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Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis

Thomas D. Parsons*, Albert A. Rizzo

Institute for Creative Technologies, University of Southern California, 13274 Fiji Way, Office 301, Marina del Rey, CA 90292-4019, USA

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Abstract

Virtual reality exposure therapy (VRET) is an increasingly common treatment for anxiety and specific phobias. Lacking is a quantitative meta-analysis that enhances understanding of the variability and clinical significance of anxiety reduction outcomes after VRET. Searches of electronic databases yielded 52 studies, and of these, 21 studies (300 subjects) met inclusion criteria. Although meta-analysis revealed large declines in anxiety symptoms following VRET, moderator analyses were limited due to inconsistent reporting in the VRET literature. This highlights the need for future research studies that report uniform and detailed information regarding presence, immersion, anxiety and/or phobia duration, and demographics.

Keywords: Virtual reality exposure therapy; Anxiety; Meta-analysis; Phobia; Affective neuroscience

1. Introduction

Anxiety and fear are concentrated emotional experiences that serve critical functions in organizing necessary survival responses (Fendt & Fanselow, 1999). Whilst properly functioning affective systems proffer responses that are adaptive, excessive trepidation is restrictive and may be a sign of dysregulated anxiety. Affective dysregulation, including

*Corresponding author. Tel.: +1 310 574 1632x1632; fax: +1 310 574 5725.
E-mail address: tparsons@ict.usc.edu (T.D. Parsons).

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anxiety disorders, specific phobias, as well as panic disorder and post-traumatic stress disorder (PTSD), may lead to significant impairments in normal life functioning. Repeated and early exposure to stress in persons with a particular genetic disposition may result in a decreased threshold for developing anxiety (Heim & Nemeroff, 1999). Over-excitation and deprivation can influence the affective system and may induce changes in the emotional circuitry of the brain that can contribute to stress-related psychopathology (Davidson, Jackson, & Kalin, 2000).

A good deal of research has shown that exposure therapy is effective for reducing negative affective symptoms (Rothbaum & Schwartz, 2002). In vivo exposure therapy has been found to have greater efficacy when compared to imaginal exposure, especially in the treatment of specific phobias (Emmelkamp, 2003). Exposure to emotional situations and prolonged rehearsal result in the regular activation of cerebral metabolism in brain areas associated with inhibition of maladaptive associative processes (Schwartz, 1998). Identical neural circuits have been found to be involved in affective regulation across affective disorders (De Raedt, 2006; Mineka, Watson, & Clark, 1998). Systematic and controlled therapeutic exposure to phobic stimuli may enhance emotional regulation through adjustments of inhibitory processes on the amygdala by the medial prefrontal cortex during exposure and structural changes in the hippocampus after successful therapy (Hariri, Bookheimer, & Mazziotta, 2000).

A novel tool for conducting exposure therapy is virtual reality exposure therapy (VRET), in which users are immersed within a computer-generated simulation or virtual environment (VE), that updates in a natural way to the users head and/or body motion. When a user is immersed in a VE, they can be systematically exposed to specific feared stimuli within a contextually relevant setting. VRET comports well with the emotion-processing model, which holds that the fear network must be activated through confrontation with threatening stimuli and that new, incompatible information must be added into the emotional network (Foa & Kozak, 1986; Wilhelm et al., 2005).

Empirical data from research assessing the efficacy of VRET on affective outcomes have been increasingly emerging over the last 10 years as VR systems have become less costly, more available and generally more usable. While much of the research to date has been comprised withcase studies, open clinical trials, and uncontrolled designs, a number of qualitative reviews (Botella et al., 2004; Glantz & Rizzo, 2003; Hodges, Anderson, Burdea, Hoffman, & Rothbaum, 2001; Krijn, Emmelkamp, Olafsson, & Biemond, 2004b; Pull, 2005) of initial VRET research have concluded that VRET has good potential as a treatment approach for several specific phobias (i.e. acrophobia, fear of driving, claustrophobia, aviophobia, and arachnophobia). The rationale for this view typically derives from early evidence that VRET produces better outcomes than imaginal exposure and that it provides equivalent outcomes and is a pragmatically attractive alternative to in vivo exposure (Emmelkamp, 2003). Further, these reviews qualitatively summarize findings from several studies that have yielded promising results with VRET in the treatment of PTSD and social anxiety disorder.

A potential problem in interpreting and reconciling findings about the nature and extent of affective changes ensuing from VRET is that a number of factors other than virtual reality exposure per se may be associated with such changes, including, for example, presence, immersion, anxiety and/or phobia duration, diagnostic groups, demographics (e.g. age, gender, and ethnicity). Furthermore, the vast majority of VRET studies have

reported on small sample sizes and made use of inadequate null hypothesis significance testing.

