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Threat Reappraisal as a Mediator of Symptom Change in Cognitive-Behavioral Treatment of Anxiety Disorders: A Systematic Review

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Abstract

Objective—Identifying mediators of therapeutic change is important to the development of interventions and augmentation strategies. Threat reappraisal is considered a key mediator underlying the effects of cognitive-behavioral therapy for anxiety disorders. The present study systematically reviewed the evidence for the threat reappraisal mediation hypothesis.

Method—In our review we included studies that: (1) investigated the threat reappraisal mediation hypothesis; (2) included adults with an anxiety disorder diagnosis; (3) employed a longitudinal design; and (4) did not report on previously published findings (to avoid the inclusion of multiple reports of the same data). After data extraction, we made review-specific quality judgments for each study using the following *a priori* criteria informed by mediation theory: (1) demonstrated statistical mediation; (2) demonstrated that CBT caused threat reappraisal; (3) demonstrated that threat reappraisal caused anxiety reduction; and (4) demonstrated specificity of the threat reappraisal-anxiety reduction relation.

Results—Of the 2,296 studies we identified, 25 met inclusion criteria. Of these studies, 56% tested and 52% established statistical mediation, 52% tested and 28% established CBT as a cause of threat reappraisal, 28% tested and 24% established threat reappraisal as a cause of anxiety reduction, and 44% tested and 36% established specificity of the threat reappraisal-anxiety reduction relation.

Conclusions—While threat reappraisal is related to anxiety symptom improvement with CBT, there are few extant studies that meet most of the criteria necessary to conclusively demonstrate that it *causes* symptom improvement in CBT and that it is not a proxy for other third variables. Recommendations for future research in this area are discussed.

Keywords

Anxiety disorders; cognitive-behavioral treatment; mediation; treatment mechanisms; systematic review

The last three decades have seen a tremendous amount of research focusing on the development of cognitive behavioral treatments (CBT) for the anxiety disorders. These efforts have paid off; CBT has demonstrated clear efficacy for the anxiety disorders (Barlow, Gorman, Shear, & Woods, 2000; Borkovec & Costello, 1993; Bryant, Moulds, Guthrie, & Nixon, 2005; Davidson et al., 2004; Foa et al., 2005; Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010; Powers, Sigmarsson, & Emmelkamp, 2008; Wolitzky-Taylor, Horowitz, Powers, & Telch, 2008), offering clinically meaningful advantages over

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psychological placebo conditions (Hofmann & Smits, 2008), and showing improvements in symptoms comparable to established pharmacotherapies (Norton & Price, 2007; Otto, Smits, & Reese, 2004). Although efficacious for the treatment of anxiety disorders, many patients who receive CBT either fail to respond or continue to experience residual symptoms following treatment discontinuation (Barlow et al., 2000; Borkovec & Costello, 1993; Davidson et al., 2004; Foa et al., 2005). For example, large clinical trials of CBT efficacy for the various anxiety disorders have yielded non-response rates up to 49% for social anxiety disorder (Davidson et al., 2004), 38% for obsessive-compulsive disorder (Foa et al., 2005), and 36% for panic disorder (Barlow et al., 2000). Accordingly, the agenda for CBT research has shifted to the development of augmentation strategies to enhance the effectiveness of CBT.

Identifying Mediators and Mechanisms of Therapeutic Change

Understanding of the mechanisms that govern anxiety symptom reduction achieved with CBT is crucial to developing effective augmentation strategies. Indeed, without knowing what leads to therapeutic change, it is difficult to identify strategies that may optimize CBT outcomes (Kazdin, 2007; Kraemer, Wilson, Fairburn, & Agras, 2002). Kazdin (2007) has proposed that identifying a mediator – i.e., an intervening variable that accounts for the effect of an independent variable (CBT) on a dependent variable (anxiety symptom severity) - is a first and key step in understanding treatment mechanisms, which he defines as explanations of why or how changes occur. The aim of this paper is to systematically review the evidence for one of the putative mediators underlying the efficacy of CBT for anxiety disorders, namely threat reappraisal.

Threat Reappraisal Mediation Hypothesis

While recognizing the role of automatic processes in anxiety disorders (e.g., preconscious attentional threat bias, inhibitory processing of safety cues; Beck, Emery, & Greenberg, 1985; Clark & Beck, 2010; Mogg & Bradley, 1998), theories forming the basis of CBT have tended to emphasize the importance of conscious cognitive processes in the maintenance of anxiety disorders (e.g., Clark & Beck, 2010; Dodson & Dozois, 2000). Among other cognitive misappraisals (e.g., elevated personal vulnerability, perceived inability to cope, downgraded estimates of safety), exaggerated appraisal of threat figures as a core (faulty) conscious cognitive process in these cognitive-behavioral accounts of anxiety disorders. Exaggerated threat appraisal is manifested by a tendency to overestimate the likelihood of harm (i.e., likelihood bias) and/or the negative consequences of anticipated harm (i.e., cost bias; cf. Clark & Beck, 2010). Panic disorder, for example, is thought to be maintained by exaggerated beliefs that panic and related bodily sensations (e.g., heart pounding, rapid breathing) will result in physical (e.g., dying), social (e.g., embarrassment) or mental (e.g., losing control) harm (Clark, 1986). Similarly, the belief that showing visible signs of anxiety in social interaction or performance situations will result in social rejection is thought to operate prominently in the maintenance of social anxiety disorder (Clark & Wells, 1995; Rapee & Heimberg, 1997). Especially when perceived self-efficacy is low, these false threat appraisals engender avoidance or escape, which, despite offering immediate relief of anxiety, is thought to interfere with the process of effectively reappraising threat, thereby creating a vicious cycle (Beck et al., 1985; Clark & Beck, 2010).

In order to disrupt this vicious cycle, CBT protocols for the anxiety disorders have traditionally set the modification of faulty threat appraisals as one of the primary targets. To this end, CBT protocols typically involve a combination of interventions, including psychoeducation regarding the adaptive nature of anxiety and the factors that maintain pathological anxiety (i.e., describing exaggerated threat appraisal as the source of

pathological anxiety), cognitive restructuring to identify and correct erroneous threat appraisals, and exposure exercises to provide disconfirming evidence regarding threat perceptions or to reestablish a sense of safety around feared stimuli (Clark & Beck, 2010; Otto, Smits, & Reese, 2004). Based on the model and corresponding therapeutic interventions, it has been hypothesized that threat reappraisal accounts, at least in part, for the positive effects of CBT on anxiety symptoms. Evidence supporting this mediation hypothesis would encourage the development of augmentation strategies that can further facilitate threat reappraisal during CBT. Conversely, if threat reappraisal is minimally important for the reduction of anxiety symptoms during CBT, refocusing some CBT strategies away from threat reappraisal and toward other important mechanisms may add to its effectiveness.

Despite growing research on the threat reappraisal mediation hypothesis (Hofmann, 2008), a published review of this research does not exist at the time of this writing. Filling this gap, the objective of the present article is to examine the state-of-the-science on the threat reappraisal mediation hypothesis. In addition to reviewing the findings, we will appraise the methodology used in extant research. As such, this systematic review may not only directly guide research on treatment development, but also help set an agenda for future research on the threat mediation hypothesis.

Framework for Evaluating the Evidence for the Threat Reappraisal Mediation Hypothesis

There is considerable heterogeneity in the quality of research on mediation (Maxwell & Cole, 2007). This state of affairs is also true for studies evaluating threat reappraisal as a mediator of CBT efficacy for the anxiety disorders. Hence, in evaluating the strength of the evidence for the threat mediation hypothesis, it is pertinent to consider the extent to which studies have met criteria critical for establishing mediation. Kazdin (2007) has provided a useful framework for testing, identifying, and critically evaluating mediators of therapeutic change. He begins by cautioning readers not to make inferences regarding mediation solely based on proof of statistical mediation. Proof of statistical mediation as it relates to the threat reappraisal mediational hypothesis involves demonstrating statistical significance of the indirect mediated *a*b* pathway (i.e., the path from treatment to threat reappraisal [path “a”] and from threat reappraisal to anxiety reduction [path “b”]; MacKinnon, 2008). The trouble with statistical mediation is that it can easily yield false positives (Kazdin, 2007; Kraemer, Wilson, Fairburn, & Agras, 2002; Maxwell & Cole, 2007). For example, Maxwell and Cole (2007) reported that many mediational hypotheses in psychology have been tested using data from cross-sectional or half-longitudinal designs. Demonstrating that *a*b* is significant in these designs can yield results consistent with mediation. However, cross-sectional mediation analyses cannot readily test one pre-condition necessary for establishing that mediation has truly occurred, namely that the independent variable (CBT) *causes* a change in the mediator (threat reappraisal), which in turn *causes* a change in the dependent variable (anxiety reduction). Indeed, *a*b* may be significant when the opposite causal path is actually true.

