One of the most effective treatments of anxiety is exposure therapy: a person is exposed to specific feared situations or objects that trigger anxiety. This exposure process may be done through actual exposure, with visualization, by imagination or using virtual reality (VR), that provides users with computer simulated environments with and within which they can interact. VR is made possible by the capability of computers to synthesize a 3D graphical environment from numerical data. Furthermore, because input devices sense the subject’s reactions and motions, the computer can modify the synthetic environment accordingly, creating the illusion of interacting with, and thus being immersed within the environment. Starting from 1995, different experimental studies have been conducted in order to investigate the effect of VR exposure in the treatment of subclinical fears and anxiety disorders. This review will discuss their outcome and provide guidelines for the use of VR exposure for the treatment of anxious patients.

A large number of people around the world suffer from anxiety disorders [1] that prevent them from doing a variety of daily-life activities such as driving, taking a plane, interacting with someone unknown or staying in crowded places. In a large proportion of anxious individuals, these commodities provoke feelings of being strangled and of imminent death so acute that they become unable to conduct a normal life. Even if these disorders tend to worsen with time and lack of clinical interventions, patients usually tend to refuse treatment because they are too frightened to go through it. In fact, even if many different kinds of treatment are available for anxiety disorders, such as behavioral treatments (relaxation, exposure, modelling and roleplay), cognitive therapies (thought stopping, mental distraction and thought recording), medication, psychodynamic therapy, family therapy and biofeedback, many studies have demonstrated that the exposure-based treatments are among the most effective [2–4]. Despite its effectiveness, exposure-based therapy presents important limitations:

- Many patients are reticent to expose themselves to the real phobic stimulus or situation
- In vivo exposure can never be fully controlled by the therapist and its intensity can be too strong for the patient
- This technique often requires that therapists accompany patients into anxiety-provoking situations in the real world at great cost to the patient, and with great time expenditure on the part of both therapist and patient.

These are the main reasons for which from the mid to late 1990s some therapists around the world have started to add the virtual reality (VR) to the in vivo exposure-based therapy, providing in-office, controlled exposure therapy to anxious patients, mitigating many of the complications of the in vivo exposure.

In 2000, the increasing success of VR in the treatment of anxiety disorders was documented by a survey performed between a panel of 62 experts in psychotherapy who affirmed that only 18 of the 38 analyzed therapeutic interventions were predicted to increase in the following 10 years. VR use was ranked third and fifth [5].
Virtual reality: from technology to presence

Since the early 1980s, when computer scientists and the media used the term for the first time, VR has been usually described as a computer-simulated environment with and within which people can interact.

VR is made possible by the capability of computers for synthesizing a 3D graphical environment from numerical data. Furthermore, because input devices sense the subject’s reactions and motions, the computer can modify the synthetic environment accordingly, creating the illusion of interacting with, and thus being immersed within the environment.

Using visual, aural or haptic devices, the subject experiences the graphical environment as if it were real. These computer-generated scenarios may represent either a model of a real-world object, such as a house, or an abstract world that does not exist in a real sense but is understood by humans as real.

A VR system is the combination of the hardware and software that enables the development of virtual environments (VEs). The hardware components receive input from user-controlled devices and convey multisensory outputs to create the illusion of a virtual world. The software component manages the hardware that makes up the VR system. Separate VR applications are then responsible for the creation of specific virtual worlds.

Typically, a VR system is composed of (Figure 1) [6,7]:

- The database construction and virtual object modeling software for building and maintaining detailed and realistic models of the virtual world. In particular, the software handles the geometry, texture, intelligent behavior, and physical modeling of hardness, inertia and surface plasticity of any object included in the virtual world
- The input tools (trackers, gloves or mice) that continually reports the position and movements of the users
- The graphic rendering system that generates, at 20–30 frames per second, the VE
- The output tools (visual, aural and haptic) that immerse the user in the VE

As we have just seen, VR is usually described as a particular collection of technological hardware and software. However, it is also possible to describe it in terms of human experience, using the concept of presence [8,9]: VR is the medium able to induce the experience of “presence” in a computer-generated world.

Presence is usually defined as the “sense of being there” [9], or as the “feeling of being in a world that exists outside the self” [10]. Different studies showed a direct connection between the intensity of the emotions experienced in VR and the level of presence elicited by it [11].

The first commercial version of a VR system was developed by Morton Heilig in 1956 [12], but the possibility to have a personalized virtual experience came only in 1968 when Ivan Sutherland developed the first head-mounted display (HMD) that allowed the user to view 3D wire frame objects. In the early 1980s, the first program that allowed people to interact and change computer generated images through bodily movements was created by Krueger [13], who was one of the first to suggest a possible role for VR in the treatment of mental health disorders [14]. VR systems became available for the consumer market between 1985 and 1990 when several video games companies started to sell quite inexpensive HMD and data gloves used to interact with the virtual worlds.

Actually, even small laboratories or private users (i.e., private clinicians) have the possibility to buy a VR system that guarantees a good quality of immersion, since the cost varies from approximately US$5000–10000 (the recent PCs or laptops are usually powerful enough to handle complex 3D simulations).

Virtual reality in healthcare

Thanks to its commercial diffusion and to the decreasing cost of technology, starting from the 1990s the use of VR in medicine has become more widespread [15]. The growing interest in medical applications of VR is also highlighted by the increasing number of scientific articles published each year on this topic: searching Medline with the keyword “virtual reality”, the total number of publications has increased from 45 in 1995 to 289 in 2006, showing an average annual growth rate of nearly 14%.

For many healthcare professionals, VR is first of all considered a technology. However, the analysis of the different VR applications clearly shows that the focus on technological devices is not the same in all areas of medicine and it is related to the specific goals of the healthcare provider.

For instance, Rubino et al. [16], McCloy and Stone [17], and Szekey and Satava [18] in their reviews describe VR as: “a collection of technologies that allow people to interact efficiently with 3D computerized databases in real time using their natural senses and skills” [17]. This definition lacks any reference to
HMD and instrumented clothing such as gloves or suits. In fact, less than 20% of VR healthcare applications in medicine are actually using any immersive equipment.

