacques, J., Robillard, G., & Renaud, P. (2006). Effectiveness of virtual reality exposure in the treatment of arachnophobia using 3D games. *Technology* and Health Care, 14(1), 19-27.
- Bouchard, S., Dumoulin, S., Robillard, G., Guitard, T., Klinger, E., Forget, H., . . . Roucaut, F. X. (2017). Virtual reality compared with in vivo exposure in the treatment of social anxiety disorder: A three-arm randomised controlled trial. *British Journal of Psychiatry*, 210(4), 276-283. doi: 10.1192/bjp.bp.116.184234

- Bouchard, S., St-Jacques, J., Robillard, G., & Renaud, P. (2007). Efficacy of a virtual reality exposure treatment for arachnophobia in children: A pilot study. *Journal de Therapie Comportementale et Cognitive*, *17*(3), 101-108. doi: 10.1016/s1155-1704(07)73238-x
- Boyd, D., & Hart, J. (2016). Potential utility of a cost-effective virtual reality system for treatment of fear of flying. *Aerospace Medicine and Human Performance*, 87(9), 830-832. doi: 10.3357/AMHP.4719.2016
- Bretón-López, J., Quero, S., Botella, C., García-Palacios, A., Baños, R. M., & Alcañiz, M.
 (2010). An augmented reality system validation for the treatment of cockroach phobia. *CyberPsychology, Behavior, and Social Networking*, 13(6), 705-710.
- Breuninger, C., Sláma, D. M., Krämer, M., Schmitz, J., & Tuschen-Caffier, B. (2017).
 Psychophysiological Reactivity, Interoception and Emotion Regulation in Patients with
 Agoraphobia During Virtual Reality Anxiety Induction. *Cognitive Therapy and Research*, 41(2), 193-205. doi: 10.1007/s10608-016-9814-9
- Brinkman, W. P., Hartanto, D., Kang, N., De Vliegher, D., Kampmann, I. L., Morina, N., . . .Neerincx, M. (2012). *A virtual reality dialogue system for the treatment of social phobia*.Paper presented at the 30th ACM Conference on Human Factors in Computing Systems.
- Cárdenas, G., Botella, C., Quero, S., Moreyra, L., De La Rosa, A., & Muñoz, S. (2009). A crosscultural validation of VR treatment system for flying phobia in the Mexican population. *Studies in Health Technology and Informatics*, 7, 141-144.
- Carlin, A. S., Hoffman, H. G., & Weghorst, S. (1997). Virtual reality and tactile augmentation in the treatment of spider phobia: A case report. *Behaviour Research and Therapy*, 35(2), 153-158.

- Carvalho, M. R. D., Freire, R. C., & Nardi, A. E. (2010). Virtual reality as a mechanism for exposure therapy. World Journal of Biological Psychiatry, 11(2 PART 2), 220-230. doi: 10.3109/15622970802575985
- Clemente, M., Rey, B., Alcaniz, M., Breton-Lopez, J., Botella, C., Rodriguez-Pujadas, A., . . .
 Banos, R. M. (2013). *FMRI assessment of small animals' phobia using virtual reality as stimulus*. Paper presented at the 7th International Conference on Pervasive Computing Technologies for Healthcare and Workshops, PervasiveHealth 2013, Venice.
- Clemente, M., Rey, B., Alcañiz, M., Bretón-López, J., Moragrega, I., Baños, R. M., . . . Ávila, C. (2010). Contributions of functional magnetic resonance in the field of psychological treatments with virtual reality. *Annual Review of CyberTherapy and Telemedicine*, 8(1), 157-160.
- Coelho, C. M., Silva, C. F., Santos, J. A., Tichon, J., & Wallis, G. (2008). Contrasting the effectiveness and efficiency of virtual reality and real environments in the treatment of acrophobia. *PsychNology Journal*, 6(2), 203-216.
- Coelho, C. M., Silvério, J. M., Da Silva, C. F., & Santos, J. A. (2014). Virtual reality in the treatment of acrophobia: Results of an experimental study. *2*, 145-149.
- Craske, M. G., & Mystkowski, J. L. (2006). Exposure therapy and extinction: Clinical studies. In
 M. G. Craske & D. Vansteenwegen (Eds.), *Fear and Learning: Basic Science to Clnical Application* (pp. 217-234). Washington, DC: American Psychological Assoication.
- Czerniak, E., Caspi, A., Litvin, M., Amiaz, R., Bahat, Y., Baransi, H., . . . Plotnik, M. (2016). A novel treatment of fear of flying using a large virtual reality system. *Aerospace Medicine and Human Performance*, 87(4), 411-416. doi: 10.3357/AMHP.4485.2016