Recognizing the pitfalls of relying solely on proof of statistical mediation, Kazdin (2007) delineated the following seven additional recommendations for research to identify a mediator: (1) the selection of mediators must be guided by theory; (2) treatment studies must include measures of potential mediators; (3) the timeline of the proposed mediator and outcome must be established; (4) studies must assess more than one mediator; (5) studies must use designs that can evaluate mediators; (6) different types of studies must provide converging evidence; and (7) treatment studies must be complemented by experiments that manipulate the mediator to provide converging evidence. For the present review of studies

testing the threat reappraisal mediation hypothesis, we have used these recommendations to develop specific criteria for evaluating the quality of evidence provided by each study included in the review. Since we review studies of the threat mediation hypothesis, all included studies meet recommendations 1 and 2, but none were designed to meet recommendation 7. Also, the present investigation summarizes the results of existing research to address recommendation 6. Thus, our criteria are based on recommendations 3, 4, and 5, and the fact that mediation must be statistically significant to be considered valid. These criteria are detailed next.

Criterion 1: Demonstrates Statistical Mediation

The first criterion for evaluating the quality of studies is whether they demonstrate either (1) significance of the indirect mediated *a*b* pathway (i.e., treatment to threat reappraisal [path a] and threat reappraisal to anxiety reduction [path b]) or (2) a reduction of the strength of the relation between treatment and anxiety symptom reduction after controlling for threat reappraisal (Baron & Kenny, 1986; MacKinnon, 2008; Kraemer, Kiernan, Essex, & Kupfer, 2008). Data can be modeled using various methods (e.g., multiple regression analyses, multilevel modeling, path analysis, structural equation modeling), and tests of the significance of the mediated pathway can take many forms (e.g., bootstrapping, MacKinnon et al., 2010; the asymmetric distribution of products tests, MacKinnon, Fritz, Williams, & Lockwood, 2007; causal steps, Baron & Kenny, 1986). It should be noted that the *b* pathway may be moderated by treatment condition (Kraemer et al., 2008), in which case the threat reappraisal mediation hypothesis would be supported if the *a*b* pathway for the *CBT* condition was significant (see Tein, Sandler, MacKinnon, & Wolchik, 2004 for techniques to test for moderated mediation).

Criterion 2: Demonstrates that CBT Causes Threat Reappraisal

The second criterion for evaluating the quality of studies is whether they demonstrate that CBT causes threat reappraisal. This criterion has been emphasized by many mediation researchers (e.g., Cole & Maxwell, 2003; Kazdin, 2007; Kraemer et al., 2008). Establishing the causal effects of CBT on the threat appraisal (the “a” path) and anxiety is most effectively achieved in studies involving random assignment of participants to CBT or a control condition. The selection of the type of control condition (e.g., waitlist, placebo, viable alternative treatment) influences the degree to which inferences can be made regarding the specificity of treatment effects. That is, evidence of significant “a” path (i.e., CBT to threat reappraisal) in studies comparing CBT to a placebo or to a viable alternative treatment indicates that the effect of CBT on threat appraisal is significant beyond the effects of the non-specific factors that the treatment conditions have in common (e.g., therapist contact, therapist support and alliance). On the other hand, studies comparing CBT to waitlist can provide evidence for CBT causing threat reappraisal, but cannot establish specificity of these effects (i.e., rule out that the effects are due to non-specific factors such as therapist contact). Importantly, a failure to demonstrate between-group differences on threat reappraisal precludes testing of the causal effects of CBT on threat appraisal (Imai et al., 2010). Indeed, in such cases, it cannot be ruled out that changes in threat reappraisal simply occurs as a function of time, regression to the mean, or some other third variable (as opposed to CBT).

Criterion 3: Demonstrates that Threat Reappraisal Causes Anxiety Reduction

The third criterion for evaluating the quality of studies is whether they demonstrate that threat reappraisal *causes* anxiety reduction. Establishing the causal effect of the mediator on outcome generally requires multiple waves of assessment of both the mediator and outcome variables in designs and analyses (i.e., longitudinal mediation analysis; Cole & Maxwell, 2003; Maxwell & Cole, 2007). With respect to the analysis, testing the causal effects of

threat reappraisal on anxiety reduction requires (at a minimum) relating previous levels of the threat appraisal to later levels of anxiety (and vice versa; i.e., bi-directional effects), while controlling for previous levels of anxiety (e.g., latent dynamic change score analysis; McArdle & Hamagami, 2001, longitudinal cross lag panel analysis; Tschacher & Ramseyer, 2009, Smits et al., 2006, Meuret et al., 2010). Simple sequential ordering of the variables (e.g., measuring the mediator before the outcome) without controlling for the prior levels of the outcome does not provide sufficient information on causality (Cole & Maxwell, 2003).

Criterion 4: Demonstrates Specificity of Threat Reappraisal – Anxiety Reduction Relation

The fourth criterion for evaluating the quality of studies is whether they demonstrate specificity of the relation between threat reappraisal and anxiety reduction. Because treatment studies do not directly manipulate the mediator variable (just the independent variable; CBT), it is difficult to rule out third-variable explanations of the effect of the mediator variable (threat reappraisal) on the outcome variable (anxiety reduction) without controlling for plausible alternative mediators. Hence, studies that include multiple mediators in their design and analysis (i.e., estimates of the "b" path) provide stronger information about the causal relations between the putative mediator and outcome by allowing tests of specificity (Kazdin, 2007). The selection of plausible alternative mediators depends on the objective of the study. For example, if the objective is to establish threat reappraisal as a specific *cognitive* mediator of CBT, alternative mediators can include variables such as therapeutic alliance (i.e., non-specific factor), whereas if the aim is to establish threat reappraisal as a specific cognitive *reappraisal* mediator of CBT, alternative mediators can include other cognitive appraisal measures, not involving threat expectancies, such as self-efficacy (Bandura, 1988) or fear expectancy (Kirsch, Tennen, Wickless, Saccone, & Cone, 1983).

Method of Review

Data Sources

In order to identify potential studies for review, the PsycInfo and MEDLINE/PubMed databases were searched. To identify studies that included CBT, the following search terms were used: cognitive behavior* therap*, cognitive therap*, or behavior* therap*. To identify studies of anxiety disorder treatment, the following search terms were added: anxiety disorder*, generalized anxiety disorder, obsessive compulsive disorder, social phobia, social anxiety disorder, specific phobia, simple phobia, panic disorder, post-traumatic stress disorder, or acute stress disorder. To identify studies that examined mechanisms of change, the following search terms were added as well: mechanism*, mediat*, change*, ingredient*, process*, threat reappraisal. All search terms were entered without limiters (e.g., terms not limited to keywords), except for the specification of English language publications. Lastly, manual searches in the lists of references from empirical studies were conducted.

Selection and Study Characteristics

We selected studies that met the following criteria: (1) aimed to examine threat reappraisal as a mediator of CBT outcome for anxiety disorders. Studies presenting analyses on datasets that were reported in previously published reports on the threat reappraisal hypothesis were excluded in order to avoid biasing the reported evidence (i.e., multiple reports of the same data) for the mediation hypothesis. Thus, results from a particular dataset are included only once in the present review. We included only the first published study on a particular dataset. (2) Included adults with a formally diagnosed anxiety disorder. The decision to limit the review to adults was guided by work suggesting that the study of cognitive distortions in children may come with additional methodological challenges that are beyond the scope of this review (Alfano, Beidel, & Turner, 2002). We operationalized formal diagnosis as the

use of a psychometrically sound procedure (e.g., Structured Clinical Interview for Axis I Disorders [SCID; First, Spitzer, Gibbon, Williams, 1995]; Anxiety Disorders Interview Schedule [ADIS; DiNardo et al., 1992]) for establishing anxiety disorder diagnoses. (3) Included longitudinal assessments, which was defined as the inclusion of at least two time-points for the assessment of mediator and outcome variables. This inclusion criterion was selected in order to rule out studies that cannot examine within-person *change* mechanisms (Kazdin, 2007; Maxwell & Cole, 2007).

Data Extraction and Synthesis

For each study, we first collected data on the following basic methodological parameters: (1) anxiety disorder studied; (2) experimental design; (3) sample size; (4) treatment duration; (5) (6) assessment schedule; (7) measure of threat appraisal; and (8) measure of anxiety disorder symptom severity. Next, we recorded for each study whether the measures of each construct had acceptable psychometric properties. Our decision (yes, no) was based on the reporting of these data in either the manuscript itself or related papers. Finally, we determined for each study whether it provided evidence (yes [+], no [-]) for: (1) statistical mediation; (2) CBT causing threat reappraisal; (3) threat reappraisal causing anxiety reduction; and (4) specificity of threat reappraisal mediation. The four authors first made each of the criteria decisions independently. Disagreement among the authors was resolved through discussion, and consensus was obtained. The second author extracted the data and entered these into a database. In addition to a qualitative review of the findings, we synthesized the findings by calculating the percentage of studies that received positive ratings for each of the four criteria for establishing mediation, separately.

