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Focus Article

Virtual reality exposure therapy for anxiety and related disorders: A meta-analysis of randomized controlled trials

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ABSTRACT

Trials of virtual reality exposure therapy (VRET) for anxiety-related disorders have proliferated in number and diversity since our previous meta-analysis that examined 13 total trials, most of which were for specific phobias (Powers & Emmelkamp, 2008). Since then, new trials have compared VRET to more diverse anxiety and related disorders including social anxiety disorder (SAD), posttraumatic stress disorder (PTSD), and panic disorder (PD) with and without agoraphobia. With the availability of this data, it is imperative to re-examine the efficacy of VRET for anxiety. A literature search for randomized controlled trials of VRET versus control or in vivo exposure yielded 30 studies with 1057 participants. Fourteen studies tested VRET for specific phobias, 8 for SAD or performance anxiety, 5 for PTSD, and 3 for PD. A random effects analysis estimated a large effect size for VRET versus waitlist ($g = 0.90$) and a medium to large effect size for VRET versus psychological placebo conditions ($g = 0.78$). A comparison of VRET and in vivo conditions did not show significantly different effect sizes ($g = -0.07$). These findings were relatively consistent across disorders. A meta-regression analysis revealed that larger sample sizes were associated with lower effect sizes in VRET versus control comparisons ($\beta = -0.007$, $p < 0.05$). These results indicate that VRET is an effective and equal medium for exposure therapy.

1. Introduction

Anxiety-related disorders (i.e., the DSM-5 anxiety disorders as well as posttraumatic stress disorder [PTSD] and obsessive compulsive disorder [OCD]) are the most prevalent class of mental disorders, with a 12-month prevalence rate of 21.3% in the United States (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). According to the American Psychological Association's Task Force for determining evidence-based treatments, exposure-based therapies are supported for the treatment of OCD, PTSD, panic disorder (PD), specific phobias, and social anxiety disorder (SAD; APA Presidential Task Force on Evidence-Based Practice, 2006). Despite demonstrable efficacy of cognitive behavioral therapy (CBT) for anxiety-related disorders (e.g., Hans & Hiller, 2013; Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012; Carpenter et al., 2018), only a minority of individuals receive this treatment (Marcks, Weisberg, & Keller, 2009). For example, in one study of therapists delivering CBT, only between 19–33% of patients treated for OCD, PTSD, SAD, or PD received in vivo exposure (Hipol & Deacon, 2013). Given this substantial treatment gap, it is imperative to consider alternative means of delivering exposure-based treatments.

Virtual reality (VR) technology offers a unique opportunity to disseminate exposure therapy. Technology is improving so that the quality of the images is better, and the cost is much lower than traditional psychotherapy (Miloff et al., 2016). In addition to being easier to disseminate, surveys indicate that many people would prefer to receive virtual reality exposure therapy (VRET) to traditional exposure therapy, with one study showing that 76% of participants chose VRET over in vivo exposure (Garcia-Palacios, Botella, Hoffman, & Fabregat, 2007). In

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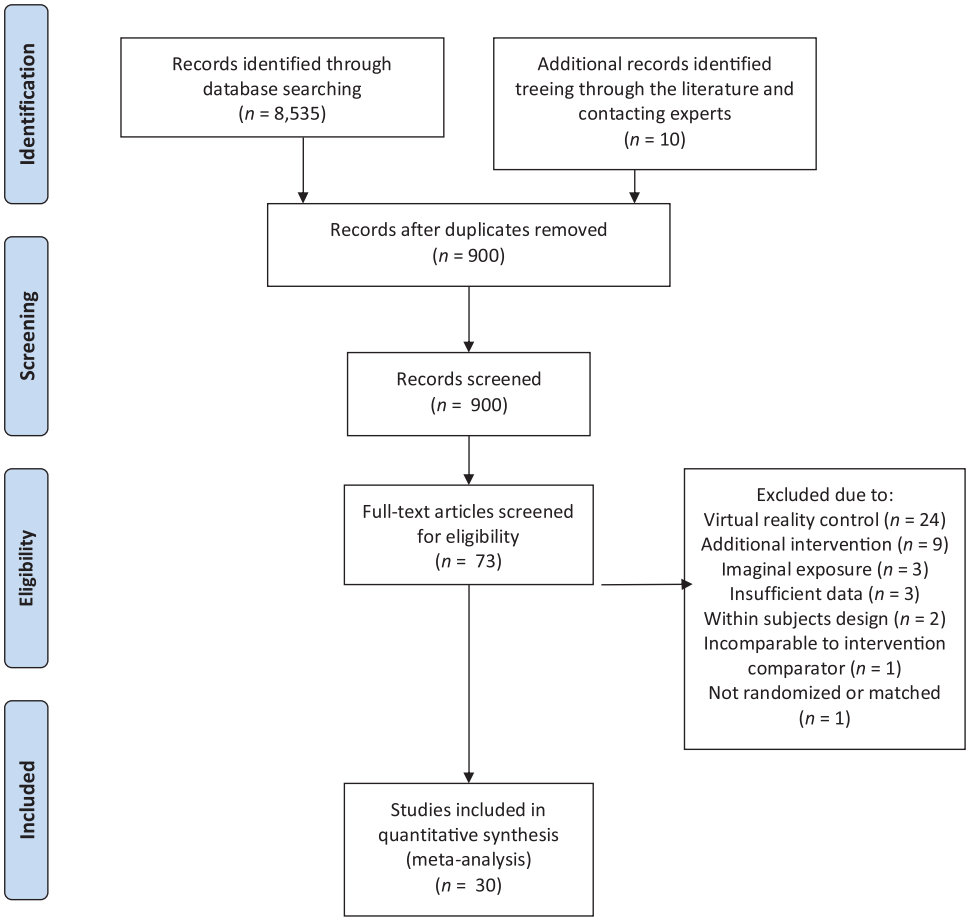

Fig. 1. Selection of studies.

a study of college students, between 81–89% of students preferred VRET to in vivo exposure therapy (Garcia-Palacios, Hoffman, Kwong See, Tsai, & Botella, 2001).

A previous meta-analysis indicated that VRET has large effect sizes relative to controls and may be more appealing to patients and easier to disseminate (Powers & Emmelkamp, 2008). In a more recent meta-analysis of VRET for specific phobias, there was no significant difference at posttreatment or follow-up between VRET and traditional in vivo exposure (Morina, Ijntema, Meyerbröker, & Emmelkamp, 2015). In addition, according to a recent individual patient data level meta-analysis, the low deterioration rate in VRET (4%) is comparable with face-to-face therapy (Fernández-Alvarez et al., in press).