However, if we shift our attention on behavioral sciences, where immersive devices are used by more than 50% of the applications, VR is described as “an advanced form of human-computer interface that allows the user to interact with and become immersed in a computer-generated environment in a naturalistic fashion” [19].

These two definitions underline two different focuses of VR in medicine: VR as a simulation tool and VR as an interaction tool.

For physicians and surgeons, the simulation focus of VR prevails on the interaction one: their ultimate goal of VR is the presentation of virtual objects to all of the human senses in a way identical to their natural counterpart [18]. As noted by Satava and Jones [20], as more and more of the medical technologies become information-based, it will be possible to represent a patient with higher fidelity to a point that the image may become a surrogate for the patient—the medical avatar. In this sense, an effective VR system should offer realistic body parts or avatars that interact with external devices such as surgical instruments as near as possible to their real models.

For clinical psychologists and psychiatrists, the interaction focus of VR prevails on the simulation one: they use VR to provide a new human–computer interaction paradigm in which users are no longer simply external observers of images on a computer screen but are active participants within a computer-generated 3D virtual world [21,22].

Starting from 1990, different companies have developed complete VR systems for the treatment of common anxiety disorders and specific phobias, such as: fear of heights, fear of flying, driving phobias, social phobia, fear of public speaking, fear of spiders, panic disorder and post-traumatic stress disorder (PTSD).

Virtual reality & the treatment of anxiety disorders

Rationale
Patients with anxiety disorders usually experience more intense levels of apprehension and worry, which usually occur for longer periods of time than the average person experiences in everyday life and often develop ritual acts, repetitive thoughts or avoidance mechanisms to protect themselves from anxiety.

Together with cognitive therapy, behavioral therapy and medication, one of the most effective treatments of anxiety is exposure therapy. Exposure therapy is a process in which a person is exposed to specific feared situations or objects that trigger anxiety. The exposure process may be performed through actual exposure, with visualization or by imagination. The rationale behind exposure therapy is that, by practicing exposure to their fears, people have the opportunity to learn that their fears are excessive, and that anxiety decreases with more and more practice (habituation). Because many people find it hard to face their fears, traditional exposure therapy typically starts with exposing a person to situations that create only mild-to-moderate symptoms of anxiety and gradually progresses to situations that create severe anxiety. With repeated exposure, feared situations begin to elicit less and less fear and anxiety for the person, and he or she feels less of an urge to avoid them.

In the last few years, researchers and clinicians have started to use VR to carry out a specific form of exposure treatment (VR exposure therapy [VRET]). VRET has the potential to control, enhance and accelerate the treatment process offering several advantages over real exposure or imagination techniques.

Compared with the in vivo exposure, VRET is completely controlled: the quality, intensity and frequency of the exposure is entirely decided by the therapist in his/her office and can be stopped any time the patient is unable to tolerate it. The flexibility of VEs also allows the patient to overpractice in situations often much worse and more exaggerated than those that are likely to be encountered in real life. This allows patients to develop a sense of mastery and the confidence to carry out the task successfully. In addition, the patient can be exposed repeatedly only to the specific feared stimuli. A typical example of this point regards the patients who only have fear of airplane landings and is clearly explained by Wiederhold [23]. Using the VRET, during a single 1-h session such a patient can practice several landings without wasting time with all other aspects of air travel.

Moreover, since the exposure takes place in a safe and controlled environment (the therapist’s office), the therapist can monitor the patient’s reactions with different instruments (e.g., psychological questionnaire and biomonitoring systems) and follow the symptom reduction.

Compared with imaginal exposure, VRET has the advantage to be highly immersive and more realistic since it has the potential to stimulate different sensory modalities through visual, auditory and sometimes tactile cues, motion and vibration that help patients to feel immersed in the experience. The feeling of presence that patients experience in these environments, involving all the sensorimotor channels, enables them to really “live” the experience in a more vivid and realistic manner than they could do through their own imagination [24]. This should translate into fewer treatment sessions, and, therefore, less cost for treatment [25,26].

In addition, during virtual exposure, the therapist can see what the patient sees, identifying the exact stimuli that are causing anxiety in patients.

In summary, the flexibility of VE allows the therapist to tailor sessions to meet the needs of each client, offering the following advantages: interactivity, flexibility, controllability, confidentiality, safety, timesaving, cost savings and repeatability. This is why, used in combination with the traditional cognitive–behavioral therapy, VRET is a promising method of increasing the likelihood of therapeutic success, at least in the field of anxiety disorders and specific phobias.
Applications
Starting from 1995, different experimental studies have been conducted in order to investigate the effect of VRET in the treatment of specific phobias (acrophobia, claustrophobia, fear of flying, fear of driving and spider phobia) and anxiety disorders (social phobia, panic disorders with agoraphobia and PTSD; for other reviews on the use of VRET in anxiety disorders see [27–36]).

The overall objective of this review is to present published journal articles that examined the effects of VRET in the treatment of anxiety and phobic symptoms. A preliminary article search was conducted using MedLine, PsycLIT and ISI Web of Science electronic database. Standard searches were performed, which used keywords related to VRET and anxiety. Reference lists of collected papers were also visually inspected to locate any cited journal articles addressing anxiety and phobic symptoms before and after VRET.

For clarity, appendices summarizing the case and randomized controlled studies for each specific phobia or anxiety disorder, each with a brief comment about the efficacy of VRET, are provided.

Acrophobia
Acrophobia, that is the pathological fear of heights, was the first phobia treated with VRET (APPENDIX 1). The results of case studies as well as of different controlled studies have shown that it may be reduced by VRET [37–46]. Follow-up observations seem to prove that the effects of the treatment are lasting [47–49].

Claustrophobia
Only two studies have been performed on the effectiveness of VRET in claustrophobia: one is a case study [50] and the other includes only four subjects. (three of whom were patients with panic disorder and claustrophobic symptoms) [51] (APPENDIX 2). Even if these two studies show positive results, they are not enough to affirm that VRET really is effective to treat claustrophobia. Further randomized controlled studies are necessary.