Until large-scale studies on the affective effects of VRET are published, statistical meta-analyses represent an interim remedy. Such analyses provide estimates of a population effect size across independent studies. They increase statistical power to detect true nonzero population effects by lowering the standard error, and consequently narrowing the confidence intervals associated with the population effect size estimate (Cohn & Becker, 2003). Hence, a quantitative meta-analysis, as opposed to a qualitative review, might facilitate a better understanding of the variability and clinical significance of affective change subsequent to VRET. In view of this need, the present study sought to examine the magnitude of VRET-related changes in six domains and an overall effect size for affective functioning across studies using meta-analytic methodologies.

2. Methods

2.1. Study selection

The overall objective of study selection was to collect published journal articles that examined anxiety symptoms before and after VRET for treatment of anxiety disorders. A preliminary article search was conducted using MedLine (1990–2006), PsycLIT (1990–2006), EMBASE (1990–2006), Cochrane Library (1990–2006), and ISI Web of Science electronic databases (1990–2006). Standard searches were performed, which used keywords containing affective domains (anxiety related), as well as references to VRET and/or anxiety. Keywords used for the search included "virtual reality exposure therapy," "virtual reality," "anxiety," "post-traumatic stress disorder," "claustrophobia," "driving," "flying," "aviophobia," "panic," "acrophobia," "agoraphobia," "social phobia," "spider," and "arachnophobia." Reference lists of collected articles were visually inspected to locate any cited journal articles addressing anxiety symptoms before and after VRET.

2.2. Study eligibility criteria

Eligibility criteria for study inclusion consisted of: (1) report of interval or ratio data, (2) anxiety symptom data presented before and after VRET, (3) use of at least one affect assessment instrument, (4) sufficient report of study results (e.g. means and standard deviations) to allow for effect size computation. All studies selected for inclusion were English-language publications. It is important to note that some studies were both repeated measure designs (before and after VRET), as well as comparisons (VRET versus cognitive behavioral therapy). For the purposes of the meta-analysis, we only used data from before and after VRET.

2.3. Data coding

After an initial meeting, two researchers independently extracted the following information from the published articles and coded: (1) number of subjects; (2) exclusion criteria; (3) affective disorder duration; (4) diagnostic groups; (5) demographics (e.g. age,

gender, and ethnicity); (6) therapeutic intervention parameters; (7) assessment measures; (8) number of sessions; and (9) summary statistics required for computation of effect sizes. Given the high level of comorbidity and possible overlap between affective disorders (De Raedt, 2006; Mineka et al., 1998), our analyses were performed first with an overall affective effect size (Anxiety Total) that included all anxiety measures used across all the studies and affective domains. Next, anxiety disorders were categorized (a priori) into the following eight affective domains: PTSD, social phobia, arachnophobia, acrophobia, panic disorder with agoraphobia, aviophobia, claustrophobia, and fear of driving. Due to the paucity of data for claustrophobia and fear of driving, meta-analytic effect sizes were completed on only the six anxiety disorder domains remaining following data extraction: PTSD, social phobia, arachnophobia, acrophobia, panic disorder with agoraphobia, and aviophobia.

2.4. Data analytic considerations

We used the random-effects meta-analytic model (Shaddish & Haddock, 1994). Analysis of continuous outcomes involved comparing standardized differences in means before and after VRET (Hedges & Olkin, 1985). Standardization allowed the study results to be transformed to a common scale (standard deviation units), which assisted pooling (Hedges, 1984; Hedges & Olkin, 1985). Adjustments were made to correct for upward bias of effect size estimation in small sample sizes. An unbiased estimation (Cohen's d) was calculated for each study in which the effect size is weighted by a sample-size based constant (Hedges, 1984; Hedges & Olkin, 1985). Standardized mean differences were calculated and analyzed for each study. In particular, $d = (M_h - M_c)/S$, where M_h and M_c are the mean scores on an anxiety measure before and after VRET, respectively, and S is the standard deviation for the pooled sample (Shaddish & Haddock, 1994). In studies that did not provide means and standard deviations, d values were computed from exact p, t or F values (Lipsey & Wilson, 2001). The variance for each d value was then calculated: variance $= (n_1 + n_2)/(n_1 n_2) + d^2/(2(n_1 + n_2))$, where n_1 and n_2 represent the sample sizes before and after VRET, respectively. The variance function was used to calculate a weighting factor for the unbiased effect size. We used the weighting factor to weight the unbiased effect-size estimate by its sampling error and then divided the result by the sum of the weighted factor for the unbiased effect size. The resulting weighted average composite unbiased effect-size estimate was established for each measure. Following general convention (Cohen, 1988), an effect size of 0.20 was considered a small effect, 0.50 a moderate effect, and 0.80 a large effect.