These meta-analyses have primarily examined trials of VRET for specific phobias (e.g., Parsons & Rizzo, 2008). The success of VRET in treating specific phobias is now reflected in APA guidelines for empirically supported treatments, which indicate that VRET is an empirically supported treatment for fear of flight (Muhlberger, Wiedemann, & Pauli, 2003; Wiederhold et al., 2002; Rothbaum, Hodges, Smith, Lee, & Price, 2000), fear of heights (Krijn et al., 2004; Emmelkamp, Krijn, Hulsbosch, de Vries, Schuemie, & van der Mast, 2002) and animal phobias (Garcia-Palacios, Hoffman, Carlin, Furness, & Botella, 2001). However, since these guidelines were enacted, there has been a growing body of literature supporting VRET for additional disorders.

It has been 10 years since we conducted the initial meta-analysis that identified 13 studies supporting the equivalence of these of VR and in vivo modalities (Powers & Emmelkamp, 2008). During this time, 30 additional papers meeting our inclusion criteria have been published on VRET, which include a wider breadth of disorders studied and a larger number of replications. This includes VRET studies for SAD (Anderson et al., 2013; Bouchard et al., 2017; Kampmann et al., 2016; Robillard, Bouchard, Dumoulin, Guitard, & Klinger, 2010), PTSD (McLay et al., 2011; Miyahira et al., 2012; Ready, Gerardi, Backscheider, Mascaro, & Rothbaum, 2010; Reger et al., 2016), generalized anxiety disorder (Repetto et al., 2013), and panic disorder with agoraphobia (Meyerbröker, Morina, Kerkhof, & Emmelkamp, 2013; Pelissolo et al., 2012). There have also been several additional specific areas of anxiety studied, including music performance anxiety (Bissonnette, Dubé, Provencher, & Moreno Sala, 2015), public speaking anxiety (Wallach, Safir, & Bar-Zvi, 2009), school phobia (Gutiérrez-Maldonado, Magallón-Neri, Rus-Calafell, & Peñaloza-Salazar, 2009), fear of falling (Levy et al., 2016), dental phobia (Gujjar, van Wijk, Sharma-Kumar, & de Jongh, in press), and arachnophobia (Miloff et al., 2016).

The current study aimed to build off our previous work examining the effectiveness of VRET for anxiety-related disorders compared to in vivo exposure alone, CBT, and control or waitlist conditions. Specifically, we hypothesized that (1) VRET would demonstrate a large overall effect size relative to control conditions, and (2) the effect size for VRET would not be significantly different from that of in vivo exposure therapy.

2. Methods

2.1. Study selection

We selected controlled trials with random or matched assignment of VRET for anxiety-related disorders. We searched the following databases: PsychINFO 1840–2018, MEDLINE 1966–2018, and the Cochrane Central Register of Controlled Trials until 2018. The searches included the terms “virtual reality” in combination with “exposure,”

Table 1
Outcome measures.

Outcome	Measure
Domain-specific subjective distress	AES, AFA, AQ, BSQ, CAPS, DES, DFS, FAM-S, FAS, FFI, FFM, FFS, FNE, FNE-B, FOFR, FSSC-R, FSQ, FQ, LSAS, MDAS, MI, PCL-C, PDBQ – A, PDS, PDSS, PPGAS, PRCP, PRCS, QAF, SCIA, SIAS, SPS, SUDS, TRGI, VAS
Behavioral	BAT, behavioral approach, flights, speech length, speech performance
Cognitive	ACQ, ASC, ATHQ, ATPS, FAM-C, SBQ, SSPS
Psychophysiological	HR, skin conductance level
General subjective distress	ASI, BAI, BDI, BDI-II, BSI, CGI, DASS, STAI, HAD, HAM-A, SCL, SCL-90-R, SDS, STAI, WSA

ACQ: agoraphobic cognitions questionnaire; AES: anxiety expectancy scale; AFA: general fear of flying questionnaire; ASC: appraisal of social concerns; ASI: anxiety sensitivity index; ATHQ: attitudes towards height questionnaire; ATPS: attitudes toward public speaking questionnaire; AQ: acrophobia questionnaire; BAI: Beck anxiety inventory; BAT: behavioral approach test; BDI: Beck depression inventory; BDI-II: Beck depression inventory II; BSI: brief symptom inventory; BSQ: bodily sensation questionnaire; CAPS: clinician-administered PTSD scale; CGI: clinical global impression; DASS: depression anxiety stress scales; DES: danger expectancy scale; DFS: dental fear scale; FAM-C: flight anxiety modality questionnaire - cognitive; FAM-S: flight anxiety modality questionnaire - somatic; FAS: flight anxiety situations questionnaire; FFI: fear of flying inventory; FFM: fear of falling measure; FFS: fear of flying scale; FOFR: fear of flying rating; FNE: fear of negative evaluation; FNE-B: fear of negative evaluation – brief form; FQ: fear questionnaire; FSQ: fear of spiders questionnaire; FSSC-R: fear survey schedule for children -revised; HAD: hospital anxiety and depression scale; HAM-A: Hamilton anxiety rating scale; HR: heart rate; LSAS: Liebowitz social anxiety scale; MDAS: modified dental anxiety scale; MI: mobility inventory; PCL-C: PTSD checklist for civilians; PDBQ – A: personality disorder brief questionnaire - avoidant; PDS: PTSD diagnostic scale; PDSS: panic disorder severity scale; PPGAS: panic, phobia and generalized anxiety scale; PRCP: personal report of confidence as a performer; PRCS: personal report of confidence as a speaker; QAF: questionnaire on attitudes toward flying; SBQ: spider beliefs questionnaire, SCIA: social contexts inducing anxiety; SCL: symptoms checklist; SCL-90-R: symptoms checklist-90-revised; SDS: Sheehan disability scale; SIAS: social interaction anxiety scale; SPS: social phobia scale; SSPS: self-statements during public speaking; STAI: state-trait anxiety inventory; SUDS: subjective units of distress; TRGI: trauma related guilty inventory; VAS: visual analogue scale; WSA: work and social adjustment scale.