Fear of flying
Fear of flying is a fairly common disorder that impacts 10–20% of the US population. It is characterized by the inability to fly or by various degrees of anxiety or stress for those who do fly. Approximately one-half of the patients who experience a fear of flying symptoms meet the criteria of specific phobias; they are fearful of something happening to the aircraft, for example, crashing. The other half of the fear of flying population are agoraphobics, with or without panic disorder; they are fearful of being trapped and having a panic attack [52].

A lot of studies have been performed in order to investigate the possibility of treating fear of flying with the VRET approach (APPENDIX 3). Compared with in vivo exposure, VRET presents the following advantages:

• It is highly cost-effective
• The different components of the flight (engines off/on, taxiing, take-off, flying and landing) can be repeated endlessly in the therapist office
• Weather conditions can be easily changed by the therapist

The literature shows that VRET could be an effective component in the treatment of fear of flying, being more successful than cognitive and behavioral techniques [23,53–65]. However, in order to strengthen the present results, it could be useful to perform new studies comparing different treatment forms, including comparable treatment conditions (same number and length of sessions, VEs that replicate in vivo situations and so on).

Fear of driving
Driving phobia, defined as a specific phobia, situational type in Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV, is characterized by intense and persistent fear of driving, which increases as a person anticipates or is exposed to driving stimuli. People with driving phobia acknowledge that their fears are excessive or unreasonable, yet are unable to drive, or tolerate driving with considerable distress. The inability to drive results in a major loss of mobility and independence, which interferes with daily activities.

Currently, the only three studies we have found in literature suggest that VRET may be a quite promising intervention for treating driving phobia [66–68], but obviously, more controlled trials and follow-up evaluations are necessary to support these preliminary findings (APPENDIX 4).

Spider phobia
Augmented VRET, consisting of the possibility to touch real objects (i.e., hairy fabric that gives sensation of feeling a spider) while watching a virtual spider through the HMD, seems to be an effective treatment for spider phobia, as concluded in the three studies presented in APPENDIX 5 [69–71]. However, to strengthen this conclusion, more research and more controlled studies are needed.

Fear of public speaking
Since it has been demonstrated that even a virtual audience can elicit anxiety [72–74], specific anxiety-provoking VEs have been created for the treatment of patients with public speaking fear. The available studies [75–79] show promising results, but also have important limitations, such as the inclusion of nonclinical samples, the use of multimodal intervention and the lack of statistical comparisons (APPENDIX 6). Other randomized controlled studies with a larger number of patients are necessary in order to guarantee the efficacy of VRET in the treatment of this disorder.

Panic disorder with agoraphobia
Agoraphobia is defined as the fear of being in places or situations from which escape might be difficult or embarrassing and is often associated with panic disorder. To date, only two studies
support the efficacy of VRET on its own in the treatment of panic disorder with agoraphobia [APPENDIX 7] [80,81]. However, Vincelli [82] and Choi [83] have demonstrated that treatments based on the experiential–cognitive therapy (ECT), a combination of psychoeducation, VR exposure, cognitive therapy, interoceptive and exposure in vivo homework assignments and relapse prevention produces the same results of the traditional cognitive–behavioral therapy, but in a smaller amount of time. Unfortunately, when VR is embedded in a multimodal intervention, such as ECT, inferring any conclusions on its effects as a therapeutic method could be deceptive.

In conclusion, VRET seems to be a promising treatment for panic disorder with agoraphobia, but other controlled studies and larger samples are necessary to understand the real advantages of this kind of therapy compared with the traditional cognitive–behavioral treatments.

Post-traumatic stress disorder
The few studies conducted in PTSD patients have shown that VRET, combined with relaxation techniques and imaginary exposure, is effective in the treatment of this diffuse disorder [APPENDIX 8] [84–86]. However, other studies are necessary to evaluate the efficacy of VRET compared with the imaginary exposure alone and to investigate the possibility to use it in patients with a PTSD caused by different traumatic events (e.g., car accident, rape or physical attack).

A brief conclusion
The presented data indicate that, in general, VRET seems to be a promising intervention for the treatment of specific phobias and anxiety disorders. However, the small sample sizes used, the substantial number of drop-outs in some VRET studies and the frequent use of multimodal interventions make it necessary to perform more controlled and randomized studies to investigate whether VRET can be recommended for use in clinical practice.

Despite these limitations, comforting data come from two very recent meta-analyses [87,88]. The first demonstrates not only that VRET is more effective than no treatment, but also that it is slightly but significantly more effective than in vivo exposure. The other analysis, concerning the affective effects of VRET, suggests that it has a statistically large effect on all affective domains and that these effects are of the magnitude described in the literature as large [89].

Expert commentary
Cost–effectiveness ratio
One of the fundamental parameters in assessing the effectiveness of therapies is the ratio existing between the ‘cost’ of administration of the therapeutic procedure and the resulting ‘benefits’. Cost refers to the expenditure not only in terms of money and time, but also in terms of emotional involvement by the person to whom the therapy is directed. The benefits regard the effectiveness of the treatment: the achievement of the target set in the shortest time possible.

As we have discussed above, exposure therapy in anxiety disorders is traditionally carried out ‘in imagination’ or else in the real world (i.e., in vivo). With imagination exposure, the subject is trained to produce the anxiety-provoking stimuli through mental images; with in vivo exposure, the subject actually experiences these stimuli in semistructured situations. Both of these methods present advantages and limitations as regards the cost–benefit ratio. In the first case, the prevalent difficulty is represented by teaching the subject to produce the images that regard experiences associated with anxiety: the majority of failures linked to this therapy are those subjects who present particular difficulties in visualizing scenes of real life. The cost of the application, however, is minimal because the therapy is administered in the physician’s office, thus avoiding situations that might be embarrassing for the patient and safeguarding his privacy. In the second case, the difficulty lies in structuring, in reality, experiences regarding the hierarchically ordered anxiety-provoking stimuli, with the result that the cost in terms of time, money and emotions is high. At the same time, the advantage of contending with real contexts increases the likelihood of effectiveness of the ‘in vivo’ procedure [90].