- De Quervain, D. J. F., Bentz, D., Michael, T., Bolt, O. C., Wiederhold, B., K., Margraf, J., &
 Wilhelm, F. H. (2011). Glucocorticoids enhance extinction-based psychotherapy.
 Proceedings of the National Academy of Sciences, 108(16), 6621-6625.
- Emmelkamp, P. M. G., Krijn, M., Hulsbosch, A. M., De Vries, S., Schuemie, M. J., & Van der Mast, C. A. P. G. (2002). Virtual reality treatment versus exposure in vivo: A comparative evaluation in acrophobia. *Behaviour Research and Therapy*, *40*(5), 509-516. doi: 10.1016/s0005-7967(01)00023-7
- Ferrand, M., Ruffault, A., Tytelman, X., Flahault, C., & Négovanska, V. (2015). A cognitive and virtual reality treatment program for the fear of flying. *Aerospace Medicine and Human Performance*, 86(8), 723-727. doi: 10.3357/AMHP4211.2015
- García-Palacios, A., Botella, C., Hoffman, H., & Fabregat, S. (2007). Comparing acceptance and refusal rates of virtual reality exposure vs. in vivo exposure by patients with specific phobias. *CyberPsychology and Behavior*, 10(5), 722-724.
- García-Palacios, A., Hoffman, H., Carlin, A., Furness, T. A., & Botella, C. (2002). Virtual reality in the treatment of spider phobia: A controlled study. *Behaviour Research and Therapy*, 40(9), 983-993.
- Gorini, A., & Riva, G. (2008). The potential of Virtual Reality as anxiety management tool: A randomized controlled study in a sample of patients affected by generalized anxiety disorder. *Trials*, *9*. doi: 10.1186/1745-6215-9-25
- Grillon, H., Riquier, F., Herbelin, B., & Thalmann, D. (2006). Virtual reality as a therapeutic tool in the confines of social anxiety disorder treatment. *International Journal on Disability* and Human Development, 5(3), 243-250.

- Gutiérrez-Maldonado, J., Magallón-Neri, E., Rus-Calafell, M., & Peñaloza-Salazar, C. (2009).
 Virtual reality exposure therapy for school phobia. *Anuario de Psicologia*, 40(2), 223-236.
- Harris, S. R., Kemmerling, R. L., & North, M. M. (2002). Brief virtual reality therapy for public speaking anxiety. *Cyberpsychology and Behavior*, 5(6), 543-550. doi: 10.1089/109493102321018187
- Hodges, L. F., Watson, B. A., Kessler, G. D., Rothbaum, B. O., & Opdyke, D. (1996). Virtually conquering fear of flying. *IEEE Computer Graphics and Applications*, 16(6), 42-49. doi: 10.1109/38.544071
- Hoffman, H. G., García-Palacios, A., Carlin, A., Furness, T. A., & Botella, C. (2003). Interfaces that heal: Coupling real and virtual objects to treat spider phobia. *International Journal of Human-Computer Interaction*, 16(2), 283-300.
- Ibrahim, N., Muhamad Balbed, M. A., Yusof, A. M., Mohammed Salleh, F. H., Singh, J., & Shahidan, M. S. (2008). Virtual reality approach in treating acrophobia: Simulating height in virtual environment. WSEAS Transactions on Computers, 7(5), 511-518.
- James, L. K., Lin, C. Y., Steed, A., Swapp, D., & Slater, M. (2003). Social anxiety in virtual environments: Results of a pilot study. *Cyberpsychology and Behavior*, 6(3), 237-243. doi: 10.1089/109493103322011515
- Jang, D. P., Ku, J. H., Choi, Y. H., Wiederhold, B. K., Nam, S. W., Kim, I. Y., & Kim, S. I. (2002). The development of Virtual Reality Therapy (VRT) system for the treatment of acrophobia and therapeutic case. *IEEE Transactions on Information Technology in Biomedicine*, 6(3 SPEC.), 213-217. doi: 10.1109/titb.2002.802374