"treatment," or "therapy." We also used "cited by" search tools and searched reference sections. Lastly, we circulated a list of studies to colleagues in the field to ask if there were any outstanding trials for inclusion, including unpublished data. We limited the trials to human subjects. Studies meeting the following criteria were included: 1) at least one VRET condition, 2) random or matched assignment to conditions, and 3) either an inactive or active control group that did not use virtual reality. Authors of selected studies were contacted directly when there were insufficient data provided in the article. A total of 30 studies with a total sample size of 1057 participants met the final inclusion criteria and were included. Of these studies, 13 had been included in the previous meta-analysis (Powers & Emmelkamp, 2008) and 17 became available since that date and are now included.

The following studies were excluded for exceptional reasons: studies with a within-subjects, cross-over design (Emmelkamp, Bruynzeel, Drost, & van der Mast, 2001; Krijn, Emmelkamp, Olafsson, Bouwman et al., 2007; Krijn, Emmelkamp, Olafsson, Schuemie, & Van Der Mast, 2007); studies that combined VRET with other interventions or treatment elements such that VRET could not be evaluated independently (Baños et al., 2011; Castro et al., 2014; Muhlberger & Wiedemann, 2003; Pitti et al., 2016; Repetto et al., 2013; Triscari, Faraci, Catalisano, DöAngelo, & Urso, 2015; Vincelli et al., 2003); studies that combined VRET with a medication or pill placebo (González Lorenzo et al., 2011; Ressler et al., 2004); studies in which the VRET condition had significantly less dosage compared to an active psychological intervention comparator (Choi et al., 2005); studies that used imaginal exposure as the comparator (the imaginal exposure condition in Reger et al., 2016; Rus-Calafell, Gutiérrez-Maldonado, Botella, & Baños, 2013; Wiederhold et al., 2002) and studies in which insufficient statistical data were available and authors could not provide it (Gamito et al., 2010; Mosso et al., 2009; North, North, & Coble, 1998). See Fig. 1 for a diagram of the study selection process.

2.2. Software

All analyses were completed with the Comprehensive Meta-Analysis software version 3.3070 (Biostat, 2014).

2.3. Procedure

In addition to outcome data, the following data were collected: sample type (diagnosed/nondiagnosed), assignment (random/matched), disorder, treatment dose (number of sessions), number of participants per condition, and year of publication. Outcome measures were classified into categories: domain-specific subjective distress, behavioral, cognitive, psychophysiological, and general subjective distress (see Table 1). Analyses were conducted using a combined score for all types of measures. Treatment and control conditions were classified into four types: VRET, in vivo exposure therapy, waitlist, and other psychological control (e.g., minimal attention, informational pamphlet).

2.4. Effect size calculation

Between-group effect sizes for each study were computed using Hedge's g (Rosenthal, 1991). Hedge's g is uniquely suited to provide unbiased effect size estimates when sample sizes are small. When the necessary data were available, effect sizes were calculated directly using this formula: $g = \bar{x}_T - \bar{x}_C = s_P$, where $\bar{x}_T$ is the mean of the treatment group, $\bar{x}_C$ is the mean of comparison group, and s_P is the pooled standard deviation. When these data were not available, g was estimated using conversion equations for significance tests. A combined effect size was computed for studies using multiple outcome measures. Hedge's g may be interpreted similarly to Cohen's d (Cohen, 1988), with a cutoff for small (0.2), medium (0.5) and large (0.8) effects. The overall mean effect size for studies combined was computed using a weighted formula, $\bar{g} = \Sigma w_j g_j / \Sigma w_j$, where w_j is the weight for each study and g_j is the effect size for each study. The random effects analysis was used, which assumes that the studies included are only a sample of the entire population of studies.

3. Results

Thirty studies met criteria for inclusion with a total of 1057 participants. Twenty studies used a waitlist control, 6 studies used another psychological control, and 14 studies used an in vivo exposure comparison. Conditions categorized as psychological controls included relaxation (Muhlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001), an attention control (Maltby, Kirsch, Mayers, & Allen, 2002), an information pamphlet (Gujjar et al., 2018), present-centered therapy (Ready et al., 2010), treatment as usual (McLay et al., 2011), and minimal attention (Miyahira et al., 2012). Fourteen studies tested VRET for specific phobias, 8 for SAD or performance anxiety, 5 for PTSD, and 3 for PD. Analyses were completed using domain-specific outcomes, except for the effect sizes reported for other outcome types specifically. Study characteristics are presented in Table 2.

3.1. Hypothesis 1: Virtual reality exposure therapy versus control conditions

Using a Hedge's g random effects analysis, we found that VRET had

Table 2
Overview of included studies by type of disorder.