Using VRET, it is possible to recreate a hierarchy of situations corresponding to reality, which they may experience in an authentic way thanks to the involvement of all their sensorimotor channels. The realistic reproduction of VEs enables the interacting individual to immerse himself in a dimension of real presence. This makes it possible to limit the costs as compared with traditional procedures of treatment and to consolidate the effectiveness of the treatment thanks to the possibility of recreating a ‘3D world’ within the walls of the clinical office [91]. On the other side, the use of VR technology requires skilled therapists able to give patients adequate psychological support and who are trained to interact with VEs.

Contraindications
Some medical conditions represent significant contraindications for the use of VR. The presence of migraine, headache, seizure disorder and vestibular abnormalities must be investigated before VR treatment because it is not compatible with this kind of therapeutic approach.

There is also some evidence that the use of 3D environments provokes changes in heart rate, and increases systolic and diastolic blood pressure and oxygen consumption, suggesting caution when these tools are used with patients with hypertension, cardiovascular and circulatory diseases.

In addition, since VR might interfere with normal psychological processes, a careful observation is necessary when using it with patients with schizophrenia, or with serious personality disorders who are pathologically predisposed to become confused by real versus virtual worlds [92].
**Cybersickness**

There is a tendency for some VR users to exhibit symptoms that parallel those of classical motion sickness both during and after the virtual experience. Cybersickness is distinct from motion sickness in that the user is often stationary but has a compelling sense of self motion through moving visual imagery. The symptoms related to cybersickness regard different target areas: visual (visual blurring, double vision, tearing, irritation redness), auditory (tinnitus and decreased hearing), vestibular (dizziness, nausea, vomiting and sweating), CNS (headache, seizures, flashbacks, disorientation and instability), musculoskeletal (neck strain, wrist strain and back pain).

Unfortunately, there is currently no foolproof method for eliminating the problem, but a gradual introduction to VEs and shorter exposure time can help to prevent symptoms.

Several existing questionnaires can be administered to assess for the risk of cybersickness before the beginning of the treatment. The most commonly used, the Simulator Sickness Questionnaire, has been shown to be a reliable indicator for predicting cybersickness in military pilots and in undergraduate populations [93]. This questionnaire is a reasonable starting point for the assessment of discomfort in patients.

**Long-term effects**

Very little is known about the long term effects of VR exposure. Ungs reported that a very small number of subjects (4.6% of the sample) experienced VR side effects, including visual flashbacks, balance disorder and lack of hand–eye coordination for longer than 24 h after the conclusion of the session [94].

In some cases, VR induces subjects to confuse the virtual experience with the real one, resembling the effects of drugs such as hallucinogens [95]. When this happens, the main risk is that people may prefer the virtual world to the real one and completely withdraw from society or, if the sense of reality becomes blurred, patients may become unable to distinguish safe from dangerous behaviors.

Addiction and social isolation are other risks that are connected to the use of VR, but they are more frequent in children and adolescents [96].
Virtual reality in anxiety disorders

Five-year view

Although it is undisputable that VR has come of age for clinical and research applications, the majority of them are still in the laboratory or investigation stage. In a recent review, Riva and colleagues identified different major issues that still limit the use of VR in psychotherapy [97]:

- The lack of standardization in VR hardware and software, and the limited possibility of tailoring the VEs to the specific requirements of the clinical or experimental setting [98]
- The lack of accepted standards for the ergonomic/usability evaluation of VEs given the clinical nature of the applications and users [99]
- The low availability of standardized protocols that can be shared by the community of researchers
- The high costs (up to $200,000) required for designing and testing a new clinical VR application
- Most VEs in use today are not user-friendly; expensive technical support or continual maintenance are often required

To address these challenges, the Italian research project FIRB-NeuroTIV is developing NeuroVR 2.0, a cost-free VR platform based on open-source software, that allows nonexpert users to easily modify a VE and to visualize it using either an immersive or nonimmersive system [100].

Most existing VEs for psychotherapy are proprietary and have a closed source, and thus cannot be tailored from the ground up to fit specific needs of different clinical applications [33]. NeuroVR addresses these issues by providing the clinical professional with a cost-free VE editor, which allows nonexpert users to easily modify a virtual scene, to best suit the needs of the clinical setting.

Using the NeuroVR Editor (FIGURE 2), the psychological stimuli/stressors appropriate for any given scenario can be chosen from a rich database of 2D and 3D objects, and easily placed into the predesigned virtual scenario by using an icon-based interface (no programming skills are required). In addition to static objects, the NeuroVR Editor allows a transparent alpha channel to be overlaid on the 3D scene videos; that is process useful when rendering image elements in separate passes, combining the resulting multiple 2D images into a single, final image.
The editing of the scene is performed in real time, and effects of changes can be checked from different views (frontal, lateral, and top).

Currently, the NeuroVR library includes different pre-designed virtual scenes, representing typical real-life situations, such as a supermarket, an apartment or a park (Figure 3). These VEs have been designed, developed and assessed in the past 10 years by a multidisciplinary research team in several clinical trials, which have involved over 400 patients [97]. On the basis of this experience, only the most effective VEs have been selected for inclusion in the NeuroVR library.

An interesting feature of the NeuroVR Editor is the ability to add new objects to the database. This feature allows the therapist to enhance the patient’s feeling of familiarity and intimacy with the virtual scene; for example, by using photos of objects/people that are part of the patient’s daily life, thereby improving the efficacy of the exposure.

The second main component of NeuroVR is the Player, which allows navigation and interaction with the VEs created using the NeuroVR Editor. The Player offers a set of standard features that contribute to increase the realism of the simulated scene. These include collision and detection to control movements in the environment, realistic walk-style motion, advanced lighting techniques for enhanced image quality and streaming of video textures using an alpha channel for transparency.

The Player can be configured for two basic visualization modalities: immersive and nonimmersive. The immersive modality allows the scene to be visualized using a HMD, either in stereoscopic or in mono-mode; compatibility with a head-tracking sensor is also provided. In the nonimmersive modality, the VE can be displayed using a desktop monitor or a wall projector. The user can interact with the VE using either keyboard commands, a mouse or a joystick, depending on the hardware configuration chosen. A future goal of the developers is also to provide software compatibility with instruments that allow collection and analysis of behavioral data, such as eye-tracking devices and sensors for psychophysiological monitoring.