- Juan, M. C., Alcañiz, M., Monserrat, C., Botella, C., Baños, R. M., & Guerrero, B. (2005). Using augmented reality to treat phobias. *IEEE Computer Graphics and Applications*, 25(6), 31-37.
- Juan, M. C., Baños, R., Botella, C., Pérez, D., Alcañiz, M., & Monserrat, C. (2006). An augmented reality system for the treatment of acrophobia: The sense of presence using immersive photography. *Presence: Teleoperators and Virtual Environments*, 15(4), 393-402.
- Juan, M. C., Botella, C., Alcañiz, M., Baños, R., Carrion, C., Melero, M., & Lozano, J. A. (2004). An augmented reality system for treating psychological disorders: Application to phobia to cockroaches. Paper presented at the Third IEEE and ACM International Symposium on Mixed and Augmented Reality, Arlington, VA.
- Kim, H. E., Hong, Y. J., Kim, M. K., Jung, Y. H., Kyeong, S., & Kim, J. J. (2017). Effectiveness of self-training using the mobile-based virtual reality program in patients with social anxiety disorder. *Computers in Human Behavior*, 73, 614-619. doi: 10.1016/j.chb.2017.04.017
- Kleim, B., Wilhelm, F. H., Temp, L., Margraf, J., Wiederhold, B. K., & Rasch, B. (2013). Sleep enhances exposure therapy. *Psychological Medicine*, *10*, 1-9.
- Klinger, E., Bouchard, S., Légeron, P., Roy, S., Lauer, F., Chemin, I., & Nugues, P. (2005).
 Virtual reality therapy versus cognitive behavior therapy for social phobia: A preliminary controlled study. *Cyberpsychology and Behavior*, 8(1), 76-88. doi: 10.1089/cpb.2005.8.76
- Krijn, M., Emmelkamp, P. M., Ólafsson, R. P., Bouwman, M., Van Gerwen, L. J., Spinhoven, P.,
 ... Van Der Mast, C. A. (2007a). Fear of flying treatment methods: Virtual reality
 exposure vs. cognitive behavioral therapy. *Aviation Space and Environmental Medicine*, 78(2), 121-128.

- Krijn, M., Emmelkamp, P. M. G., Biemond, R., De Wilde De Ligny, C., Schuemie, M. J., & Van Der Mast, C. A. P. G. (2004). Treatment of acrophobia in virtual reality: The role of immersion and presence. *Behaviour Research and Therapy*, 42(2), 229-239. doi: 10.1016/s0005-7967(03)00139-6
- Krijn, M., Emmelkamp, P. M. G., Ólafsson, R. P., Schuemie, M. J., & Van Der Mast, C. A. P. G. (2007b). Do self-statements enhance the effectiveness of virtual reality exposure therapy? A comparative evaluation in acrophobia. *Cyberpsychology and Behavior*, *10*(3), 362-370. doi: 10.1089/cpb.2006.9943
- Levy, F., Leboucher, P., Rautureau, G., & Jouvent, R. (2015). E-virtual reality exposure therapy in acrophobia: A pilot study. *Journal of Telemedicine and Telecare*, 22(4), 215-220. doi: 10.1177/1357633X15598243
- López-Soler, C., Castro, M., Alcántara, M., & Botella, C. (2011). The virtual reality system
 EMMA-childhood in the psychological treatment of a minor with posttraumatic stress
 disorder. [Sistema de realidad virtual emma-infancia en el tratamiento psicológico de un
 menor con estrés postraumático] *Revista de Psicopatologia y Psicología Clínica, 16*(3), 189-206.
- Malbos, E., Rapee, R. M., & Kavakli, M. (2011). Isolating the effect of virtual reality based exposure therapy for agoraphobia: A comparative trial. *Annual Review of CyberTherapy and Telemedicine*, 9(1), 36-40.
- Malbos, E., Rapee, R. M., & Kavakli, M. (2013). A controlled study of agoraphobia and the independent effect of virtual reality exposure therapy. *Australian and New Zealand Journal of Psychiatry*, 47(2), 160-168. doi: 10.1177/0004867412453626
- Meyerbroeker, K., Morina, N., Kerkhof, G. A., & Emmelkamp, P. M. G. (2013). Virtual reality exposure therapy does not provide any additional value in agoraphobic patients: A

randomized controlled trial. *Psychotherapy and Psychosomatics*, 82(3), 170-176. doi: 10.1159/000342715