Study	Control	n[a]	No. of sessions	Primary outcome measures	Additional outcome measures	Primary outcome Hedges's g
Specific Phobia						
Rothbaum et al. (1995)	Waitlist	17	8	AQ	ATHQ	2.61
Rothbaum, Hodges, Smith, Lee, and Price (2000)	Waitlist	30	8	FFI, QAF		0.59
	In vivo	30	8	FFI, QAF		−0.57
Muhlberger et al. (2001)	Relaxation	28	1	AES, AFA, DES, FFS, SUDS	ASI, BAT HR, BAT, SCL	0.57
Garcia-Palacios, Hoffman, Carlin, Furness, and Botella (2002)	Waitlist	23	4	FSQ, SUDS	BAT	1.62
Maltby, Kirsch, Mayers, and Allen (2002)	Attention Control	43	5	FAM-somatic, FAS – anticipatory, FAS – generalized, FAS – in-flight	FAM-cognitive	0.73
Emmelkamp et al. (2002)	In vivo	33	3	AQ-anxiety, AQ-avoidance	ATHQ, BAT	0.06
Krijn et al. (2004)	Waitlist	28	3	AQ-anxiety, AQ-avoidance	ATHQ, BAT	1.10
Rothbaum et al. (2006)	In vivo	58	4	FFI, QAF		0.18
	Waitlist	54	4	FFI, QAF		0.75
Krijn, Emmelkamp, Olafsson, Bouwman et al. (2007)	Waitlist	49	4	FAM, FAS		0.48
	In vivo	53	4	FAM, FAS		−0.06
Gutiérrez-Maldonado et al. (2009)	Waitlist	36	8	FSSC-R		0.20
Michaliszyn, Marchand, Bouchard, Martel, and Poirier-Bisson (2010)	In vivo	32	8	FSQ	BAT, SBQ	−0.27
Levy et al. (2016)	Waitlist	16	12	FFM	BDI, SDS-family, SDS-social, STAI-state, STAI-trait	1.42
Gujjar et al. (2018)	Information pamphlet	30	1	DFS, MDAS, SUDS, VAS	BAT	2.19
Minns et al. (2018)	Waitlist	77	1	Anticipatory fear, FSQ, peak BAT fear	BAT	0.77
Social Anxiety						
Harris, Kemmerling, and North (2002)	Waitlist	14	4	LSAS, PRCS	ATPS, HR, STAI	0.91
Klinger et al. (2005)	In vivo	36	12	LSAS, SCIA	HAD – anxiety, HAD - depression, SDS- family, SDS-social, SDS-work	0.37
Robillard, Bouchard, Dumoulin, Guitard, and Klinger (2010)	Waitlist	29	16	FNE, LSAS, SPS	ASC-consequences, ASC-probability, BDI-II, STAI-trait	1.53
	In vivo	30	16	FNE, LSAS, SPS	ASC-consequences, ASC-probability, BDI-II, STAI-trait	0.61
Anderson et al. (2013)	In vivo	50	8	FNE-brief, PRCS, peak anxiety during speech	Speech duration	−0.61
	Waitlist	50	8	FNE-brief, PRCS, peak anxiety during speech	Speech duration	0.76
Kampmann et al. (2016)	In vivo	32	10	FNE-brief, LSAS, PDBQ-A	DASS depression, DASS stress, DASS anxiety, speech duration	−0.55
	Waitlist	31	10	FNE-brief, LSAS, PDBQ-A	DASS depression, DASS stress, DASS anxiety, speech duration	0.61
Bouchard et al. (2017)	In vivo	39	14	FNE, LSAS, SIAS, SPS	BAT, BDI-II	0.56
	Waitlist	37	14	FNE, LSAS, SIAS, SPS	BAT, BDI-II	1.53
Performance Anxiety						
Wallach, Safir, and Bar-Zvi (2009)	In vivo	58	12	FNE, LSAS-avoidance, LSAS-fear	SSPS	0.08
	Waitlist	58	12	FNE, LSAS-avoidance, LSAS-fear	SSPS	1.14
Bissonnette, Dubé, Provencher, and Moreno Sala (2015)	No intervention	17	6	PRCP	STAI	0.14
PTSD						
Difede et al. (2007)	Waitlist	18	7	CAPS	BDI, BSI	1.18
Ready, Gerardi, Backscheider, Mascaro, and Rothbaum (2010)	Present-centered therapy	10	10	CAPS	BDI	0.10
McLay et al. (2011)	TAU[b]	20	9	CAPS		0.67
Miyahira et al. (2012)	Minimal attention	22	10	CAPS, PDS, TRGI	BDI-II	0.34
Reger et al. (2016)	Waitlist	77	10	CAPS, PCL-C	BAI, BDI-II	0.59
Panic Disorder w/ or w/o Agoraphobia						
Botella et al. (2007)	In vivo	24	9	ASI, avoidance of target, fear of target, belief of fear, FQ-agoraphobia, PDSS	BDI	0.23

(*continued on next page*)

Table 2 (*continued*)

Study	Control	*n*[a]	No. of sessions	Primary outcome measures	Additional outcome measures	Primary outcome Hedges's *g*
	Waitlist	25	9	ASI, avoidance of target, fear of target, belief of fear, FQ-agoraphobia, PDSS	BDI	1.61
Panic Disorder w/ Agoraphobia						
Pelissolo et al., (2012)	In vivo	60	12	FQ – agoraphobia, PDSS, PPGAS	ACQ, BDI, FQ – anxiety depression, HAM-A, SDS, STAI-trait, STAI-state, WSA	−0.30
Meyerbröker, Morina, Kerkhof, and Emmelkamp (2013)	Waitlist	40	10	BSQ, MI-alone, PDSS	ACQ	0.54
	In vivo	46	10	BSQ, MI-alone, PDSS	ACQ	−0.51

ACQ: agoraphobic cognitions questionnaire; AES: anxiety expectancy scale; AFA: general fear of flying questionnaire; ASC: appraisal of social concerns; ASI: anxiety sensitivity index; ATHQ: attitudes towards height questionnaire; ATPS: attitudes toward public speaking questionnaire; AQ: acrophobia questionnaire; BAI: Beck anxiety inventory; BAT: behavioral approach test; BDI: Beck depression inventory; BDI-II: Beck depression inventory II; BSI: brief symptom inventory; BSQ: bodily sensation questionnaire; CAPS: clinician-administered PTSD scale; CGI: clinical global impression; DASS: depression anxiety stress scales; DES: danger expectancy scale; DFS: dental fear scale; FAM: flight anxiety modality questionnaire; FAS: flight anxiety situations questionnaire; FFI: fear of flying inventory; FFM: fear of falling measure; FFS: fear of flying scale; FOFR: fear of flying rating; FNE: fear of negative evaluation; FQ: fear questionnaire; FSQ: fear of spiders questionnaire; FSSC-R: fear survey schedule for children -revised; HAD: hospital anxiety and depression scale; HAM-A: Hamilton anxiety rating scale; HR: heart rate; LSAS: Liebowitz social anxiety scale; MDAS: modified dental anxiety scale; MI: mobility inventory; PCL-C: PTSD checklist for civilians; PDBQ – A: personality disorder brief questionnaire - avoidant; PDS: PTSD diagnostic scale; PDSS: panic disorder severity scale; PPGAS: panic, phobia and generalized anxiety scale; PRCP: personal report of confidence as a performer; PRCS: personal report of confidence as a speaker; QAF: questionnaire on attitudes toward flying; SBQ: spider beliefs questionnaire; SCIA: social contexts inducing anxiety; SCL: symptoms checklist; SCL-90-R: symptoms checklist-90-revised; SDS: Sheehand disability scale; SIAS: social interaction anxiety scale; SPS: social phobia scale; SSPS: self-statements during public speaking; STAI: state-trait anxiety inventory; SUDS: subjective units of distress (during BAT or exposure); TRGI: trauma related guilty inventory; VAS: visual analogue scale (for dental fear); WSA: work and social adjustment scale.

[a] *n* represents the number of participants included in each comparison.

[b] The treatment as usual (TAU) condition in McLay et al. (2011), was not prescribed an intervention but was able to receive services including cognitive processing therapy, prolonged exposure, group therapy, etc.