Currently, the NeuroVR library includes a limited number of VEs addressing specific phobias (e.g., fear of public speaking and agoraphobia) and eating disorders. However, new pre-designed environments will be developed in the next few years: it is envisioned that Blender user community, consisting currently of 250,000 people worldwide will contribute to extend the NeuroVR library, developing new VEs which can be tailored by the clinical professionals for a range of clinical and experimental needs.

A final critical issue related to the use of VRET in the treatment of anxiety-related disorders is the lack of availability of a VR system in the real life context of the patient: both the cost and the setting of the system limit its use to the healthcare center/hospital/therapist’s office. To overcome this issue, a VRML/X3D exporter for experiencing the environments on the Web and a player for PDAs and smartphones are planned features (Figure 4). The final goal is the development of a VRET system able to [101]:

- Present and structure emotionally relevant contents in a home setting
- Verify the adherence of the patient and eventually alert the patient/therapist
- Track in real-time the emotional level of the patient and record it for later assessment by the therapist
- Provide a feedback to the patient that is able to help him in coping with the contents
- Automatically contact the therapist if the emotional level of the patient is higher than a preset cut-off value

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Key issues

- An emerging new treatment for anxiety disorders is virtual reality exposure therapy (VRET), integrating different virtual reality experiences with traditional cognitive–behavioral techniques.
- VRET uses a computer-generated environment to recreate a feared stimulus and provide the opportunity for habituation.
- The feeling of actual presence offered by the use of VRET enables the patient to experience the treatment in a more vivid and realistic manner than they could through their own imagination.
- Through the use of virtual environments, it is possible to gradually expose the patient to feared situations.
- The therapist sees what the patient sees. In this way it is easier to identify the exact stimuli that are causing anxiety in patients.
- Patients are more receptive to VRET treatment than imaginal treatment. VR therapy appears to have more face validity for them, increasing the adherence to treatment.
- VR allows the situation to be graded so that the patient can start at the easiest level and progress to the most difficult.
- Different controlled studies have verified the efficacy of VRET in different anxiety disorders: simple phobias, panic disorders with agoraphobia, post-traumatic stress disorders and fear of public speaking.
- A new open source software, NeuroVR, provides the therapist with an easy way to test this approach in his/her own clinical practice.

References

Papers of special note have been highlighted as:
- of interest
- of considerable interest


Virtual reality anxiety disorders


**Excellent meta-analysis about the effects of virtual reality exposure therapy in anxiety disorders.**


**Good meta-analysis describing the affective outcomes of virtual reality exposure therapy.**


**Key book about cybertherapy.**


**Excellent paper describing the NeuoroVR software.**

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Appendices

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<td>2 + 2</td>
<td>VRET = IVE in reduction of anxiety and avoidance</td>
<td>Stable results at 6-month follow-up</td>
<td>Order effect cannot be ruled out</td>
<td>[38]</td>
</tr>
<tr>
<td>Emmelkamp et al. (2002)</td>
<td>38, 5 drop-outs (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (VRET vs IVE)</td>
<td>3</td>
<td>VRET = IVE in reduction of anxiety and avoidance</td>
<td>Stable results at 6-month follow-up</td>
<td>Order effect cannot be ruled out</td>
<td>[48]</td>
</tr>
<tr>
<td>Jang et al. (2002)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>1</td>
<td>Symptom improvement</td>
<td></td>
<td></td>
<td>[40]</td>
</tr>
<tr>
<td>Krijn et al. (2004)</td>
<td>37, 12 drop-outs (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (VRET with HMD vs VRET with CAV vs WL)</td>
<td>3</td>
<td>VRET-HMD = VRET-CAVE; VRET-HMD and VRET-CAVE &gt; WL</td>
<td>Stable results at 6-month follow-up</td>
<td>The level of immersion (HMD vs CAVE) does not influence the effectiveness of the treatment</td>
<td>[49]</td>
</tr>
<tr>
<td>Coelho et al. (2006)</td>
<td>10 (clinical sample)</td>
<td>Uncontrolled study</td>
<td>1 (VRET)</td>
<td>3</td>
<td>Significant improvements in every post-test measure, in behavioral performance, in the subjective feeling of fear and in the attitudes towards height-related situations for all subjects</td>
<td>Stable results at 1-year follow-up</td>
<td>Order effect cannot be ruled out</td>
<td>[47]</td>
</tr>
<tr>
<td>Krijn et al. (2007)</td>
<td>26 (clinical sample)</td>
<td>Randomized crossover design</td>
<td>2 (VRET followed by VRET + VRET-CSS vs VRET + VRET-CSS followed by VRET)</td>
<td>2 + 2</td>
<td>VRET = VRET-CSS</td>
<td>At 6-month follow-up, most gains during treatment were not fully retained</td>
<td>VRET, regardless of addition of coping self-statements, decreased anxiety and avoidance of height situations, and improved attitudes towards heights</td>
<td>[43]</td>
</tr>
</tbody>
</table>

CAVE: Cave Automatic Virtual Environment; CTR: No-treatment control group; HMD: Head-mounted display; IVE: In vivo exposure; VRET-CSS: Virtual reality exposure therapy + coping self statements; WL: Waiting list (patients waiting for the treatment); VRT: Virtual reality therapy; VRET: Virtual reality exposure therapy.
## Appendix 2. Claustrophobia.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botella et al. (1998)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>8 + 1 IVE</td>
<td>Reduction of anxiety and avoidance; symptoms improvement</td>
<td>Stable results at 1-month follow-up</td>
<td>A multiple baseline showed fluctuations in scores for 2 of the patients, indicating lack of stability of symptom severity before treatment; VRET was not compared with other treatments</td>
<td>[50]</td>
</tr>
<tr>
<td>Botella et al. (2000)</td>
<td>1 claustrophobic + 3 panic disorder with claustrophobic fear (clinical sample)</td>
<td>Multiple-baseline design</td>
<td>1 (VRET)</td>
<td>8</td>
<td>Reduction of anxiety and avoidance; symptom improvement</td>
<td>Stable results at 1- and 3-month follow-ups</td>
<td></td>
<td>[51]</td>
</tr>
</tbody>
</table>