Prior to combining studies in the meta-analysis, we assessed the homogeneity of the effect size (Hedges & Olkin, 1985). Cochran's Q-statistic (Cochran, 1954) was computed by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, weighting each study's contribution in the same manner as in the meta-analysis (Hedges, 1984; Hedges & Olkin, 1985). The Q-statistic is distributed approximately as chi-square with $k-1$ degrees of freedom (k = number of studies), and tests the null hypothesis that all studies are evaluating the same effect. In general, p-values less than 0.01 for the Q-statistic are considered to indicate significant differences across studies (Lau, Ioannidis, & Schmid, 1997). After finding evidence for the presence of heterogeneity in study outcomes, subsequent pooled analyses used random-effects estimating methods

(Shaddish & Haddock, 1994). Further, we removed heterogeneous measures that may have introduced bias. To further ensure that our findings were not impacted by bias, we completed subsequent meta-analyses using random-effects models stratified by study type and for all studies combined.

2.5. Moderator variables

An attempt was made to evaluate the potential influence on anxiety and specific phobia effect sizes of several potential moderators, using categorical models. Personal characteristics such as the level of hypnotizability and absorption may act as moderators that mediate the effectiveness of VRET (Wiederhold & Wiederhold, 2000; Witmer & Singer, 1998). Additionally, virtual reality system characteristics may moderate the level of presence felt (Krijn et al., 2004a). Further, personality characteristics may also be related to successful treatment with VRET. Moderators were selected on the basis of prior research identifying these variables as candidate moderators of affective changes. For example, prior research has suggested that self-reports of presence, levels of immersion, anxiety and/or phobia duration, demographics (e.g. age, gender, and ethnicity) may influence treatment results (see Krijn et al., 2004b). An analysis was carried out to determine the influence of these moderator variables upon treatment effects.

3. Results

3.1. Literature search

The results of the literature search produced 52 studies that had evaluated anxiety and/or phobia before and after VRET. Among these studies, 21 articles met the eligibility criteria for inclusion in the meta-analysis. Table 1 lists included studies' sample size, affective domain assessed, and number of VRET sessions. Across studies the maximum combined sample size used for aggregated effect size calculations was 300 subjects.

3.2. Tests of homogeneity of variance

For all studies combined, initial assessment of homogeneity of variance revealed evidence of significant heterogeneity ($p = 0.01$). To increase homogeneity, we removed extraneous measures until homogeneity was achieved. Further, to increase the dependability of our findings, we completed subsequent meta-analyses using random-effects models stratified by study type and for all studies combined.

3.3. Mean effect sizes

The average weighted effect sizes were calculated for each of the six affective domains and an overall affective effect size (Anxiety Total). This involved combining the standardized effect sizes within each affective domain (within and across domains for Anxiety Total) into a composite-mean weighted effect size, and examining each domain's significance. Table 2 shows the average weighted effect sizes, standard error of the effect sizes, confidence limits, and percentage of variance accounted for by VRET (Table 3).

Table 1
Summary of studies included in the meta-analysis

Authors	*N*	Grouping	Sessions	Sample	Standardized assessments	Control group
Anderson, Zimand, Hodges, and Rothbaum (2005)	10	Social phobia	8	Clinical	Yes	None
Bouchard, Cote, St-Jacques, Robillard, and Renaud (2006)	11	Arachnophobia	5	Clinical	Yes	None
Choi et al. (2005)	20	Agoraphobia	6	Clinical	Yes	In vivo
Cote and Bouchard (2005)	28	Arachnophobia	7	Clinical	Yes	None
Difede, Cukor, Patt, Giosan, and Hoffman (2006)	9	PTSD	7.5	Clinical	Yes	Bibliotherapy
Emmelkamp et al. (2002)	17	Acrophobia	3	Clinical	Yes	In vivo
Emmelkamp, Bruynzeel, Drost, and van der Mast (2001)	10	Acrophobia	4	Clinical	Yes	None
Garcia-Palacios, Hoffman, Carlin, Furness, and Botella (2002)	12	Arachnophobia	4	Clinical	Yes	Waitlist
Harris, Kemmerling, and North (2002)	8	Social phobia	4	Non-clinical	Yes	Waitlist
Hoffman, Garcia-Palacios, Carlin, Furness, and Botella-Arbona (2003)	8	Arachnophobia	3	Clinical	Yes	Waitlist
Klinger et al. (2005)	18	Social phobia	12	Clinical	Yes	In vivo
Krijn et al., 2004a, 2004b	17	Acrophobia	3	Clinical	Yes	Waitlist
Maltby, Kirsch, Mayers, and Allen (2002)	20	Aviophobia	5	Clinical	Yes	Attention
Muhlberger, Herrmann, Wiedemann, Ellgring, and Pauli (2001)	15	Aviophobia	4	Clinical	Yes	Relaxation
North, North, and Coble (1996)	30	Agoraphobia	8	Unclear	No	Waitlist
Rothbaum, Hodges, Ready, Graap, and Alarcon (2001)	9	PTSD	8	Clinical	Yes	Waitlist
Rothbaum et al. (1995)	10	Acrophobia	5	Clinical	Yes	Waitlist
Rothbaum, Hodges, Smith, Lee, and Price (2000)	15	Aviophobia	4	Clinical	Yes	Waitlist
Rothbaum et al. (2006)	25	Aviophobia	4	Clinical	Yes	In vivo
Roy et al. (2003)	4	Social phobia	12	Unclear	No	Waitlist
Vincelli et al. (2003)	4	Agoraphobia	12	Clinical	Yes	Waitlist