Study name	Outcome	Hedges's g	Comparison	Standard error	Time point	Variance	Lower limit	Upper limit	Z-Value	p-Value
Anderson et al., 2013	Combined	0.757	VRE vs WL	0.292	Post	0.085	0.186	1.329	2.597	0.009
Bissonnette et al., 2015	PRCP	0.140	VRET vs Control	0.462	Post	0.213	-0.765	1.045	0.303	0.762
Botella et al., 2007	Combined	1.612	VR vs WL	0.453	Post	0.205	0.723	2.500	3.556	0.000
Bouchard et al., 2017	Combined	1.526	VR vs WL	0.369	Post	0.136	0.803	2.250	4.134	0.000
Difede et al., 2007	CAPS	1.183	VR vs WL	0.493	Post	0.243	0.217	2.149	2.400	0.016
Garcia-Palacios et al., 2002	Combined	1.616	VR vs WL	0.474	Post	0.225	0.686	2.545	3.408	0.001
Gujjar et al. 2018	Combined	2.185	VRET vs Information pamphlet	0.455	Post	0.207	1.293	3.077	4.800	0.000
Gutierrez-Maldonado et al., 2009	FSSC-R	0.197	VR vs WL	0.327	Post	0.107	-0.443	0.838	0.603	0.546
Harris, Kemmerling, & North, 2002	Combined	0.914	VR vs WL	0.543	Post	0.295	-0.150	1.978	1.683	0.092
Kampmann et al., 2016	Combined	0.607	VR vs WL	0.359	Post	0.129	-0.096	1.310	1.691	0.091
Krijn et al., 2004	Combined	1.099	VR vs WL	0.403	Post	0.163	0.308	1.889	2.724	0.006
Krijn et al., 2007	Combined	0.481	VR vs WL	0.293	Post	0.086	-0.093	1.054	1.643	0.100
Levy et al., 2016	FFM	1.421	VR vs WL	0.539	Post	0.290	0.365	2.477	2.638	0.008
Maltby et al., 2002	Combined	0.728	VR vs Attention control	0.312	Post	0.097	0.118	1.339	2.338	0.019
McLay et al., 2011	CAPS	0.674	VR vs TAU	0.441	Post	0.195	-0.191	1.539	1.527	0.127
Meyerbroeker et al., 2013	Combined	0.537	VR vs WL	0.330	Post	0.109	-0.111	1.184	1.625	0.104
Minns et al., 2018	Combined	0.773	VRET vs WL	0.234	Post	0.055	0.314	1.232	3.300	0.001
Miyahira et al., 2012	Combined	0.340	VR vs Minimal attention	0.417	Post	0.173	-0.476	1.156	0.816	0.414
Muhlberger et al., 2001	Combined	0.573	VR vs Relaxation	0.379	Post	0.144	-0.171	1.316	1.510	0.131
Ready et al., 2010	CAPS	0.098	VRET vs Present-centered therapy	0.597	Post	0.356	-1.072	1.268	0.164	0.870
Reger et al., 2016	Combined	0.586	VR vs WL	0.236	Post	0.056	0.123	1.049	2.479	0.013
Robillard et al., 2010	Combined	1.527	CBT-VR vs WL	0.414	Post	0.172	0.715	2.340	3.687	0.000
Rothbaum et al., 1995	AQ-Total	2.609	VR vs WL	0.647	Post	0.419	1.340	3.877	4.031	0.000
Rothbaum et al., 2000	Combined	0.588	VR vs WL	0.364	Post	0.133	-0.126	1.302	1.613	0.107
Rothbaum et al., 2006	Combined	0.751	VR vs WL	0.279	Post	0.078	0.204	1.297	2.693	0.007
Wallach et al., 2009	Combined	1.143	VRCBT vs WL	0.291	Post	0.085	0.573	1.713	3.929	0.000
		0.879		0.099		0.010	0.685	1.073	8.873	0.000

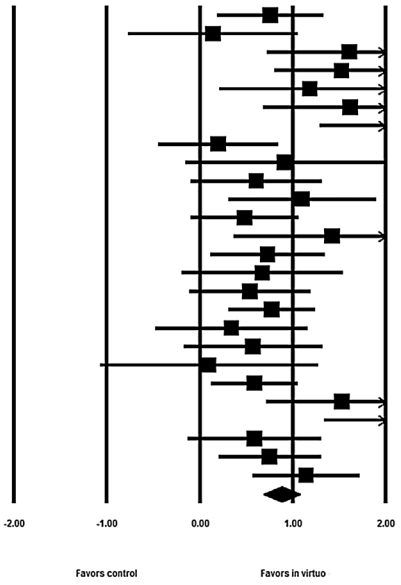

Fig. 2. Forest plot of VRET vs. waitlist and control comparisons.

Study name	Outcome	Hedges's g	Comparison	Standard error	Time point	Variance	Lower limit	Upper limit	Z-Value	p-Value
Anderson et al., 2013	Combined	-0.612	VRE vs EGT	0.286	Post	0.082	-1.174	-0.051	-2.137	0.033
Botella et al., 2007	Combined	0.229	VR vs in vivo	0.399	Post	0.159	-0.553	1.010	0.574	0.566
Bouchard et al., 2017	Combined	0.557	VR vs in vivo	0.323	Post	0.104	-0.076	1.190	1.724	0.085
Emmelkamp et al., 2002	Combined	0.063	VR vs in vivo	0.340	Post	0.116	-0.604	0.730	0.185	0.854
Kampmann et al., 2016	Combined	-0.549	VR vs in vivo	0.353	Post	0.125	-1.241	0.144	-1.553	0.120
Klinger et al., 2005	Combined	0.371	VR vs in vivo	0.329	Post	0.108	-0.274	1.015	1.127	0.260
Krijn et al., 2007	Combined	-0.056	VR vs in vivo	0.273	Post	0.075	-0.591	0.479	-0.206	0.837
Meyerbroeker et al., 2013	Combined	-0.514	VRET vs in vivo	0.298	Post	0.089	-1.098	0.071	-1.723	0.085
Michaliszyn et al., 2010	FSQ-F	-0.268	VRET vs in vivo	0.346	Post	0.120	-0.947	0.410	-0.775	0.438
Pelissolo et al., 2012	Combined	-0.295	VRET vs CBT	0.257	Post	0.066	-0.798	0.208	-1.151	0.250
Robillard et al., 2010	Combined	0.613	CBT-VR vs CBT	0.366	Post	0.134	-0.105	1.330	1.672	0.094
Rothbaum et al., 2000	Combined	-0.568	VR vs in vivo	0.363	Post	0.132	-1.280	0.143	-1.566	0.117
Rothbaum et al., 2006	Combined	0.181	VR vs in vivo	0.260	Post	0.068	-0.329	0.691	0.695	0.487
Wallach et al., 2009	Combined	0.076	VRCBT vs CBT	0.259	Post	0.067	-0.433	0.584	0.292	0.770
		-0.065		0.108		0.012	-0.276	0.146	-0.607	0.544