*IVE: In vivo exposure.*

## Appendix 3. Fear of flying.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rothbaum et al. (1996)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>2 (within subject: AMT + VRET)</td>
<td>7 AMT followed by 6 VRET</td>
<td>Reduction of discomfort, anxiety, avoidance and depression; symptom improvement; the participant could fly comfortably in vivo after treatment</td>
<td>Both components were effective</td>
<td></td>
<td>[62]</td>
</tr>
<tr>
<td>North et al. (1997)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>5</td>
<td>Gradual reduction of discomfort during sessions; symptom improvement; participant could fly comfortably in vivo after treatment</td>
<td></td>
<td></td>
<td>[58]</td>
</tr>
<tr>
<td>Wiederhold et al. (1998)</td>
<td>2 (1 phobic + 1 normal)</td>
<td>Uncontrolled study</td>
<td>1 (VRET)</td>
<td>1</td>
<td>Reduction in skin conductance immediately after the session</td>
<td></td>
<td></td>
<td>[64]</td>
</tr>
<tr>
<td>Kahan et al. (2000)</td>
<td>31, 6 drop-outs (clinical sample)</td>
<td>Uncontrolled study</td>
<td>1 (AMT + VRET)</td>
<td>Average of 5.75</td>
<td>68% of treated patients were able to make a real flight after treatment. No other measures were reported</td>
<td>Patients continued to fly but with anxiety</td>
<td>Results were not presented for each treatment separately; there were no subjective or objective measures of subjects’ anxiety; some patients took medication or other psychological treatments before and/or during treatment; so any conclusion about the effectiveness of VRET is precluded</td>
<td>[53]</td>
</tr>
<tr>
<td>Klein (2000)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>2 (within subject: AMT + VRET)</td>
<td>21 (3 AMT + 18 VRET + homework)</td>
<td>After treatment, the patient was able to fly with a reduction of fear and anxiety</td>
<td>Multimodal intervention: the different treatment components were not evaluated separately</td>
<td></td>
<td>[54]</td>
</tr>
</tbody>
</table>

*AMT: Anxiety management training (cognitive and relaxation techniques and psycho-education); APGT: Attention-placebo group treatment; CBT: Cognitive–behavioral therapy (cognitive restructuring, interoceptive exposure and imaginative exposure to feared situations); IET: Systematic desensitization with imaginal exposure therapy; IVE: In vivo Exposure; WL: Waiting list (patients waiting for the treatment); VRET: Virtual reality exposure therapy.*
<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rothbaum et al. (2000)</td>
<td>45, 4 drop-outs</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (AMT + VRET vs AMT + IVE vs WL)</td>
<td>8 (4 AMT + 4 VRET or IVE)</td>
<td>AMT+VRET = AMT+IVE; AMT+VRET &gt; WL; AMT+IVE &gt; WL</td>
<td>No differences between the two treatments; stable results at 1-year follow-up, although a significant number of patients reported using either alcohol or drugs to reduce anxiety on flights</td>
<td>VRET situations (virtual flight, taxing, take-off and landing) were different from IVE situations (walking through an airport and sitting in a stationary aircraft)</td>
</tr>
<tr>
<td>Muhlberger et al. (2001)</td>
<td>30, 10 drop-outs</td>
<td>Randomized partly uncontrolled study; between subjects design</td>
<td>2 (AMT followed by VRET vs AMT followed by relaxation)</td>
<td>4 h AMT followed by 4 simulated flights vs 4 h AMT followed by 2 relaxation sessions</td>
<td>VRET &gt; RELAXATION on fear of flying questionnaire; VRET = RELAXATION on the other measurements</td>
<td>At 6-month follow-up, most group differences disappeared; VRET resulted in a better outcome on only one of five standardized flight anxiety measures</td>
<td>Educational and nonspecific factors seem to have a relatively large impact on flying behavior and fear of flying. Nonetheless, for APGT participants only, degree of anxiety reported at post-treatment was unrelated to the ability to fly successfully. In contrast, reduced scores on measures of flight anxiety for VRET participants was significantly associated with successfully flying</td>
</tr>
<tr>
<td>Maltby et al. (2002)</td>
<td>45 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (AMT + VRET vs APGT)</td>
<td>5</td>
<td>65% of VRET and 57% of APGT participants flew during a test flight. Both groups showed significant improvement following treatment on standardized self-report measures of flight anxiety, with a better outcome for the VRET group on four of five of these measures</td>
<td>At 6-month follow-up, only one participant who received IET, eight of the 10 participants who received VRGET with no physiological feedback, and 10 of the 10 participants who received VRGET with physiological feedback, reported an ability to fly without medication or alcohol</td>
<td></td>
</tr>
<tr>
<td>Rothbaum et al. (2002)</td>
<td>24, 6 drop-outs</td>
<td>12-month follow up study [61]</td>
<td>2 (AMT + VRET vs AMT + IVE)</td>
<td>At 12-month follow-up; AMT+VRET = AMT+IVE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wiederhold et al. (2002)</td>
<td>30 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (VRET with no physiological feedback vs VRET with physiological feedback vs IET)</td>
<td>8</td>
<td>VRET with physiological feedback &gt; VRET with no physiological feedback &gt; IET</td>
<td>At 3-month follow-up, only one participant who received IET, eight of the 10 participants who received VRGET with no physiological feedback, and 10 of the 10 participants who received VRGET with physiological feedback, reported an ability to fly without medication or alcohol</td>
<td>Physiological feedback may add to the efficacy of VR treatment</td>
</tr>
</tbody>
</table>

AMT: Anxiety management training (cognitive and relaxation techniques and psycho-education); APGT: Attention-placebo group treatment; CBT: Cognitive–behavioral therapy (cognitive restructuring, interoceptive exposure and imaginative exposure to feared situations); IET: Systematic desensitization with imaginal exposure therapy; IVE: In vivo Exposure; WL: Waiting list (patients waiting for the treatment); VRET: Virtual reality exposure therapy.
### Appendix 3. Fear of flying (cont.)