Results

Study Selection

As can be seen in Figure 1, the search strategy yielded 2,296 potentially eligible records published between 1956 and November 2011. After initial screening, 83 full-text articles were identified and assessed further for eligibility. Fifty-eight studies were then excluded due to no examination of threat reappraisal as a mechanism of treatment outcome, and four publications were excluded due to the use of repeated datasets. Accordingly, 25 studies met inclusion criteria and were selected for this review (see Table 1).

Of the 25 studies, the majority focused on panic disorder ($N = 9$) and social anxiety disorder ($N = 8$), followed by obsessive-compulsive disorder (OCD; $N = 3$), post-traumatic stress disorder (PTSD; $N = 2$), acute stress disorder ($N = 1$), specific phobia ($N = 1$), and a mixed sample of patients with panic disorder or social anxiety disorder ($N = 1$). Twenty-four of 25 studies (96%) involved the evaluation of a treatment package that included both cognitive restructuring and behavioral exercises (i.e., exposure or behavioral experiments), while one study examined an intervention that utilized strict exposure treatment without cognitive restructuring (Overton & Menzies, 2005). Thirteen studies (52%) employed a randomized controlled design, 10 studies (40%) employed a within-subjects design (i.e., either results for an alternative treatment condition were not included in the reported data, or there was no treatment comparison condition), while the remainder ($N = 2$; 8%) utilized a single-subject design. Among the 13 studies that compared CBT against an alternative procedure, 4 included waitlist comparator, 2 included a pill condition (either active or placebo), and 7 included a psychosocial treatment comparator (e.g., IPT, relaxation, biofeedback). Sample sizes ranged from 8 to 525, with a total N across the studies of 1,986. Most studies employed existing or slightly modified versions of psychometrically sound self-report measures of threat appraisal ($N = 21$; 84%), while 4 studies (16%) asked participants to indicate the strength of belief in a set of patient-identified task-related threat appraisals

(idiosyncratic approach). All studies used acceptable measures of anxiety symptom severity (see Table 1).

Data Synthesis

Evidence for Statistical Mediation (Criterion 1)—Results are presented in Table 2 and Figure 2. Fourteen of 25 studies (56%) investigated statistical mediation and 13 (52%) demonstrated either a significant mediated pathway or a reduction of the strength of the relation between treatment and anxiety reduction after controlling for threat reappraisal. One study (4%) did not observe significant mediation. In this study, Hoffart (1995) found that improvements in self-efficacy, but not threat reappraisal, accounted for symptom improvement observed among 46 patients with panic disorder with agoraphobia receiving a six-week course of CBT or guided mastery therapy. Ten studies (40%) examined the relation between threat reappraisal and anxiety symptom severity reduction (i.e., the “b” paths), but did not conduct a full test of mediation. Most of these studies ($N = 9$) documented significant findings, but Bryant and colleagues (2001) only observed significant relations between threat reappraisal and reduction of depressive symptoms, but not anxiety symptom severity reduction. Lastly, there was one study (4%) that did not include analyses linking threat reappraisal to symptom reduction (Grenier, O'Connor, & Bélanger, 2008).

Evidence for CBT Causing Threat Reappraisal (Criterion 2)—As can be seen in Table 2 and Figure 2, 13 of 25 studies (52%) manipulated CBT. Seven studies (28%) demonstrated evidence for a causal relation between CBT and threat reappraisal. Four of these studies (Casey, Newcombe, & Oei, 2005; Hofmann, 2004; Smits, Powers, Cho, & Telch, 2004; Taylor & Alden, 2008) demonstrated that CBT outperformed waitlist in changing threat appraisal, while the other 3 studies (Bryant, Moulds, Guthrie, & Nixon, 2001; Rapee, Gaston, & Abbott, 2009; Woody, Whittal, & McLean, 2011) documented advantages of CBT over a credible treatment condition in terms of threat reappraisal, thus demonstrating that these causal effects were specific to CBT (as opposed to treatment).

Interestingly, 6 studies (24%) involved the manipulation of CBT in their design and analysis, but failed to demonstrate that CBT caused threat reappraisal (Hoffart, 1995; Hoffart, Borge, Sexton, H., & Clark, D. (2009); Hofmann et al., 2007; McManus, Clark, & Hackman, 2000; Meuret et al., 2010; Raes, Koster, Loeys, & DeRaedt, 2011). In each of these studies, threat appraisal did change with treatment but did not differ between CBT and a credible comparison condition (e.g., pharmacotherapy, stress management, interpersonal therapy, breathing retraining), thus making it impossible to rule the possibility that this change was due to time or some other third variable (not involving CBT or treatment). The remainder of studies (N=12) did not include a manipulation of CBT in their design or analysis, and thus could not test the causal effects of CBT on threat reappraisal.

Evidence for Threat Reappraisal Causing Anxiety Reduction (Criterion 3)—Results are presented in Table 2 and Figure 2. Seven studies (28%) examined whether threat reappraisal causes anxiety reduction and 6 (24%) demonstrated that threat reappraisal resulted in subsequent reductions in anxiety (Bouchard et al., 2007; Hedley, Hoffart, & Sexton, 2001; Hoffart, Sexton, Hedley, & Martinsen, 2008; Meuret et al., 2010; Smits et al., 2006; Teachman et al., 2010). Three of these studies documented bi-directional effects, showing that threat reappraisal caused anxiety reduction and anxiety reduction caused threat reappraisal. One study (4%) did not observe a causal effect of threat reappraisal on anxiety reduction, but instead found that anxiety reduction caused threat reappraisal (Woody et al., 2011).

Five studies attempted to establish causality of the mediator to outcome effects, but did not appropriately model the data to make strong causal inferences. In these studies (Hoffart et al., 2009; Hofmann, 2004; Overton & Menzies, 2005; Taylor & Alden, 2008; Wilson & Rapee, 2005), threat reappraisal in earlier phases of the study protocol was merely correlated with symptom improvements in later phases of the protocol, but testing of causality (e.g., by controlling for earlier levels of anxiety symptoms) was absent. The remaining 13 studies did not attempt to establish causality of the threat reappraisal – anxiety reduction relation.

Evidence for Specificity of the Threat Reappraisal – Anxiety Reduction Relation (Criterion 4)—As shown in Table 2 and Figure 2, 11 studies (44%) controlled for one or more plausible alternative mediators, and 9 (36%) observed significant relations between threat reappraisal and anxiety reduction after controlling for one or more plausible alternative mediators. Alternative mediator candidates included enhanced self-efficacy (Bouchard et al., 2001; Casey, Newcombe, Oei, 2005), increased perceived control (Meuret et al., 2010; Overton & Menzies, 2005) or partnership satisfaction (Vögele et al., 2010), reduced fear expectancy (Smits et al., 2006), uncertainty (Overton & Menzies, 2005), or negative mental representation (Rapee, Gaston, & Abbott, 2009), reduced self-focus and safety behaviors and increased self-disclosure and acceptance by others (Hoffart, Borge, Sexton, & Clark, 2009), and reduced perfectionism or change in personal significance (Woody et al., 2011). With the exception of increased partner satisfaction and self-disclosure as well as reduced perfection, personal significance and uncertainty, relations with anxiety reduction were also significant for all rival mediators in these studies.

Two studies (8%) found that the relation between threat reappraisal and anxiety reduction was no longer significant after controlling for enhanced self-efficacy (Foa & Rauch, 2004; Hoffart, 1995), while the remaining 14 studies did not attempt to rule out third-variable explanations of the threat reappraisal-anxiety relation.

Discussion

Summary of Findings

The present study sought to review the evidence for the threat reappraisal mediation hypothesis for CBT treatment of anxiety disorders. To this end, we identified studies that aimed to test this mediation hypothesis and appraised each study on a number of criteria critical to establishing mediation (Cole & Maxwell, 2003; Maxwell & Cole & 2007; Kazdin, 2007). Our review yielded a number of important findings. First, the threat reappraisal mediation hypothesis has received considerable empirical attention; we identified 25 studies. Interestingly, however, the vast majority of these studies included samples of adults suffering from panic disorder or social anxiety disorder. In fact, our search did not yield any studies that focused on generalized anxiety disorder, and studies including adults with OCD, PTSD, acute stress disorder, and specific phobia were small in number. Accordingly, it was not possible to examine whether threat reappraisal mediation of CBT efficacy varied across the anxiety disorders.

Second, there was strong evidence for a significant relation between threat reappraisal and anxiety symptom severity reduction. The studies that also specifically tested for statistical mediation, which comprised half of the studies included in the review, further demonstrated significance of the mediated threat reappraisal to anxiety reduction pathway or, alternatively, a reduction of the strength of the relation between treatment and anxiety reduction after controlling for threat reappraisal. Collectively, these findings are consistent with the cognitive-behavioral model, which posits that improvements in maladaptive thinking and anxiety symptoms during CBT occur in tandem (Beck et al., 1985; Clark & Beck, 2010).