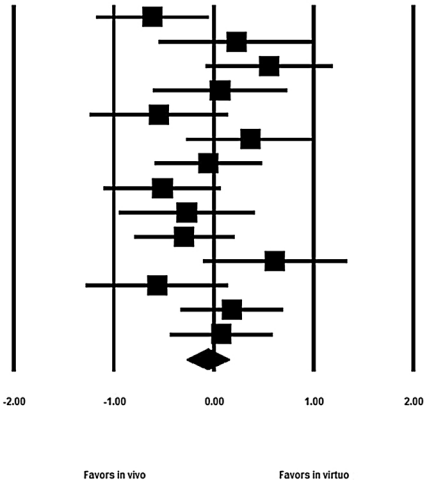

Fig. 3. Forest plot of VRET vs. in vivo comparisons.

an overall large effect size compared to waitlist and control conditions (g = 0.88, SE = 0.10, 95% CI: 0.69–1.07). When considered separately, VRET had medium to large effect size compared to psychological control conditions (g = 0.78, SE = 0.27, 95% CI: 0.25–1.31) and a large effect compared to waitlist conditions (g = 0.90, SE = 0.11, 95% CI: 0.69–1.11). At follow-up, results were maintained (n = 4; g = 0.90, SE = 0.48, 95% CI: −0.05 to 1.85). A forest plot of VRET versus control conditions at posttreatment is presented in Fig. 2.

For other types of outcome measures, VRET had a large effect versus waitlist and psychological controls on behavioral outcomes (g = 0.87, SE = 0.19, 95% CI: 0.49–1.25), a large effect on cognitive outcomes (g = 1.15, SE = 0.24, 95% CI: 0.68–1.63), a medium effect on psychophysiological outcomes (g = 0.64, SE = 0.42, 95% CI: −0.19 to 1.46), and a small to medium effect on measures of general subjective distress (g = 0.49, SE = 0.11, 95% CI: 0.27–0.71).

3.2. Hypothesis 2: Virtual reality exposure will not be significantly different from in vivo exposure

Using a Hedge's g random effects analysis, we compared VRET to in vivo exposure conditions. We obtained a mean overall effect size of Hedge's g = −0.07 (SE = 0.11, 95% CI: −0.28 to 0.15), indicating a small nonsignificant effect in favor of in vivo conditions. At follow-up, there was a small nonsignificant effect in favor of in vivo conditions (n = 7; g = -0.22, SE = 0.22, 95% CI: −0.65 to 0.22). A forest plot of VRET versus in vivo conditions at posttreatment is presented in Fig. 3.

For other types of outcome measures, there was a small nonsignificant effect in favor of in vivo conditions on behavioral measures (g = −0.11, SE = 0.17, 95% CI: −0.44 to 0.23) and a small nonsignificant effect on cognitive measures (g = −0.01, SE = 0.12, 95% CI: −0.25 to 0.23). There was a small nonsignificant effect in favor of in virtuo conditions on measures of general distress (g = 0.01, SE = 0.13, 95% CI: −0.25 to 0.27). No data were available for

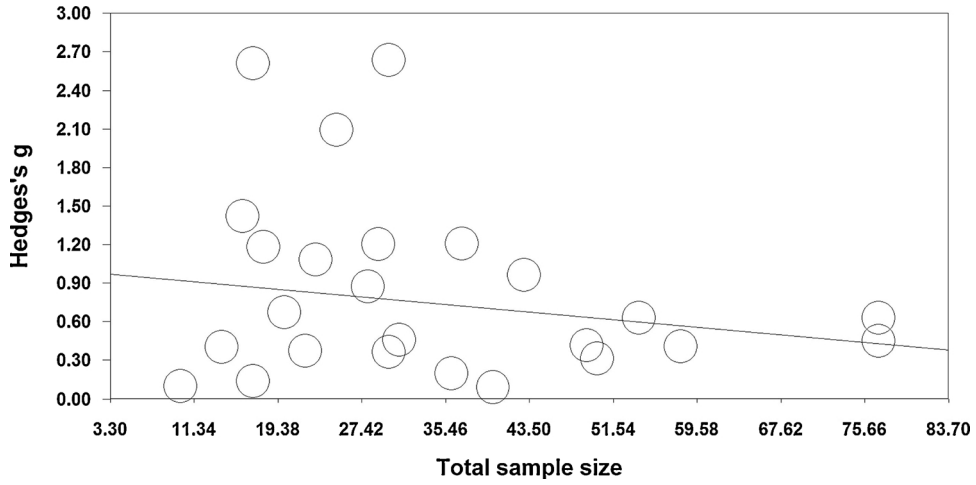

Fig. 4. Meta-regression of total sample size on Hedge's *g* for control and waitlist comparisons.