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muhlberger et al. (2003)</td>
<td>45, 8 drop-outs (clinical sample)</td>
<td>Randomized controlled study: between subjects design</td>
<td>4 (CBT + VRET with motion simulation vs CBT + VRET without motion simulation vs CBT vs WL)</td>
<td>1 h CBT followed by 4 simulated flights (with or without motion simulation) vs 1 h CBT</td>
<td>CBT + VRET &gt; CBT &gt; WL</td>
<td>Stable results at 6-month follow-up</td>
<td>Motion simulation did not enhance treatment effectiveness; CBT condition took only 1 h while CBT + VRET took approximately 140 min</td>
<td>[57]</td>
</tr>
<tr>
<td>Wiederhold et al. (2003)</td>
<td>30 (clinical sample)</td>
<td>3-year follow up study</td>
<td>3 (VRET with physiological and visual feedback vs VRETno vs IET with physiological feedback only)</td>
<td>Of the participants in the VRGET group who had flown successfully by the end of treatment, all had maintained their ability to fly at follow-up. Of the participants in the VRGETno group who had flown successfully by the end of treatment, two were no longer able to fly. Of the participants in the IET group who had flown successfully, all were still able to fly</td>
<td>The addition of teaching self-control via visual feedback of physiological signals serves to maintain treatment gains in long-term follow-up</td>
<td>[65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rothbaum et al. (2006)</td>
<td>83, 8 drop-outs (clinical sample)</td>
<td>Randomized controlled study: between subjects design</td>
<td>3 (AMT + VRET vs AMT + IVE vs WL)</td>
<td>10 (4 AMT + 6 VRET or IVE)</td>
<td>AMT+VRET = AMT+IVE AMT+VRET &gt; WL AMT+IVE &gt; WL</td>
<td>Stable results at 6- and 12-month follow-ups for &gt;70% of respondents</td>
<td></td>
<td>[59]</td>
</tr>
<tr>
<td>Wallach et al. (2007)</td>
<td>4 (clinical sample)</td>
<td>Uncontrolled, pilot study</td>
<td>1 (VRET)</td>
<td>Reduction of anxiety and fear; symptoms improvement; the participants could fly in vivo after treatment</td>
<td>Small sample size; lack of a control group; lack of objective measures</td>
<td></td>
<td>[63]</td>
<td></td>
</tr>
</tbody>
</table>

AMT: Anxiety management training (cognitive and relaxation techniques and psycho-education); APGT: Attention-placebo group treatment; CBT: Cognitive–behavioral therapy (cognitive restructuring, interoceptive exposure and imaginative exposure to feared situations); IET: Systematic desensitization with imaginal exposure therapy; IVE: In vivo Exposure; WL: Waiting list (patients waiting for the treatment); VRET: Virtual reality exposure therapy; VRETno: VRET without visual feedback.
### Appendix 4. Fear of driving.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wald et al. (2000)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>3</td>
<td>Peak anxiety decreased within and across sessions; anxiety and avoidance and phobia-related interference in daily functioning declined between pre- and post-treatment</td>
<td>Stable results at 1- and 7-month follow-ups</td>
<td></td>
<td>[67]</td>
</tr>
<tr>
<td>Walsh et al. (2003)</td>
<td>14, 7 drop-outs (patients with driving phobia following a motor-vehicle accident)</td>
<td>Open trial</td>
<td>1 (CBT + VRET)</td>
<td>12</td>
<td>Significant reduction of distress, fear of diving, post-traumatic stress and depression</td>
<td>Half of the patients did not demonstrate an anxiety response during the VR exposure; multimodal intervention: the different treatment components were not evaluated separately</td>
<td></td>
<td>[68]</td>
</tr>
<tr>
<td>Wald (2004)</td>
<td>5 (clinical sample)</td>
<td>Multiple baseline across subjects design</td>
<td>1 (VRET)</td>
<td>8</td>
<td>Significant improvement in driving anxiety and avoidance in three patients; marginal improvement in one patient and no treatment gains in the last patient</td>
<td>Some loss of treatment gains at 3-months follow-up, but the scores remained below the pretreatment levels</td>
<td>Only little change in actual driving frequency for any of the patients</td>
<td>[66]</td>
</tr>
</tbody>
</table>

CBT: Cognitive behavioural therapy (cognitive restructuring, interoceptive exposure, and imaginative exposure to feared situations).

### Appendix 5. Spider phobia.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carlin et al. (1997)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>12</td>
<td>Reduction of fear, anxiety and avoidance; symptom improvement</td>
<td>Paradigm based on VRET with tactile augmentation</td>
<td></td>
<td>[69]</td>
</tr>
<tr>
<td>Garcia-Palacios et al. (2002)</td>
<td>23 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (VRET augmented vs CTR)</td>
<td>Average of 4</td>
<td>VRET augmented &gt; WL; 83% of the VRET group showed a significant reduction of fear, anxiety and avoidance</td>
<td>Paradigm based on VRET with tactile augmentation</td>
<td></td>
<td>[70]</td>
</tr>
<tr>
<td>Hoffman et al. (2003)</td>
<td>8 clinically phobic and 28 nonclinical students</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (VRET augmented vs VRET vs WL)</td>
<td>3</td>
<td>VRET augmented &gt; VRET &gt; WL in reduction of behavioral avoidance and subjective fear</td>
<td>Tactile augmentation makes the VRET more effective</td>
<td></td>
<td>[71]</td>
</tr>
</tbody>
</table>