Total $N = 300$.

3.4. Potential moderators of effect size

For clinical variables, such as presence, immersion, anxiety and/or phobia duration, demographics (e.g. age, gender, and ethnicity), it was not possible to calculate correlation coefficients because numerous studies did not report exact values, and, for some parameters, the number of studies was too small to meaningfully interpret the *r* value.

Table 2
Average random effect sizes, including the variance and confidence limits for the mean effect sizes, for the affective domains and the anxiety total

Domain	Average random effect size	Effect size variance	95% CI		*R*	%
			Lower	Upper		
PTSD	0.87	0.01	0.64	1.10	0.40	0.16
Social phobia	0.96	0.10	0.34	1.59	0.43	0.19
Arachnophobia	0.92	0.12	0.25	1.59	0.42	0.18
Acrophobia	0.93	0.06	0.44	1.43	0.42	0.18
Panic disorder with agoraphobia	1.79	0.02	1.52	2.06	0.67	0.44
Aviophobia	1.59	0.05	1.16	2.01	0.62	0.39
Anxiety Total	0.95	0.02	0.69	1.21	0.43	0.18

Note: All reported random effect sizes reflect large effects for VRET on decrease of negative affective symptoms. PTSD, post-traumatic stress disorder; %, percent of variance accounted for by VRET. The average weighted effect sizes were calculated for each of the six affective domains and an overall affective effect size (Anxiety Total). This involved combining the standardized effect sizes within each affective domain (within and across domains for Anxiety Total) into a composite-mean weighted effect size, and examining each domain's significance. Total $N = 300$.

4. Discussion

The results of this meta-analysis revealed that VRET had statistically large effects on all affective domains, as well as all anxiety/phobia groupings evaluated. These effects were of the magnitude described in the literature as large (Cohen, 1992, 1988). Thus, VRET appears effective from a clinical psychology standpoint (bearing in mind that patients in most studies were selected after consideration of a variety of inclusion and exclusion criteria, meaning this conclusion may not generalize to unselected patients).

4.1. Limitations of meta-analysis

Findings from this meta-analysis must be interpreted with caution given limitations of meta-analysis in general and data available for this analysis in particular. Meta-analysis is limited by the quality of studies included, and we attempted to address this by having fairly strict study inclusion criteria. As in any review of studies in a given area, it is possible that studies with nonsignificant results are underreported. The practice of publishing only studies with significant outcomes may create a distortion of the subject under investigation, especially if a meta-analysis is done (Rosenthal, 1979). The random-effect model was utilized in the present analysis because heterogeneity was apparent and that the random effects model tends to yield more generalizable parameter estimates.

It is important to note that, for some variables, meta-analyses were based on relatively few subjects. Whereas the effects found in arachnophobia were based upon a pooled sample of 59 patients, some other effects (e.g. PTSD) were based on fewer than 20 individuals. A further issue, by virtue of introducing possible bias to meta-analytic findings, is that when multiple studies are published by the same investigative team, it is