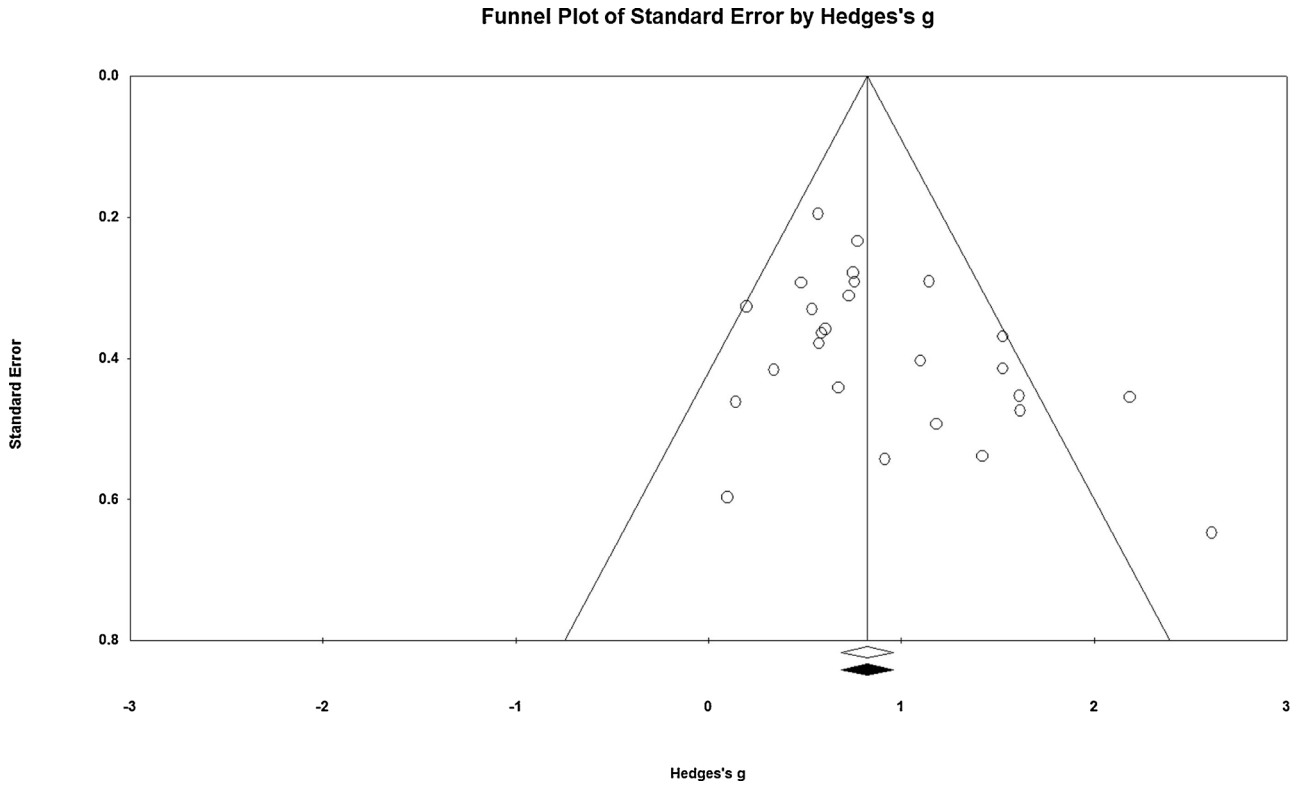

Fig. 5. Funnel plot for control and waitlist comparisons.

psychophysiological outcomes within in vivo and in virtuo comparisons.

3.3. By disorder

3.3.1. Specific phobias

The pooled effect size for 12 studies comparing VRET to psychological placebo or waitlist conditions for specific phobias yielded a large effect size for VRET ($g = 0.95$, SE = 0.17, 95% CI: 0.63–1.28). The pooled effect size for 5 studies comparing VRET to in vivo exposure for specific phobias showed a small nonsignificant effect in favor of in vivo conditions ($g = -0.08$, SE = 0.14, 95% CI: −0.35 to 0.19).

3.3.2. Social anxiety disorder and performance anxiety

The pooled effect size for 7 studies comparing VRET to psychological placebo or waitlist conditions for SAD and performance anxiety showed a large effect size for VRET ($g = 0.97$, SE = 0.18, 95% CI: 0.62–1.31). The pooled effect size for 6 studies comparing VRET to in vivo exposure for SAD and performance anxiety a small nonsignificant effect in favor of virtuo conditions ($g = 0.06$, SE = 0.22, 95% CI: −0.36 to 0.49).

3.3.3. Posttraumatic stress disorder

The pooled effect size for 5 studies comparing VRET to psychological placebo or waitlist conditions for PTSD yielded a medium effect size for VRET ($g = 0.59$, SE = 0.17, 95% CI: 0.26 −0.92). There were no VRET versus in vivo exposure studies for PTSD.

3.3.4. Panic disorder

The 2 studies that compared VRET to psychological placebo or

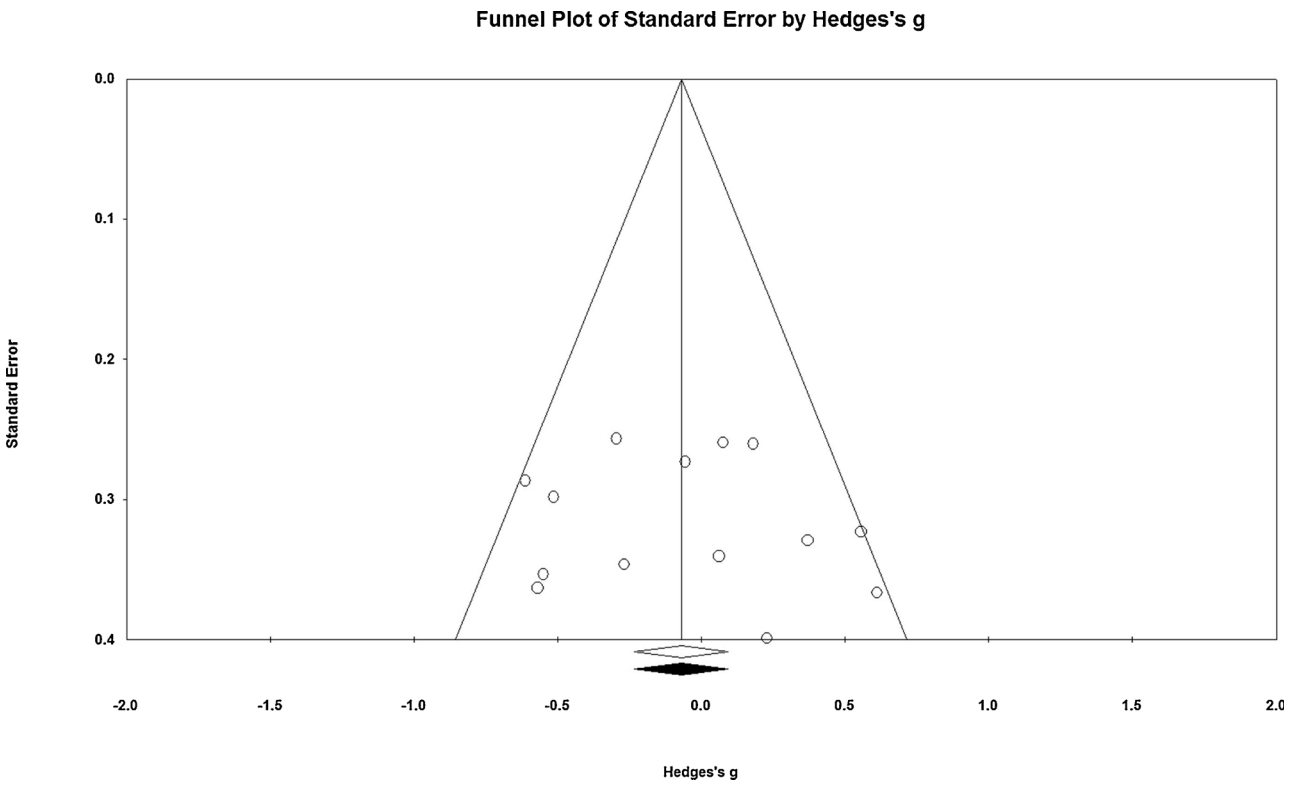

Fig. 6. Funnel plot for in vivo comparisons.

waitlist for PD showed a large effect size for VRET ($g = 1.03$, SE = 0.54, 95% CI: −0.02 to 2.08). The 3 studies that compared VRET to in vivo exposure for PD showed a small nonsignificant effect in favor of in vivo conditions ($g = -0.26$, SE = 0.19, 95% CI: −0.63 to 0.10).