- Meyerbröker, K., Morina, N., Kerkhof, G., & Emmelkamp, P. M. G. (2011). Virtual reality exposure treatment of agoraphobia: A comparison of computer automatic virtual environment and head-mounted display. *Annual Review of CyberTherapy and Telemedicine*, 9(1), 41-45.
- Michaliszyn, D., Marchand, A., Bouchard, S., Martel, M. O., & Poirier-Bisson, J. (2010). A randomized, controlled clinical trial of in virtuo and in vivo exposure for spider phobia. *Cyberpsychology, Behavior, and Social Networking, 13*(6), 689-695. doi: 10.1089/cyber.2009.0277
- Milgram, P., & Kishino, F. (1994). Taxonomy of mixed reality visual displays. *IEICE Transactions on Information and Systems*, *E77-D*(12), 1321-1329.
- Miller, L., Silva, C., Bouchard, S., Bélanger, C., & Taucer-Samson, T. (2012). Using virtual reality and other computer technologies to implement cognitive-behavior therapy for the treatment of anxiety disorders in youth. In T. E. Davis Iii, T. H. Ollendick & L.-G. Öst (Eds.), *Intensive One-Session Treatment of Specific Phobias* (pp. 227-251): Springer New York.
- Moore, K., Wiederhold, B. K., Wiederhold, M. D., & Riva, G. (2002). Panic and agoraphobia in a virtual world. *Cyberpsychology and Behavior*, 5(3), 197-202. doi: 10.1089/109493102760147178
- Mühlberger, A., Herrmann, M. J., Wiedemann, G., Ellgring, H., & Pauli, P. (2001). Repeated exposure of flight phobics to flights in virtual reality. *Behaviour Research and Therapy*, 39(9), 1033-1050. doi: 10.1016/s0005-7967(00)00076-0

- Mühlberger, A., Sperber, M., Wieser, M. J., & Pauli, P. (2008). A Virtual reality behavior avoidance test (VR-BAT) for the assessment of spider phobia. *Journal of CyberTherapy & Rehabilitation*, 1(2), 147-158.
- Mühlberger, A., Wiedemann, G., & Pauli, P. (2003). Efficacy of a one-session virtual reality exposure treatment for fear of flying. *Psychotherapy Research*, *13*(3), 323-336.
- North, M. M., M., N. S., & Coble, J. R. (1998). Virtual Reality Therapy: An effective treatment for the fear of public speaking. *International Journal of Virtual Reality* 3(2), 2-6.
- Opriş, D., Pintea, S., García-Palacios, A., Botella, C., Szamosközi, Ş., & David, D. (2012).
 Virtual reality exposure therapy in anxiety disorders: A quantitative meta-analysis.
 Depression and Anxiety, 29(2), 85-93. doi: 10.1002/da.20910
- Pallavicini, F., Algeri, D., Repetto, C., Gorini, A., & Riva, G. (2009). Biofeedback, virtual reality and mobile phones in the treatment of generalized anxiety disorder (gad): A phase-2 controlled clinical trial. *Journal of Cyber Therapy and Rehabilitation*, 2(4), 315-327.
- Parrish, D. E., Oxhandler, H. K., Duron, J. F., Swank, P., & Bordnick, P. (2016). Feasibility of Virtual Reality Environments for Adolescent Social Anxiety Disorder. *Research on Social Work Practice*, 26(7), 825-835. doi: 10.1177/1049731514568897
- Parsons, T. D., & Rizzo, A. A. (2008). Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, 39(3), 250-261. doi: 10.1016/j.jbtep.2007.07.007
- Peñate, W., Pitti, C. T., Bethencourt, J. M., de la Fuente, J., & Gracía, R. (2008). The effects of a treatment based on the use of virtual reality exposure and cognitive-behavioral therapy applied to patients with agoraphobia. *International Journal of Clinical and Health Psychology*, 8(1), 5-22.