Third, the evidence for the hypothesis that threat reappraisal *drives* the efficacy of CBT for anxiety disorders was not strong, because the testing of many important criteria for mediation was absent from most studies. Specifically, less than one-third (28%) of the studies reviewed established CBT as a cause of threat reappraisal, less than one-fourth (24%) of the studies reviewed established threat reappraisal as a cause of anxiety reduction, only 36% of studies reviewed demonstrated specificity of the threat reappraisal-anxiety reduction relation, and no studies met all these more stringent criteria for establishing mediation. Importantly, of the studies that tested the criteria, most did provide evidence consistent with hypothesis. For example, of the 13 studies that investigated whether CBT causes threat reappraisal, 7 (54%) reported positive results, while the other 6 found no differences between CBT and a credible comparison condition (which may merely suggest that threat reappraisal is a mediator not specific to CBT). Similarly, evidence for threat reappraisal causing anxiety reduction was observed in 6 of 7 (87%) studies that examined this criterion. Likewise, evidence for specificity of the threat reappraisal-anxiety reduction relationship was found in 9 of 11 (82%) studies that tested this criterion. It should also be noted that no studies tested and established evidence for all four criteria. The importance of testing and obtaining positive results for all criteria was underscored by the study completed by Woody and colleagues (2011). Indeed, they demonstrated statistical mediation (criterion 1), showed evidence of CBT causing threat reappraisal (criterion 2) and specificity of the threat reappraisal-anxiety reduction relation (criterion 4), but also showed that threat reappraisal did *not* cause anxiety reduction (criterion 3), and therefore raised concerns about the validity of the threat reappraisal mediation hypothesis of symptom change in OCD. Thus, conclusions can be misleading if studies did not attempt to rule out false positives by testing these four criteria.

Fourth, in reviewing the evidence for specificity of threat reappraisal mediation, we observed strong relations between changes in anxiety symptom severity and most rival mediators. These rival mediator variables included improvements in other cognitive appraisal processes such as self-efficacy, perceived control, and fear expectancy, in addition to reduced negative mental representation of self, self-focus, and safety behaviors, as well as increased acceptance by others. Thus, these studies suggest that even if threat reappraisal is a mediator of symptom improvement in CBT, other factors may independently explain additional variance in symptom improvement. It is important to point out here that many of these studies did not document that these alternative change mechanisms acted as causative agents in the CBT-anxiety symptom improvement relation.

The present review was prompted by the observation that CBT is effective for treating anxiety disorders, but also leaves ample room for improvement. As we consider the development of new treatments or augmentation strategies, the results of our review suggest that, given the state of the current research, it is difficult to make a strong case for threat reappraisal as a *singular* target for these interventions. While the evidence for threat reappraisal mediation to date is promising, such recommendation would require additional evidence suggesting that threat reappraisal is a causative agent and not merely a consequence of symptom change or a proxy for some other therapeutic change process, something that has not yet been well established. In the next section, we discuss specific considerations for investigations (in addition to our 4 criteria) that can build on extant work in this important area.

Directions for Future Research

Determining the Optimal Assessment Interval—Any study that involves more than two assessment occasions yields data that can be modeled to test causal relations. However, as has been demonstrated by Cole and Maxwell (2003; see also Gollob & Reichardt, 1991),

estimates of mediation effects are not accurate when the time interval between assessments does not match the time interval during which the hypothesized causal effects occur. Hence, it is important to conduct studies that can determine the time interval that must elapse for CBT to have an effect on threat appraisal and for threat reappraisal to have an effect on anxiety reduction (Cole & Maxwell, 2003). There is some work suggesting that this interval may be brief and therefore not adequately captured even by weekly assessments. For example, placebo-controlled studies with claustrophobic persons have shown that 30 minutes of CBT yields significant improvement in threat appraisals (Powers, Smits, Whitley, Brustritsky, & Telch, 2006; Powers, Smits, & Telch, 2004). Similarly, as predicted by theory (Clark & Beck, 2010) and evidenced by findings reported by Smits et al. (2006), the causative effects of threat reappraisal on anxiety reduction can also be evident within one session. In order to advance research on the threat mediation hypothesis, we must first empirically establish the time frame during which the indirect effects (i.e., CBT to threat reappraisal and threat reappraisal to anxiety reduction) unfold. Here, it is important to consider the possibility that differences may exist across the different anxiety disorders.

Evaluating the Stationarity Assumption—Related to determining the optimal assessment interval is evaluating the assumption inherent to many regression models of causation, namely stationarity. Stationarity has been defined as constancy in the causal structure over time (Cole & Maxwell, 2003), which in the case of the threat reappraisal mediation hypothesis implies that the effects of CBT on threat appraisal and threat reappraisal on anxiety do not change during the course of treatment. Clearly, testing the stationarity assumption is critical to selecting appropriate assessment intervals as well as optimal data analytic approaches (Cole & Maxwell, 2003). Tests of stationarity can be easily be performed in both multi-wave SEM models (by allowing the cross lags to differ over time) and in longitudinal, multilevel models (by adding the interaction between time and the mediator in the level 1 model predicting outcome; Hedeker & Gibbons, 2006). Moreover, studies that examine the stationarity assumption may, by doing this, assist in the testing of the role of threat reappraisal in more complex therapeutic change models. Consider, for example, the possibility that non-specific change processes (e.g., therapeutic alliance, expectancy) are critically involved in the effects of any psychosocial treatment, including CBT for the anxiety disorders, as some have suggested (e.g., Messer & Wampold, 2002; Roth, 2010). In many CBT protocols for anxiety disorders, techniques thought to be critical to achieve threat reappraisal (e.g., exposure, behavioral experiments, cognitive restructuring) are not introduced until after a few weeks (Otto et al., 2004). Analyses of session-by-session data of anxiety symptoms, however, show that notable changes in symptoms can be observed prior to the introduction of these techniques (Penava, Otto, Maki, & Pollack, 1998; Teachman, Marker, & Smith-Janik, 2008; van Minnen & Foa, 2006). Collectively, these findings could suggest that therapeutic alliance established early on in treatment may promote higher expectancy, which results in initial reductions of anxiety symptom severity. This improvement in anxiety may, in turn, motivate a patient to decrease behavioral avoidance (i.e., engage in behavioral experiments and exposure), which may in turn lead to later threat reappraisal followed by continued anxiety reduction. Obviously, this is just one of many possible pathways explaining how threat reappraisal may be involved in anxiety symptom improvement with CBT. We present it here simply to illustrate that the causal effects of CBT on threat appraisal (and other mediators) and the causal effects of threat reappraisal (and other mediators) on anxiety may vary over the course of treatment.

Evaluating Moderated Mediation—As is this case for treatment efficacy, treatment mechanisms may also vary across patients, even among individuals who experience similar levels of symptom improvement. One moderator candidate is the type of anxiety disorder, recognizing that, although anxiety disorders share many features in common, there are a

number of distinguishing features which may influence mechanisms of change. A similar rationale could be made for testing the presence of psychiatric comorbidity, sex, ethnicity, or other demographic characteristics as moderators of therapeutic mechanisms. With respect to testing the mechanism of action of CBT, it may also be worthwhile to consider possible genetic influences. Here, it is noteworthy to mention that recent research has shown that extinction learning, the process thought to reflect threat reappraisal (Hofmann, 2008), is impaired in carriers of the BDNF Met allele (Soliman et al., 2010), suggesting that the BDNF Val66Met single nucleotide polymorphism may be a viable moderator candidate. Lastly, it would be interesting to test whether treatment mechanisms vary as a function of the nature of the CBT intervention. Indeed, although questioned by some (Hofmann, 2008), it is possible that different mechanisms are evident for CBT interventions that emphasize behavioral interventions versus CBT interventions that emphasize cognitive interventions.

Including Multi-Method Assessments—The inclusion of multi-method assessments would likely further bolster future investigations in this area in two significant ways. First, relying on one single method such as self-report can introduce challenges with respect to the interpretation of the path coefficients. Specifically, if not modeled appropriately, shared method variance inherent in this approach can artificially inflate the path coefficients (Maxwell & Cole, 2007). An example of a method for assessing threat appraisal that does not rely on self-report is a reaction time paradigm. Completed on a computer, this task indexes threat appraisal by comparing differences in the time it takes for individuals to endorse or reject threat interpretations of ambiguous stimuli (Beard & Amir, 2009). Second, multi-method assessment may also involve measuring mediator constructs at different levels of analyses, and thereby help discern mechanisms of change (Kazdin, 2007). For example, recent research has associated cognitive reappraisal with decreased activation in the amygdala and increased activation in a number of systems implicated in the control of emotion (e.g., medial prefrontal and anterior temporal regions; McRae, Hughes, Chopra, Gabrieli, Gross, & Ochsner, 2010). Including assessment of change in these neural systems alongside threat appraisal may help explain how threat reappraisal results in anxiety reduction, thereby meeting the more stringent criterion for establishing a change mechanism (Kazdin, 2007).