3.4. Moderators

Because effect sizes of VRET versus control and VRET versus in vivo exposure are not comparable, moderator analyses were conducted separately. Both types of comparisons had sufficient heterogeneity to conduct moderator analyses ($I^2 = 45.34$ and $I^2 = 39.85$, respectively). A meta-regression analysis showed that larger total sample size was associated with lower study effect size in VRET versus control conditions ($\beta = -0.005$, $p < 0.05$) but not with VRET and in vivo comparisons ($p = 0.70$). A graph of sample size and effect size in control conditions is presented in Fig. 4. There was no effect for the number of treatment sessions in either VRET versus control ($p = 0.87$) or in vivo comparisons ($p = 0.67$). Publication year did not significantly predict effect size in control conditions ($p = 0.62$) or VRET versus in vivo comparisons ($p = 0.20$).

3.5. Publication bias

The "file-drawer problem" (Rosenthal, 1991) refers to the possibility that the literature may be biased by studies that had non-significant results and were therefore not published. This would lead a meta-analysis to overestimate the true effect size of a phenomenon.

We used a funnel plot asymmetry test to detect publication bias. Because effect sizes of VRET versus control and VRET versus in vivo exposure are not comparable, funnel plots were generated separately. A funnel plot of standard error and effect size for VRET versus control comparisons revealed some funnel plot asymmetry (Fig. 5). The Duval and Tweedie (2000) trim and fill procedure did not impute any studies and did not adjust the effect size. A funnel plot of standard error and effect size within VRET and in vivo comparisons did not reveal asymmetry, and the Duval and Tweedie (2000) trim and fill procedure did not impute any studies or adjust the effect size (Fig. 6).

4. Discussion

This meta-analysis of 30 VRET trials (participants $N = 1057$) supported the study hypotheses. Consistent with hypothesis 1, VRET showed a large effect size compared to waitlist conditions and a medium to large effect size compared to psychological controls. Consistent with hypothesis 2, VRET was not significantly more or less effective than in vivo exposure. An analysis across each disorder showed that these effect sizes were relatively consistent.

These findings differ somewhat from the previous meta-analysis (Powers & Emmelkamp, 2008). First, the effect size for VRET versus control conditions was somewhat weaker, with a previous estimate of Hedge's $g = 1.08$ versus the current $g = 0.88$. Second, the previous meta-analysis found a significant small effect size favoring VRET ($g = 0.34$) whereas the current meta-analysis found a small non-significant effect in favor of in vivo conditions ($g = -0.07$). The previous meta-analysis included a smaller number of trials (5 in vivo comparisons and 11 control comparisons) and thus, the previous conclusions may have been influenced underpowered studies.

Despite the differences with the previous meta-analysis, there is consensus between the two that VRET is effective for anxiety-related disorders and is not inferior to in vivo exposure. Given that some survey studies have indicated a preference for VRET over in vivo exposure (Garcia-Palacios et al., 2001, 2007), VRET should be considered both an attractive and effective clinical tool.

Interestingly, our findings are similar to a recent meta-analysis on 64 trials of internet-delivered CBT for anxiety and depression (Andrews et al., 2018), which found an overall large effect size for internet-delivered CBT ($g = 0.80$) and equal effectiveness with face-to-face CBT. In addition, these results generally seem to be maintained at follow-up (Andersson, Rozental, Shafran, & Carlbring, 2018), as were the results in the present meta-analysis. It seems that, across the board,

technologically based delivery of clinical tools is proving its value, and even equality to traditional treatment (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). This is important to making evidence-based treatment more accessible to those who are unable (e.g., due to mobility or geographic limitations) or unwilling (e.g., due to perceived stigmatization) to receive in-person treatment.

5. Limitations

These findings do, however, need to be considered in the context of several limitations. Most notably, this meta-analysis of VRET for anxiety-related disorders is limited by the number of trials for many diagnoses. With no studies meeting study criteria for GAD or OCD, it is still too early to draw conclusions about the efficacy of VRET for these clinical domains. Likewise, the inclusion and exclusion of trials present a number of important considerations. First, we did not require that participants were diagnosed with an anxiety disorder ($n = 9$ trials with nondiagnosed participants; although many of the studies without diagnosed participants screened for clinical elevations on questionnaires). While this allowed for greater quantity in the analysis, the applications for clinical settings are clearer when conclusions can be drawn from diagnosed samples. Second, in order to preserve homogeneity in the sample, a number of conditions and trials had to be excluded for exceptional reasons (e.g., VRET combined with another intervention outside of traditional CBT techniques, VRET compared to imaginal exposure). This necessity negated the inclusion of a number of VRET trials; for example, one study did use a VRET intervention for GAD (Repetto et al., 2013), but used progressive muscle relaxation and biofeedback in conjunction with exposure. Additionally, a large number of trials used non-exposure VR conditions as a control. While a great deal more data on VRET for anxiety-related conditions would be available with the inclusion of these trials, the absence of a non-VR control condition makes it impossible to parse the effectiveness of VR as a medium for exposure therapy. Lastly, this analysis did not use an index for study quality or risk of bias, and so was not able to test for quality or bias as moderators.

6. Conclusion

To conclude, this meta-analysis indicates that, for a number of the anxiety-related disorders, VRET has a large effect size compared to control conditions and an equal effect size to that of in vivo exposure. These results were consistent for different disorders, with a medium or large effect size for VRET compared to controls for specific phobias, SAD and performance anxiety, PTSD, and PD. In cases where VRET is preferable or more accessible, VRET can be considered an acceptable and efficacious alternative to in vivo exposure for the treatment of anxiety-related disorders.

Author notes

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from various book publishers.

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