- Pérez-Ara, M. A., Quero, S., Botella, C., Baños, R., Andreu-Mateu, S., García-Palacios, A., &
 Bretón-López, J. (2010). Virtual reality interoceptive exposure for the treatment of panic disorder and agoraphobia. *Annual Review of CyberTherapy and Telemedicine*, 8(1), 61-64.
- Pertaub, D. P., Slater, M., & Barker, C. (2002). An experiment on public speaking anxiety in response to three different types of virtual audience. *Presence: Teleoperators and Virtual Environments*, 11(1), 68-78. doi: 10.1162/105474602317343668
- Pitti, C. T., Peñate, W., de la Fuente, J., Bethencourt, J. M., Roca-Sánchez, M. J., Acosta, L., . . . Gracia, R. (2015). The combined use of virtual reality exposure in the treatment of agoraphobia. *Actas españolas de psiquiatría, 43*(4), 133-141.
- Powers, M. B., Briceno, N. F., Gresham, R., Jouriles, E. N., Emmelkamp, P. M. G., & Smits, J.
 A. J. (2013). Do conversations with virtual avatars increase feelings of social anxiety? *Journal of Anxiety Disorders*, 27(4), 398-403. doi: 10.1016/j.janxdis.2013.03.003
- Powers, M. B., & Emmelkamp, P. M. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders*, 22(3), 561-569. doi: 10.1016/j.janxdis.2007.04.006
- Quero, S., Nebot, S., Rasal, P., Bretón-López, J., Baños, R. M., & Botella, C. (2014a). The use of communication and information technologies in the treatment of small animals phobia in childhood [La utilización de las tecnologías de la información y la comunicación en el tratamiento de la fobia a animales pequeños en la infancia]. *Behavioral Psychology-Psicología Conductual, 22*(2), 257-276.
- Quero, S., Pérez-Ara, M. Á., Bretón-López, J., García-Palacios, A., Baños, R. M., & Botella, C. (2014b). Acceptability of virtual reality interoceptive exposure for the treatment of panic

disorder with agoraphobia. *British Journal of Guidance & Counselling*, 42(2), 123-137. doi: 10.1080/03069885.2013.852159

- Repetto, C., Gaggioli, A., Pallavicini, F., Cipresso, P., Raspelli, S., & Riva, G. (2013). Virtual reality and mobile phones in the treatment of generalized anxiety disorders: A phase-2 clinical trial. *Personal and Ubiquitous Computing*, *17*(2), 253-260. doi: 10.1007/s00779-011-0467-0
- Riva, G., Gaggioli, A., Gorini, A., Carelli, L., Repetto, C., Algeri, D., & Vigna, C. (2009).
 Virtual reality as empowering environment for personal change: The contribution of the applied technology for neuro-psychology laboratory. *Anuario de Psicologia, 40*(2), 171-192.
- Robillard, G., Wiederhold, B. K., Wiederhold, M. D., Larouche, S., & Bouchard, S. (2004). *An open trial to confirm the external validity of virtual reality exposure treatment of fear of flying*. Paper presented at the 38th Annual convention of the Association for the Advancement of Behavior Therapy, New Orleans LA.
- Rothbaum, B. O. (2009). Using virtual realty to help our patients in the real world. *Depression* and Anxiety, 26(3), 209-211. doi: 10.1002/da.20556
- Rothbaum, B. O., Anderson, P., Zimand, E., Hodges, L., Lang, D., & Wilson, J. (2006). Virtual reality exposure therapy and standard (in vivo) exposure therapy in the treatment of fear of flying. *Behavior Therapy*, *37*(1), 80-90.
- Rothbaum, B. O., Hodges, L., Anderson, P. L., Price, L., & Smith, S. (2002). Twelve-month follow-up of virtual reality and standard exposure therapies for the fear of flying. *Journal* of Consulting and Clinical Psychology, 70(2), 428-432.