The type of the measurements used in future studies is crucial for an additional reason. Unreliable measures, whether for the mediator, the outcome, competing mediators, or control variables, can bias estimates of the path coefficients in complex ways (either up or down, depending on the relative reliabilities of each measure that affects each path coefficient; Cole & Maxwell, 2003). As noted by Cole and Maxwell (2003), since few psychological measures are perfectly reliable, future research should consider latent variable SEM models with carefully selected multiple measures of the underlying constructs. These latent variables are “without error” (see Cole and Maxwell, 2003), yielding more accurate estimates of the path coefficients.

Study Limitations

As is the case for any systematic review, the conclusions of the present review are influenced by the manner in which we appraised and used evidence from available studies (Gough, 2007). In synthesizing the evidence for the threat appraisal mediation hypothesis, we conducted an assessment of quality and relevance at different stages of the review. At the start of the review process, we elected to limit the inclusion of studies to those that aimed to examine the threat reappraisal mediation hypothesis, employed a longitudinal design, included adults with an anxiety disorder diagnosis, and did not report on previously published findings covered by other studies in this review. While ensuring high relevance of

the evidence and reducing multiple publication bias (Higgins & Green, 2011), this approach comes with the risk of excluding studies that contained useful information (Gough, 2007).

After data extraction, we appraised each study on the quality of its results with respect to the aims of the present investigation. Thus, we opted for making review-specific as opposed to generic quality judgments, implying that our study ratings do not reflect the overall quality of the study per se, but rather about the extent to which the evidence from each respective study helps address the review question (Gough, 2007). We made these review-specific quality judgments using *a priori* criteria informed by mediation theory, thereby allowing results of each study to be evaluated based on meeting the criteria. The results of the assessment process presented here reflect the consensus among four individuals and have yet to be replicated by an independent group of investigators. In addition, the aggregation of data obtained from quality judgments of each individual study may result in different conclusions than a meta-analysis, which can have the advantage of increasing power to detect meaningful effects.

Conclusions

Identifying mediators of therapeutic change is critical to treatment development. The current article reviewed the evidence of the relative importance of threat reappraisal to the efficacy of CBT for the anxiety disorders. The results suggest that, while threat reappraisal is related to CBT outcome, it may be premature to designate it as a critical or singular target for novel intervention or augmentation strategies. Although most of the studies that actually test the criteria necessary for mediation do provide support for the threat reappraisal mediation hypothesis, most fail to test these important criteria. Thus, although the extant evidence supports the threat reappraisal mediation hypothesis, conclusive evidence, from studies that test most if not all of the Kazdin mediation criteria, has yet to be provided. We have offered a number of suggestions that can hopefully guide future work in this important area of inquiry.

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References

Alfano CA, Beidel DC, Turner SM. Cognition in childhood anxiety: Conceptual methodological and developmental issues. Clinical Psychology Review. 2002; 22(8):1209–1238. doi:10.1016/S0272-7358(02)00205-2. [PubMed: 12436811]

Bandura A. Self-efficacy conception of anxiety. Anxiety Research. 1988; 1:77–98.

Barlow DH, Gorman JM, Shear M, Woods SW. Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: A randomized controlled trial. JAMA: Journal of the American Medical Association. 2000; 283(19):2529–2536. doi:10.1001/jama.283.19.2529.

Baron R, Kenny D. The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology. 1986; 51(6):1173–1182. doi:10.1037//0022-3514.51.6.1173. [PubMed: 3806354]

Beard C, Amir N. Interpretation in Social Anxiety: When Meaning Precedes Ambiguity. Cognitive Therapy & Research. 2009; 33(4):406–415. doi:10.1007/s10608-009-9235-0. [PubMed: 20046862]

Beck, AT.; Emery, G.; Greenberg, R. Anxiety disorders and phobias: A cognitive perspective. Basic Books; New York: 1985.

Borkovec TD, Costello E. Efficacy of applied relaxation and cognitive-behavioral therapy in the treatment of generalized anxiety disorder. Journal of Consulting and Clinical Psychology. 1993; 61(4):611–619. doi:10.1037/0022-006X.61.4.611. [PubMed: 8370856]

Bouchard S, Gauthier J, Nouwen A, Ivers H, Vallières A, Simard S, et al. Temporal relationship between dysfunctional beliefs, self-efficacy and panic apprehension in the treatment of panic disorder with agoraphobia. Journal of Behavior Therapy and Experimental Psychiatry. 2007; 38(3): 275–292. doi:10.1016/j.jbtep.2006.08.002. [PubMed: 17157264]

Bryant R, Moulds M, Guthrie R. Cognitive strategies and the resolution of acute stress disorder. Journal of Traumatic Stress. 2001; 14(1):213–219. doi:10.1023/A:1007856103389.

Bryant RA, Moulds ML, Guthrie RM, Nixon RV. The Additive Benefit of Hypnosis and Cognitive-Behavioral Therapy in Treating Acute Stress Disorder. Journal of Consulting & Clinical Psychology. 2005; 73(2):334–340. doi:10.1037/0022-006X.73.2.334. [PubMed: 15796641]

Casey L, Newcombe P, Oei T. Cognitive mediation of panic severity: The role of catastrophic misinterpretation of bodily sensations and panic self-efficacy. Cognitive Therapy and Research. 2005; 29(2):187–200. doi:10.1007/s10608-005-3164-3.

Clark DM. A cognitive approach to panic. Behaviour Research and Therapy. 1986; 24(4):461–470. doi:10.1016/0005-7967(86)90011-2. [PubMed: 3741311]

Clark, DM.; Wells, A. A cognitive model of social phobia.. In: Heimberg, RG.; Liebowitz, MR.; Hope, DA.; Schneier, FR.; Heimberg, RG.; Liebowitz, MR.; Schneier, FR., editors. Social phobia: Diagnosis, assessment, and treatment. Guilford Press; New York, NY US: 1995. p. 69-93.

Clark, D.; Beck, A. Cognitive therapy of anxiety disorders: Science and practice. Guilford Press; New York: 2010.

Cole DA, Maxwell SE. Testing mediational models with longitudinal data: Questions and tips in the use of structural equation modeling. Journal of Abnormal Psychology. 2003; 112:558–577. [PubMed: 14674869]

Davidson J, Foa E, Huppert J, Keefe F, Franklin M, Compton J, et al. Fluoxetine, comprehensive cognitive behavioral therapy, and placebo in generalized social phobia. Archives of General Psychiatry. 2004; 61(10):1005–1013. doi:10.1001/archpsyc.61.10.1005. [PubMed: 15466674]

DiNardo, PA.; Brown, TA.; Barlow, DH. Anxiety Disorders Interview Schedule for DSM-IV. Center for Anxiety and Related Disorders at Boston University; Boston, MA: 1994.

Dobson, KS.; Dozois, DJA. Historical and philosophical bases of the cognitive-behavioral therapies.. In: Dobson, KS., editor. Handbook of cognitive-behavioral therapies. 2nd ed.. Guilford Press; New York: 2001. p. 3-39.

First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/NP): Non-patient Edition. American Psychiatric Press; Washington, DC: 2002.

Foa EB, Liebowitz MR, Kozak MJ, Davies S, Campeas R, Franklin ME, Tu X. Randomized, placebo-controlled trial of exposure and ritual prevention, clomipramine, and their combination in the treatment of obsessive-compulsive disorder. The American Journal of Psychiatry. 2005; 162(1): 151–161. doi:10.1176/appi.ajp.162.1.151. [PubMed: 15625214]

Foa E, Rauch S. Cognitive changes during prolonged exposure versus prolonged exposure plus cognitive restructuring in female assault survivors with posttraumatic stress disorder. Journal of Consulting and Clinical Psychology. 2004; 72(5):879–884. doi:10.1037/0022-006X.72.5.879. [PubMed: 15482045]

Foa E, Franklin M, Perry K, Herbert J. Cognitive biases in generalized social phobia. Journal of Abnormal Psychology. 1996; 105(3):433–439. doi:10.1037//0021-843X.105.3.433. [PubMed: 8772013]

Gollob, HF.; Reichardt, CS. Interpreting and estimating indirect effects assuming time lags really matter.. In: Collins, LM.; Horn, JL., editors. Best Methods for the Analysis of Change. American Psychological Association; Washington, DC: 1991. p. 243-59.

Gough D. Weight of evidence: a framework for the appraisal of the quality and relevance of evidence. Research Papers in Education. 2007; 22:213–228.

Grenier S, O'Connor K, Bélanger C. Obsessional beliefs, compulsive behaviours and symptom severity: Their evolution and interrelation over stages of treatment. Clinical Psychology & Psychotherapy. 2008; 15(1):15–27. doi:10.1002/cpp.560. [PubMed: 19115424]

Hedeker, D.; Gibbons, RD. Longitudinal Data Analysis. John Wiley & Sons; Hoboken, N.J.: 2006.

Hedley L, Hoffart A, Sexton H. The change process in a cognitive-behavioral therapy: Testing a cognitive, a behavioral, and an integrated model of panic disorder with agoraphobia. Psychotherapy Research. 2001; 11(4):401–413. doi:10.1093/ptr/11.4.401.