CTR: No-treatment control group; WL: Waiting list (patients waiting for the treatment); VRET: Virtual reality exposure therapy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>North et al. (1998)</td>
<td>16, 2 drop-outs (nonclinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (VRET vs CTR*)</td>
<td>5</td>
<td>VRET &gt; CTR; significant reduction of anxiety and increased ability to face real world situations in the VRET group; no changes in the CTR group</td>
<td></td>
<td>Nontclinical sample</td>
<td>[79]</td>
</tr>
<tr>
<td>Harris et al. (2002)</td>
<td>14 (nonclinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (VRET vs CTR)</td>
<td>4</td>
<td>VRET &gt; CTR; significant reduction of anxiety in the VRET group</td>
<td></td>
<td>Nontclinical sample</td>
<td>[77]</td>
</tr>
<tr>
<td>Anderson et al. (2003)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>4 AMT + 1 IVT + 4 VRET</td>
<td>Decline in specific anxiety symptoms</td>
<td>Multimodal intervention: the different treatment components were not evaluated separately</td>
<td>[75]</td>
<td></td>
</tr>
<tr>
<td>Anderson et al. (2003)</td>
<td>1 (clinical sample)</td>
<td>Case study</td>
<td>1</td>
<td>2 IVT + 5 VRET + 1 relapse prevention</td>
<td>Decline in specific anxiety symptoms</td>
<td>Multimodal intervention: the different treatment components were not evaluated separately</td>
<td>[75]</td>
<td></td>
</tr>
<tr>
<td>Klinger et al. (2004)</td>
<td>36 (clinical sample)</td>
<td>Controlled not randomized study; between subjects design</td>
<td>2 (VRET + IVE vs CBGT + IVE)</td>
<td>12</td>
<td>VRET = CBGT (no statistical comparison)</td>
<td></td>
<td>Statistical comparisons were not made; participants were not randomly allocated</td>
<td>[78]</td>
</tr>
<tr>
<td>Anderson et al. (2005)</td>
<td>10 (clinical sample)</td>
<td>Open clinical trial</td>
<td>1 (AMT + VRET)</td>
<td>4 AMT + 4 VRET</td>
<td>Decreases on all self-report measures of public-speaking anxiety from pre- to post-treatment</td>
<td>Stable results at 3-month follow-up</td>
<td>Uncontrolled study; multimodal intervention: the different treatment components were not evaluated separately</td>
<td>[76]</td>
</tr>
</tbody>
</table>

AMT: Anxiety management training (cognitive and relaxation techniques and psychoeducation); CBGT: Cognitive–behavioral group therapy; CTR: No-treatment control group; CTR*: Control group (subjects were exposed to a trivial VR scene and encouraged to manage their phobia using visualization techniques or self exposure to the feared situations); IVE: In vivo exposure; IVT: Talking in front of a video camera and watching the videotape; VRET: Virtual reality exposure therapy.
### Appendix 7. Panic disorder with agoraphobia.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Experimental design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>North et al.</td>
<td>60 (nonclinical students with some degree of agoraphobia)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (VRET vs CTR)</td>
<td>8</td>
<td>VRET &gt; CTR; significant decrease in negative attitudes towards agoraphobic situations for VRET group</td>
<td>Nonclinical sample</td>
<td></td>
<td>[81]</td>
</tr>
<tr>
<td>Jang et al.</td>
<td>7, 7 drop-outs (clinical sample)</td>
<td>Open uncontrolled study</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
<td>Participants were not able to feel present in the virtual environment; the study was stopped</td>
<td></td>
</tr>
<tr>
<td>Vincelli et al.</td>
<td>12 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (ECT vs CBT vs WL)</td>
<td>ECT = 8; CBT = 12</td>
<td>ECT = CBT; ECT &gt; WL; CBT &gt; WL; ECT and CBT reduced the number of panic attacks, the level of depression and both state and trait anxiety</td>
<td></td>
<td>Small sample size; multimodal intervention: the different treatment components were not evaluated separately; ECT produced the same results of using 33% fewer sessions than CBT</td>
<td>[82]</td>
</tr>
<tr>
<td>Choi et al.</td>
<td>40 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>2 (ECT vs PCP)</td>
<td>ECT = 4; PCP = 12</td>
<td>ECT = PCP</td>
<td>At 6-month follow-up: PCP &gt; ECT</td>
<td>Multimodal intervention: the different treatment components were not evaluated separately; ECT produced the same results of using 33% fewer sessions than PCP immediately after the treatment, but the effect was not retained at 6-month follow-up</td>
<td>[83]</td>
</tr>
<tr>
<td>Botella et al.</td>
<td>37 (clinical sample)</td>
<td>Randomized controlled study; between subjects design</td>
<td>3 (VRET vs IVE vs WL)</td>
<td>9</td>
<td>VRET = IVE; VRET &gt; WL; IVE &gt; WL</td>
<td>Stable results at 1-year follow-up</td>
<td></td>
<td>[80]</td>
</tr>
</tbody>
</table>

CBT: Cognitive–behavioral therapy (cognitive restructuring, interoceptive exposure and imaginative exposure to feared situations); CTR: No-treatment control group; ECT: Experiential cognitive therapy (psychoeducation, virtual reality exposure, cognitive therapy, interoceptive exposure, exposure in vivo homework assignments and relapse prevention); IVE: In vivo exposure; PCP: Panic control program; WL: Waiting list (patients waiting for the treatment); VRET: Virtual reality exposure therapy.

### Appendix 8. Post-traumatic stress disorder.

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Design</th>
<th>Condition(s)</th>
<th>Sessions</th>
<th>Short-term outcome</th>
<th>Follow-up</th>
<th>Notes and limitations</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rothbaum et al.</td>
<td>1 (Vietnam combat veteran)</td>
<td>Case study</td>
<td>1</td>
<td>14</td>
<td>Participant experienced a 34% decrease on clinically-rated PTSD and a 45% decrease on self-rated PTSD; global symptom improvement</td>
<td>Stable results at 6-month follow-up</td>
<td>Multimodal intervention: the different treatment components were not evaluated separately</td>
<td>[85]</td>
</tr>
<tr>
<td>Rothbaum et al.</td>
<td>16, 7 drop-outs (Vietnam combat veterans)</td>
<td>Open clinical trial</td>
<td>1 (VRET + IET + PE + relaxation)</td>
<td>8–16</td>
<td>Significant reduction in symptoms associated with reported traumatic experiences</td>
<td>Stable results at 6-month follow-up</td>
<td>Uncontrolled study; multimodal intervention: the different treatment components were not evaluated separately</td>
<td>[86]</td>
</tr>
<tr>
<td>Difede et al.</td>
<td>1 (survivor of the World Trade Center attack)</td>
<td>Case study</td>
<td>1</td>
<td>6</td>
<td>90% reduction of PTSD symptoms after completing the VRET</td>
<td></td>
<td></td>
<td>[84]</td>
</tr>
</tbody>
</table>

IET: Systematic desensitization with imaginal exposure therapy; PE: Psychoeducation; PTSD: Post-traumatic stress disorder; VRET: Virtual reality exposure therapy.