- Rothbaum, B. O., Hodges, L., Smith, S., Lee, J. H., & Price, L. (2000). A controlled study of virtual reality exposure therapy for the fear of flying. *Journal of Consulting and Clinical Psychology*, 68(6), 1020-1026. doi: 10.1037//0022-006x.68.6.1020
- Rothbaum, B. O., Hodges, L. F., Kooper, R., Opdyke, D., Williford, J. S., & North, M. (1995).
 Virtual reality graded exposure in the treatment of acrophobia: A case report. *Behavior Therapy*, 26(3), 547-554. doi: 10.1016/s0005-7894(05)80100-5
- Roy, S., Klinger, E., Légeron, P., Lauer, F., Chemin, I., & Nugues, P. (2003). Definition of a VRbased protocol to treat social phobia. *Cyberpsychology and Behavior*, 6(4), 411-420. doi: 10.1089/109493103322278808
- Rus-Calafell, M., Gutiérrez-Maldonado, J., Botella, C., & Baños, R. M. (2013). Virtual reality exposure and imaginal exposure in the treatment of fear of flying: A pilot study. *Behavior Modification*, 37(4), 568-590. doi: 10.1177/0145445513482969
- Safir, M. P., Wallach, H. S., & Bar-Zvi, M. (2012). Virtual reality cognitive-behavior therapy for public speaking anxiety: One-year follow-up. *Behavior Modification*, 36(2), 235-246. doi: 10.1177/0145445511429999
- Slater, M., Pertaub, D. P., Barker, C., & Clark, D. M. (2006). An experimental study on fear of public speaking using a virtual environment. *Cyberpsychology and Behavior*, 9(5), 627-633. doi: 10.1089/cpb.2006.9.627
- Slater, M., Pertaub, D. P., & Steed, A. (1999). Public speaking in virtual reality: Facing an audience of avatars. *IEEE Computer Graphics and Applications*.
- St-Jacques, J., Bouchard, S., & Bélanger, C. (2010). Is virtual reality effective to motivate and raise interest in phobic children toward therapy? A clinical trial study of in vivo with in virtuo versus in vivo only treatment exposure. *Journal of Clinical Psychiatry*, 71(7), 924-931. doi: 10.4088/JCP.08m04822blu

- Tortella-Feliu, M., Botella, C., Llabrés, J., Bretón-López, J. M., del Amo, A. R., Baños, R. M., & Gelabert, J. M. (2011). Virtual reality versus computer-aided exposure treatments for fear of flying. *Behavior Modification*, 35(1), 3-30.
- Vincelli, F., Anolli, L., Bouchard, S., Wiederhold, B. K., Zurloni, V., & Riva, G. (2003).
 Experiential cognitive therapy in the treatment of panic disorders with agoraphobia: A controlled study. *Cyberpsychology and Behavior*, 6(3), 321-328. doi: 10.1089/109493103322011632
- Wald, J. (2004). Efficacy of virtual reality exposure therapy for driving phobia: A multiple baseline across-subjects design. *Behavior Therapy*, 35(3), 621-635. doi: 10.1016/s0005-7894(04)80035-2
- Wald, J., & Taylor, S. (2000). Efficacy of virtual reality exposure therapy to treat driving phobia:
 A case report. *Journal of Behavior Therapy and Experimental Psychiatry*, *31*(3-4), 249-257. doi: 10.1016/s0005-7916(01)00009-x
- Wald, J. L., Liu, L., & Reil, S. (2000). Concurrent validity of a virtual reality driving assessment for persons with brain injury. *Cyberpsychology and Behavior*, *3*(4), 643-654. doi: 10.1089/109493100420232
- Walshe, D. G., Lewis, E. J., Kim, S. I., O'Sullivan, K., & Wiederhold, B. K. (2003). Exploring the use of computer games and virtual reality in exposure therapy for fear of driving following a motor vehicle accident. *Cyberpsychology and Behavior*, 6(3), 329-334. doi: 10.1089/109493103322011641
- Wallach, H. S., Safir, M. P., & Bar-Zvi, M. (2009). Virtual reality cognitive behavior therapy for public speaking anxiety: A randomized clinical trial. *Behavior Modification*, *33*(3), 314-338. doi: 10.1177/0145445509331926