Higgins, JPT.; Green, S., editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. Available from www.cochrane-handbook.org

Hoffart A. Cognitive mediators of situation fear in agoraphobia. Journal of Behavior Therapy and Experimental Psychiatry. 1995; 26(4):313–320. doi:10.1016/0005-7916(95)00043-7. [PubMed: 8675718]

Hoffart A, Borge F, Sexton H, Clark D. Change processes in residential cognitive and interpersonal psychotherapy for social phobia: A process-outcome study. Behavior Therapy. 2009; 40(1):10–22. doi:10.1016/j.beth.2007.12.003. [PubMed: 19187813]

Hoffart A, Sexton H, Hedley L, Martinsen E. Mechanisms of change in cognitive therapy for panic disorder with agoraphobia. Journal of Behavior Therapy and Experimental Psychiatry. 2008; 39(3):262–275. doi:10.1016/j.jbtep.2007.07.006. [PubMed: 17727812]

Hofmann S. Cognitive mediation of treatment change in social phobia. Journal of Consulting and Clinical Psychology. 2004; 72(3):392–399. doi:10.1037/0022-006X.72.3.392.

Hofmann SG. Cognitive processes during fear acquisition and extinction in animals and humans: implications for exposure therapy of anxiety disorders. Clinical Psychology Review. 2008; 28:199–210. doi:10.1016/j.cpr.2007.04.009. [PubMed: 17532105]

Hofmann SG. Common misconceptions about cognitive mediation of treatment change: a commentary to Longmore and Worrell (2007). Clinical Psychology Review. 2008; 28(1):67–70. doi:10.1016/j.cpr.2007.03.003. [PubMed: 17481790]

Hofmann S, Smits J. Cognitive-behavioral therapy for adult anxiety disorders: A meta-analysis of randomized placebo-controlled trials. Journal of Clinical Psychiatry. 2008; 69(4):621–632. [PubMed: 18363421]

Hofmann S, Meuret A, Rosenfield D, Suvak M, Barlow D, Gorman J, et al. Preliminary evidence for cognitive mediation during cognitive-behavioral therapy of panic disorder. Journal of Consulting and Clinical Psychology. 2007; 75(3):374–379. doi:10.1037/0022-006X.75.3.374. [PubMed: 17563154]

Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. Psychological Methods. 2010; 15(4):309–334. doi:10.1037/a0020761. [PubMed: 20954780]

Kazdin AE. Mediators and mechanisms of change in psychotherapy research. Annual Review of Clinical Psychology. 2007; 3:1–27. doi: 10.1146/annurev.clinpsy.3.022806.091432.

Kirsch I, Tennen H, Wickless C, Saccone AJ, Cody S. The role of expectancy in fear reduction. Behavior Therapy. 1983; 14:520–533.

Kraemer H, Wilson G, Fairburn C, Agras W. Mediators and moderators of treatment effects in randomized clinical trials. Archives of General Psychiatry. 2002; 59(10):877–884. doi:10.1001/archpsyc.59.10.877. [PubMed: 12365874]

Kraemer HC, Kiernan M, Essex M, Kupfer DJ. How and why criteria defining moderators and mediators differ between the Baron & Kenny and MacArthur approaches. Health Psychology. 2008; 27(2 Suppl):S101–108. [PubMed: 18377151]

MacKinnon, DP. Introduction to statistical mediation analysis. Taylor & Francis Group/Lawrence Erlbaum Associates; New York, NY: 2008.

MacKinnon DP, Elliot DL, Thoemmes F, Kuehl KS, Moe EL, Goldberg L, Ranby KW. Long-term effects of a worksite health promotion program for firefighters. American Journal of Health Behavior. 2010; 34(6):695–706. [PubMed: 20604695]

MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. Psychological Methods. 2002; 7:83–104. [PubMed: 11928892]

Maxwell SE, Cole DA. Bias in cross-sectional analyses of longitudinal mediation. Psychological Methods. 2007; 12(1):23–44. doi:10.1037/1082-989X.12.1.23. [PubMed: 17402810]

McArdle, JJ.; Hamagami, F. Latent difference score structural models for linear dynamic analyses with incomplete longitudinal data.. In: Collins, LM.; Sayer, AG., editors. New methods for the analysis of change. American Psychological Association; Washington, DC: 2001. p. 139-175.

McManus F, Clark D, Hackmann A. Specificity of cognitive biases in social phobia and their role in recovery. Behavioural and Cognitive Psychotherapy. 2000; 28(3):201–209. doi:10.1017/S1352465800003015.

McRae K, Hughes B, Chopra S, Gabrieli JDE, Gross JJ, Ochsner KN. Journal of Cognitive Neuroscience. 2010; 22:248–262. doi: 10.1162/jocn.2009.21243. [PubMed: 19400679]

Messer S, Wampold B. Let's face facts: Common factors are more potent than specific therapy ingredients. Clinical Psychology: Science and Practice. 2002; 9(1):21–25. doi:10.1093/clipsy.9.1.21.

Meuret A, Rosenfield D, Seidel A, Bhaskara L, Hofmann S. Respiratory and cognitive mediators of treatment change in panic disorder: Evidence for intervention specificity. Journal of Consulting and Clinical Psychology. 2010; 78(5):691–704. doi:10.1037/a0019552. [PubMed: 20873904]

Mogg K, Bradley BP. A cognitive-motivational analysis of anxiety. Behaviour Research and Therapy. 1998; 36:809–848. doi:10.1016/S0005-7967(98)00063-1. [PubMed: 9701859]

Mueser K, Rosenberg S, Xie H, Jankowski M, Bolton E, Lu W, et al. A randomized controlled trial of cognitive-behavioral treatment for posttraumatic stress disorder in severe mental illness. Journal of Consulting and Clinical Psychology. 2008; 76(2):259–271. doi:10.1037/0022-006X.73.5.945. [PubMed: 18377122]

Norton PJ, Price EC. A meta-analytic review of adult cognitive-behavioral treatment outcome across the anxiety disorders. Journal of Nervous and Mental Disease. 2007; 195(6):521–531. doi: 10.1097/01.nmd.0000253843.70149.9a. [PubMed: 17568301]

Otto MW, Smits JAJ, Reese HE. Cognitive-behavioral therapy for the treatment of anxiety disorders. Journal of Clinical Psychiatry. 2004; 65(5):34–41. [PubMed: 15078117]

Overton S, Menzies R. Cognitive change during treatment of compulsive checking. Behaviour Change. 2005; 22(3):172–184. doi:10.1375/bech.2005.22.3.172.

Penava SJ, Otto MW, Maki KM, Pollack MH. Rate of improvement during cognitive-behavioral group treatment for panic disorder. Behaviour Research and Therapy. 1998; 36:665–673. [PubMed: 9682523]

Powers MB, Smits JAJ, Telch MJ. Disentangling the effects of safety-behavior utilization and safety-behavior availability during exposure-based treatment: A placebo-controlled trial. Journal of Consulting and Clinical Psychology. 2004; 72(3):448–454. doi: 10.1037/0022-006X.72.3.448. [PubMed: 15279528]

Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB. A meta-analytic review of prolonged exposure for posttraumatic stress disorder. Clinical Psychology Review. 2010; 30(6):635–641. Doi:10.1016/j.cpr.2010.04.007. [PubMed: 20546985]

Powers MB, Sigmarsson SR, Emmelkamp PMG. A meta-analytic review of social phobia treatments. International Journal of Cognitive Therapy. 2008; 1:94–113. doi:10.1521/ijct.2008.1.2.94.

Powers MB, Smits JAJ, Whitley D, Bystritsky A, Telch MJ. The effect of attributional processes concerning medication taking on return of fear. Journal of Consulting and Clinical Psychology. 2008; 76(3):478–490. doi: 10.1037/0022-006X.76.3.478. [PubMed: 18540741]

Raes AK, Koster EHW, Loeys T, Raedt RD. Pathways to change in one-session exposure with and without cognitive intervention: An exploratory study in spider phobia. Journal of Anxiety Disorders. 2011; 25(7):964–971. doi:10.1016/j.janxdis.2011.06.003. [PubMed: 21741797]

Rapee R, Heimberg R. A cognitive-behavioral model of anxiety in social phobia. Behaviour Research and Therapy. 1997; 35(8):741–756. doi:10.1016/S0005-7967(97)00022-3. [PubMed: 9256517]

Rapee RM, Gaston JE, Abbott MJ. Testing the Efficacy of Theoretically Derived Improvements in the Treatment of Social Phobia. Journal of Consulting & Clinical Psychology. 2009; 77(2):317–327. doi:10.1037/a0014800. [PubMed: 19309190]

Roth W. Diversity of effective treatments of panic attacks: What do they have in common? Depression and Anxiety. 2010; 27(1):5–11. doi:10.1002/da.20601. [PubMed: 20049938]

Smits JAJ, Powers M, Cho Y, Telch M. Mechanism of change in cognitive-behavioral treatment of panic disorder: Evidence for the fear of fear mediational hypothesis. Journal of Consulting and

Clinical Psychology. 2004; 72(4):646–652. doi:10.1037/0022-006X.72.4.646. [PubMed: 15301649]

Smits JAJ, Rosenfield D, McDonald R, Telch M. Cognitive mechanisms of social anxiety reduction: An examination of specificity and temporality. Journal of Consulting and Clinical Psychology. 2006; 74(6):1203–1212. doi:10.1037/0022-006X.74.6.1203. [PubMed: 17154749]

Soliman F, Glatt C, Bath K, Levita L, Jones R, Pattwell S, Casey B. A genetic variant BDNF polymorphism alters extinction learning in both mouse and human. Science (New York, N.Y.). 2010; 327(5967):863–866. doi:10.1126/science.1181886.