Table 3
A list of measures included in each affective domain

Affective group	Test	*N*	*K*	*Q*
PTSD	Clinician administered PTSD scale Impact of event scale	18	2	2.18
Social phobia	Liebowitz social anxiety scale State-trait anxiety inventory-state Personal report of communication apprehension Sheehan Sheehan incapacity scale	40	4	7.36
Arachnophobia	Fear of spider questionnaire Perceived self efficacy toward spiders	59	4	12.83
Acrophobia	Acrophobia questionnaire Attitude towards heights questionnaire	54	4	7.11
Agoraphobia	Spielberger trait anxiety inventory Anxiety sensitivity index Body sensation questionnaire Panic belief questionnaire Agoraphobic cognition questionnaire Fear questionnaire	54	3	7.34
Aviophobia	Anxiety expectancy scale Danger expectancy scale Anxiety sensitivity index Subjective units of discomfort Fear of flying inventory Questionnaire on attitudes toward flying	75	4	7.64

Note: *N*, sample size across studies for an affective grouping and *Q*, results of analyses of grouping specific homogeneity of the effect sizes (*Q*, Cochran's Q-statistic and *K*, number of studies).

not always clear whether there is overlap in the samples of different studies (i.e. follow-up studies).

A further issue for this meta-analysis, as is true of any systematic review, is deciding which trials or studies to include and which to exclude. While some researchers (e.g. Cochrane Collaboration) view the randomized trial (RCT) as the only acceptable evidence on treatment outcome, many systematic reviews are indeterminate because they include insufficient RCTs whilst they reject large numbers of non-randomized controlled studies. This is particularly true in studies of VRET, a domain where RCT methodology is limited.

Some studies meta-analyzed did not have control groups, and were not randomized clinical trials, limiting the confidence that affective enhancements were directly related to or caused by VRET. Even though we attempted to identify possible moderators of affective improvements, this was not possible because necessary information was not reported or reported in insufficient detail. This lack of information related to affective improvements and presence, immersion, anxiety and/or phobia duration, demographics (e.g. age, gender, and ethnicity) may reflect a limited range of values given the selection criteria employed by most studies. Thus, the findings of this meta-analysis may not generalize to patients with anxiety disorders in general. Similarly,

a host of other factors that could not be directly analyzed might moderate affective regulation, including differences among treatment centers in terms of beliefs about best practices concerning VRET, timing of sessions, and concurrent psychopharmacological treatment.

Caution is also invited in interpreting the clinical significance of what are statistically large affective improvements. Specifically, effect size classification is somewhat arbitrary in its distinctions between magnitudes (Cohen, 1988). Hence, while a statistical consideration of data may describe 0.80 as a large effect size, statistical and clinical significance are not synonymous (Ogles, Lunnen, & Bonesteel, 2001) and an effect size is not fully informative for clinical interpretation.

4.2. Methodological implications for future studies

Our study findings have several implications for future research concerning affective effects of VRET. The large effect sizes determined in this study suggest that in order for studies to have adequate power (above 0.80) to detect affective effect of VRET (using single group, repeated measure design, and two-tailed tests with alpha set at 0.05), they would require a minimum sample size of 30 subjects (actual power = 0.82). Obviously, this is a minimal standard, and adequate evaluation of affective effects, at least using instruments applied to anxiety disorders thus far, would ideally involve samples much larger than this. Thus, while in future small-sample studies detecting significant effects would be of interest, studies with positive findings will probably be of interest only if they are adequately powered.

Another issue is that it may behoove research groups to reach consensus regarding critical variables that should be examined as possible indicators of treatment efficacy in multi-center studies. Attempts to perform moderator analyses to identify factors that may play a role in anxiety decline were unsuccessful because mean values of potential moderator variables were too narrow in range to allow meaningful analyses or were not adequately reported. Future studies should seek uniformity in reporting in detail various patient, disorder, treatment, and VRET procedural variables. For example, it may be critical to identify the optimal type of virtual environments for treatment success (although this itself is beset by methodological controversy), percentages of patients showing changes on clinical outcome measures of a given VRET protocol, the number of patients belonging to a diagnostic group (such as specific phobia, before and after VRET), and the relationship of these factors to affective outcome. It is anticipated that such reporting will facilitate identification of factors underlying affective improvement due to VRET.

5. Conclusions

Given the currently available data, it appears that VRET is relatively effective from a psychotherapeutic standpoint in carefully selected patients. VRET can reduce anxiety and phobia symptoms. Whether the affective enhancements are directly related to VRET, or some other factor, remains to be specified, as do the clinical predictors for such improvements. The meta-analytic findings parallel qualitative reviews revealing that VRET has potential for the treatment of anxiety and several specific phobias. Further, this meta-analysis extends the existing literature through facilitation

of a better understanding of the variability and clinical significance of affective improvement subsequent to VRET. There is a need for additional well-designed and adequately powered studies investigating the affective outcomes of VRET, more extensive and uniform reporting of data, and for meta-analysis of the VRET effects on cognition, depression, and quality of life.

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