- Wiederhold, B. K., Gevirtz, R., & Wiederhold, M. D. (1998). Fear of flying: A case report using virtual reality therapy with physiological monitoring. *Cyberpsychology and Behavior*, 1(2), 97-103.
- Wiederhold, B. K., Jang, D. P., Gevirtz, R. G., Kim, S. I., Kim, I. Y., & Wiederhold, M. D.
 (2002). The treatment of fear of flying: A controlled study of imaginal and virtual reality graded exposure therapy. *IEEE Transactions on Information Technology in Biomedicine*, 6(3 SPEC.), 218-223.
- Wiederhold, B. K., & Wiederhold, M. D. (2003). Three-year follow-up for virtual reality exposure for fear of flying. *Cyberpsychology and Behavior*, *6*(4), 441-445.
- Wiederhold, M. D., & Wiederhold, B. K. (2013). Virtual reality and pharmaceuticals: Enhanced synergy to improve clinical care. *CyberTherapy & Rehabilitation*, 6(1), 10-12.
- Wilhelm, F. H., Pfaltz, M. C., Gross, J. J., Mauss, I. B., I., K. S., & Wiederhold, B. K. (2005).
 Mechanisms of virtual reality exposure therapy: The role of the Behavioral activation and behavioural inhibition systems. A. *pplied Psychophysiology and Biofeedback*, 30(3), 271-284.
- Wrzesien, M., Alcañiz, M., Botella, C., Burkhardt, J. M., Bretón-López, J., Ortega, M., & Brotons, D. B. (2013). The therapeutic lamp: Treating small-animal phobias. *IEEE Computer Graphics and Applications*, 33(1), 80-86.
- Yuen, E. K., Herbert, J. D., Forman, E. M., Goetter, E. M., Comer, R., & Bradley, J. C. (2013).
 Treatment of social anxiety disorder using online virtual environments in second life.
 Behavior Therapy, 44(1), 51-61. doi: 10.1016/j.beth.2012.06.001

Table 1. Main private mental health centers that offer VR-EBT or AR-EBT treatments

Spain	http://www.previsl.com	-Specific phobias (travel by plane, heights, enclosed
		spaces, spiders, cockroaches).
	http://www.labpsitec.es	-Agoraphobia
		-Panic disorder.
		-Fear of public speaking.
		-Post-traumatic stress disorder.
		-Adjustment disorder.
		-Pathological gambling.
		-Fibromyalgia
		-Eating disorders.
United States	http://www.virtuallybetter.com	-Specific phobias (heights, storms, travel by plane,
		school).
		-Social anxiety and fear of public speaking.
		-Post-traumatic stress disorder.
		-Pain distraction.
		-Drug and alcohol addictions.
	http://www.vrphobia.com	-Specific phobias (enclosed spaces, driving, travel by
		plane, heights, needles and blood, spiders, storms,
		school).
		-Agoraphobia
		-Panic disorder.
		-Social anxiety and fear of public speaking.
		-Attention deficit hyperactivity disorder.
		-Chronic pain
		-Post-traumatic Stress Disorder
Belgium	http://www.vrphobia.eu	-Specific phobias (enclosed spaces, driving, travel by
		plane, heights, needles and blood, spiders, storms,
		school).

		-Agoraphobia
		-Panic disorder.
		-Social anxiety and fear of public speaking.
		-Attention deficit hyperactivity disorder.
		-Chronic pain.
		-Post-traumatic Stress Disorder.
Canada	http://invirtuo.com	-Specific phobias (travel by plane, heights, enclosed
		spaces, injections, dogs, cats, insects).
		-Agoraphobia
		-Panic disorder.
		-Social anxiety and fear of public speaking.
		-Generalized anxiety disorder.
		-Obsessive-compulsive disorder.
Mexico	http://www.solucionesvirtuales.com.mx	-Fear or flying
		-Agoraphobia
		-Panic disorder.
		-Obsessive-compulsive disorder.
		-Post-traumatic Stress Disorder.
		-Social anxiety and fear of public speaking.