Taylor C, Alden L. Self-related and interpersonal judgment biases in social anxiety disorder: Changes during treatment and relationship to outcome. International Journal of Cognitive Therapy. 2008; 1(2):125–137. doi:10.1680/ijct.2008.1.2.125.

Teachman BA, Marker CP, Clerkin EM. Catastrophic Misinterpretations as a Predictor of Symptom Change During Treatment for Panic Disorder. Journal of Consulting & Clinical Psychology. 2010; 78(6):964–973. doi:10.1037/a0021067. [PubMed: 20954759]

Teachman BA, Marker CD, Smith-Janik SB. Automatic associations and panic disorder: Trajectories of change over the course of treatment. Journal of Consulting and Clinical Psychology. 2008; 76:988–1002. [PubMed: 19045967]

Tein JY, Sandler IN, MacKinnon DP, Wolchik SA. How did it work? Who did it work for? Mediation in the context of a moderated prevention effect for children of divorce. Journal of Consulting and Clinical Psychology. 2004; 72:617–624. [PubMed: 15301646]

Tschacher W, Ramseyer F. Modeling psychotherapy process by time-series panel analysis (TSPA). Psychotherapy Research. 2009; 19:469–481. doi:10.1080/10503300802654496. [PubMed: 19585371]

van Minnen A, Foa EB. The effect of imaginal exposure length on outcome of treatment for PTSD. Journal of Traumatic Stress. 2006; 19(4):427–438. [PubMed: 16929519]

Vögele C, Ehlers A, Meyer A, Frank M, Hahlweg K, Margraf J. Cognitive mediation of clinical improvement after intensive exposure therapy of agoraphobia and social phobia. Depression and Anxiety. 2010; 27(3):294–301. doi:10.1002/da.20651. [PubMed: 20037922]

Wolitzky-Taylor KB, Horowitz JD, Powers MB, Telch MJ. Psychological approaches in the treatment of specific phobias: A meta-analysis. Clinical Psychology Review. 2008; 28(6):1021–1037. doi: 10.1016/j.cpr.2008.02.007. [PubMed: 18410984]

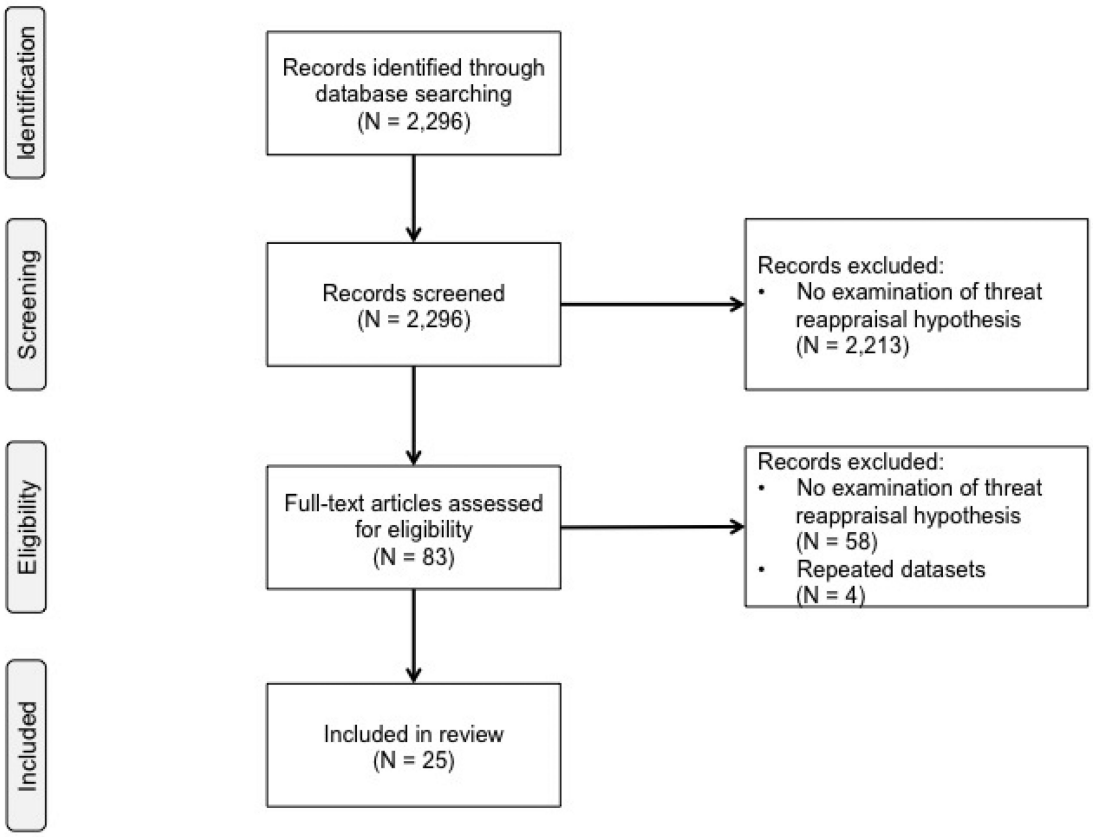

Figure 1.
Flow Diagram for Study Selection.

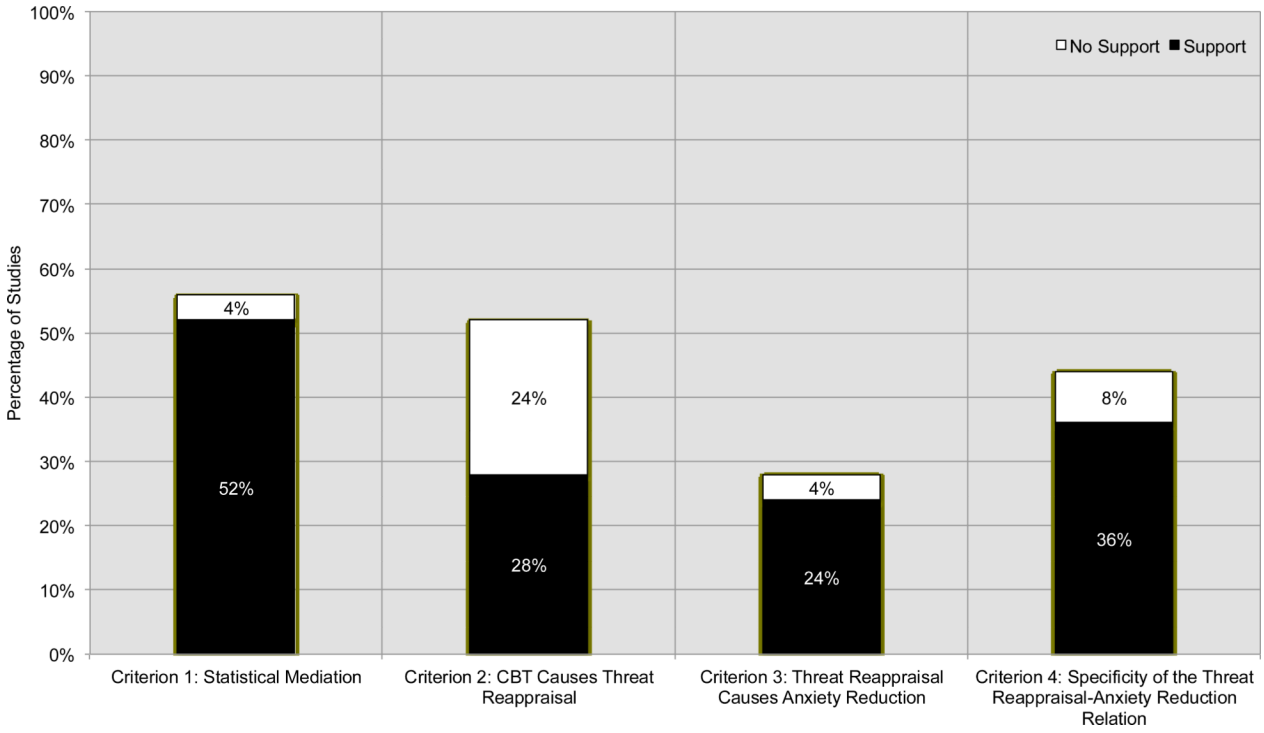

Figure 2.
Tests and Evidence for Each Criterion of Mediation.