	Psycho- education	Cognitive restructuring	Breathing training	VR exposure	Interoceptive exposure	Relaxation training
Wiederhold et al. (2002)			Х	X		
Rothbaum et al. (2000, 2002, 2006)	Х	Х	Х	X	Х	
Botella et al. (2004)	Х			X		
Mühlberger et al. (2001, 2002)	Х	Х		Х		
Maltby et al. (2002)	Х	Х		Х		Х

Table 2. Comparative of components for fear of flying included in some VR-EBT protocol treatments



Figure 1. Botella's team AR mobile phone systems for cockroach phobia treatment



Figure 2. Botella's team VR and AR environments for treating specific phobias

Table 3. VR-EBT sessions for social anxiety disorder and fear of public speaking

	Roy et al. (2003)	Wallach et al. (2009)	Anderson et al. (2013)
Session	-Therapy presentation &	-Therapy presentation &	-Therapy presentation &
1	psychoeducation	psychoeducation	psychoeducation
Session	-VRET (performance	-Training in automatic thoughts	-VRET including:
	_		- V KET including.
2	environment)	identification	-Self-focused attention
Session	-VRET (performance	-Cognitive restructuring	-
	_		-Perceptions of self and others
3	environment)		
Session	-VRET (intimacy environment)	-VRET	-Perceptions of emotional
	- VKE1 (mumacy environment)	-VKEI	control
4		-Cognitive restructuring	
			-Rumination
Session	-VRET (intimacy environment)	- VRET	-
5			-Realistic goal setting for social
		-Cognitive restructuring	situations
			_
Session	-VRET (scrutiny environment)	- VRET.	
6		-Cognitive restructuring	
Session	-VRET (scrutiny environment)	- VRET	-
7			
		-Cognitive restructuring	
Session	-VRET (assertiveness	- VRET	-Relapse prevention
8	environment)		
		-Cognitive restructuring	
Session	-VRET (assertiveness	-VRET	-
9	environment)		

		-Cognitive restructuring	
Session	-VRET (environment chosen by	- VRET	
10	the patient)	-Cognitive restructuring	
Session	-VRET (environment chosen by	- VRET	
11	the patient)	-Cognitive restructuring	
Session	-VR (environment chosen by the	-Relapse prevention	
12	patient)		



Figure 3. VR environments for panic disorder and agoraphobia treatment (Botella et al., 2004)



Figure 4. VR-interoceptive exposure vs traditional interoceptive exposure (Pérez-Ara et al., 2010)

	Vincelli et al. (2003)	Botella et al. (2007b)
Session 1	-Psychoeducation	-Psychoeducation
	-Establishment of the VRET hierarchy	
Homework:	-Record of panic	-Catastrophic interpretations recording
		-Record of panic
Session 2	-Cognitive assessment	-Slow breathing training
	-Scheduling of in vivo self-exposure	-Cognitive restructuring
Homework:	-Record of panic	-Practicing slow breathing
	-In vivo self-exposure	-Record of panic
Session 3	- Cognitive restructuring	- VRET
	-VRET	- VR-interoceptive exposure
Homework:	-Record of panic	-Record of panic.
	-In vivo self-exposure	
Session 4	-VRET	-VRET
	-Cognitive restructuring	-VR-interoceptive exposure
		-Cognitive restructuring
Homework:	-Record of panic	-Record of panic
	-In vivo self-exposure	
Session 5	- VRET	-VRET
	-Interoceptive exposure	- VR-interoceptive exposure
		-Cognitive restructuring
Homework:	-Record of panic	-Record of panic
	-In vivo interoceptive exposure	
Session 6	- VRET	-VRET
	-Interoceptive exposure	-VR-interoceptive exposure

	-Cognitive restructuring	-Cognitive restructuring
Homework:	-Record of panic	-Record of panic
	-In vivo interoceptive exposure	
Session 7	- VRET	-VRET
	-Interoceptive exposure	-VR-interoceptive exposure
	-Cognitive restructuring	-Cognitive restructuring
Homework:	-Record of panic	-Record of panic
	-In vivo interoceptive exposure	
Session 8	-Cognitive restructuring	-VRET
	-Relapse prevention	- VR-interoceptive exposure
		-Cognitive restructuring
Homework:		-Record of panic
Session 9		-Relapse prevention