Table 1

Study Characteristics

Study	Disorder	Design	*N*	Treatment Duration	Threat Appraisal Measure	Symptom Severity Measure	Assessment Frequency*
Bouchard et al. (2007)	Panic Disorder	Single-subject	12	18 weeks	Idiosyncratic appraisals	Panic apprehension	Daily, from 6 wks pre- to 6 wks post-
Bryant et al. (2001)	Acute Stress Disorder	RCT (CTRL=SC)	45	4 weeks	TCQ-Reappraisal	IES	Pre-, post-, 6- month follow up
Casey et al. (2005)	Panic Disorder Social	RCT (CTRL=WL)	60	11 weeks	BBSIQ	PAS	Pre-, post-
Foa et al. (1996)	Anxiety Disorder	Within-subjects	15	14 weeks	PCQ	SPAI	Pre- , post-
Foa & Rauch (2004)	PTSD	Within-subjects	54	8-11 weeks	PTCI-World	PSS-I	Pre-, post-, follow up
Grenier et al. (2008)	OCD	Single-subject	8	24 weeks	Idiosyncratic appraisals	YBOCS	Pre-, mid-, post-
Hedley et al. (2001)	Panic Disorder	Within-subjects	58	11 weeks	ACQ, BSQ	MI	Pre-, post-
Hoffart (1995)	Panic Disorder	RCT (CTRL=GMT)	46	3 weeks	Task-relevant appraisals	Situational fear	Pre-, post-
Hoffart et al. (2009)	Social Anxiety Disorder	RCT (CTRL=IPT)	80	10 weeks	Modified SPCQ	SPWSS	Weekly
Hoffart et al. (2008)	Panic Disorder	Within-subjects	188	6-11 weeks	ACQ	MI	Pre-, post-
Hofmann (2004)	Social Anxiety Disorder	RCT (CTRL= WL)	90	11 weeks	SCQ	SPAI	Pre-, post-, follow up
Hofmann et al. (2007)	Panic Disorder	RCT (CTRL= PLA, imipramine)	91	12 weeks	TRF	PDSS	Pre-, post-, follow up
McManus et al. (2000)	Social Anxiety Disorder	RCT (CTRL=fluoxetine)	23	-#	Modified SPCQ	FNE, SIAS, SPS	Pre-, post-
Meuret et al. (2010)	Panic Disorder	RCT (CTRL=CART)	41	4 weeks	ASI/BSQ	PDSS	Pre-, session 5
Mueser et al. (2008)	PTSD	Within-subjects	33	11-15 weeks	PTCI	CAPS	Pre-, post-, 2 follow ups
Overton & Menzies (2005)	OCD	Within-subjects	14	11 weeks	Idiosyncratic appraisals	MOCI, YBOCS SRS	Weekly, pre-, post-
Raes et al. (2011)	Specific Phobia	RCT (CTRL=CT)	31	1 week	Thought Checklist	SPQ, FSQ	Pre-, post-, follow up
Rapee et al. (2009)	Social Phobia	RCT (CTRL=SM)	195	12 weeks	Modified PCQ	SIAS, SPS, ADIS- IV	Pre-, post-
Smits et al. (2004)	Panic Disorder	RCT (CTRL=WL)	130	9 weeks	ASI, BSQ	Panic frequency, FQ-Ago, SPRAS, SDS	Pre-, post-

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Study	Disorder	Design	*N*	Treatment Duration	Threat Appraisal Measure	Symptom Severity Measure	Assessment Frequency*
Smits et al. (2006)	Social Anxiety Disorder	Within-subjects	53	1 week	Modified ASC	Fear during speech task	Post-exposures
Taylor & Alden (2008)	Social Anxiety Disorder	RCT (CTRL=WL)	42	11 weeks	PCQ, CSW-S	Social Phobia Composite	Pre-, post-
Teachman et al. (2010)	Panic Disorder Panic Disorder/	Within-subjects	43	11 weeks	BBSIQ	PDSS	Weekly
Vogële et al. (2010)	Social Anxiety Disorder	within-subjects	525	4-10 days	ACQ	MI for PD, SCL-IS for SP	Pre-, 2 follow- ups
Wilson & Rapee (2005)	Social Anxiety Disorder	within-subjects	36	12 weeks	CONSE-Q	SIAS, SPS, ADIS- IV	Pre-, post-, follow up
Woody et al. (2011)	OCD	RCT (CTRL=SMT)	73	12 weeks	OBQ	YBOCS, OAQ	Pre-, post-, 2 follow-ups

Note. ACQ = Agoraphobic Cognitions Questionnaire; ADIS-IV = clinical severity ratings; ASC = Appraisal of Social Concerns; ASI = Anxiety Sensitivity Index; BBSIQ = Brief Bodily Sensations Interpretations Questionnaire; BSQ = Body Sensations Questionnaire; CAPS = Clinician Administered PTSD Scale; CART = capnometry-assisted respiratory training; CONSE-Q = Consequences of Negative Social Events Questionnaire; CSW-S = Contingencies of Self-Worth Questionnaire-Social; CTRL = comparison condition; FNE = Fear of Negative Evaluation questionnaire; FQ-Ago = Fear Questionnaire-Agoraphobia subscale; FSQ = Fear of Spiders Questionnaire; GMT= Guided Mastery Therapy; IES = Impact of Event Scale; MI = Mobility Inventory for Agoraphobia; MOCI =Maudsley Obsessional-Compulsive Inventory; OAQ = Obsessional Activity Questionnaire; OCD = obsessive-compulsive disorder; PAS = Panic and Agoraphobia Scale; PCQ = Probability and Cost Questionnaire; PDSS = Panic Disorder Severity Scale; PLA = Pill placebo; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview; PTCI = Posttraumatic Cognitions Inventory; PTSD = posttraumatic stress disorder; RCT – randomized controlled trial; SC = supportive counseling; SCQ = Social Cost Questionnaire; SCL-IS = Symptom Checklist-90-Revised-Interpersonal Sensitivity; SDS = Sheehan Disability Scale; SIAS = Social Interaction Anxiety Scale; SM = Stress Management; SMT = Stress Management Training; SPAI = Social Phobia and Anxiety Inventory; SPCQ = Social Probability and Cost Questionnaire; SPQ = Spider Phobia Questionnaire; SPRAS = Sheehan Patient-Rated Anxiety Scale; SPS = Social Phobia Scale; SPWSS = Social Phobia Weekly Summary Scale; SRS = Self-Rating of Severity; TCQ = Thought Control Questionnaire; TRF = Thoughts Rating Form; WL = Waitlist; YBOCS = Yale-Brown Obsessive Compulsive Scale.

*Several studies employed different assessment schedules for threat appraisal and symptom severity; for these studies, we record here the schedule for the measure that had the lowest number of occasions.

#data was not reported in manuscript.

Table 2

Appraisal of Quality of the Evidence

		Evidence for Each Criterion			
Study	**Disorder**	**Criterion 1: Statistical Mediation**	**Criterion 2: CBT Causes Threat Reappraisal**	**Criterion 3: Threat Reappraisal Causes Anxiety Reduction**	**Criterion 4: Specificity of Threat Reappraisal- Anxiety Reduction Relation**
Bouchard et al. (2007)	Panic Disorder	-	-	+	+§
Bryant et al. (2001)	Acute Stress Disorder	-	+*	-	-
Casey et al. (2005)	Panic Disorder	+	+	-	+§
Foa et al. (1996)	Social Anxiety Disorder	+	-	-	-§§
Foa & Rauch (2004)	PTSD	-	-	-	-
Grenier et al. (2008)	OCD	-	-	-	-
Hedley et al. (2001)	Panic Disorder	-	-	+	-
Hoffart (1995)	Panic Disorder	-	-**	-	-§§
Hoffart et al. (2008)	Panic Disorder	-	-	+≠	-
Hoffart et al. (2009)	Social Anxiety Disorder	+	-**	-	+§
Hofmann (2004)	Social Anxiety Disorder	+	+	-	-
Hofmann et al. (2007)	Panic Disorder	+	-**	-	-
McManus et al. (2000)	Social Anxiety Disorder	-	-**	-	-
Meuret et al. (2010)	Panic Disorder	+	-**	+≠	+§
Mueser et al. (2008)	PTSD	+	-	-	-
Overton & Menzies (2005)	OCD	-	-	-	+
Raes et al. (2011)	Specific Phobia	+	-**	-	-
Rapee et al. (2009)	Social Anxiety Disorder	+	+*	-	+§
Smits et al. (2004)	Panic Disorder	+	+	-	-
Smits et al. (2006)	Social Anxiety Disorder	+	-	+≠	+§
Taylor & Alden (2008)	Social Phobia	-	+	-	-
Teachman et al. (2010)	Panic Disorder Panic Disorder/	-	-	+	-

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		Evidence for Each Criterion			
Study	**Disorder**	**Criterion 1: Statistical Mediation**	**Criterion 2: CBT Causes Threat Reappraisal**	**Criterion 3: Threat Reappraisal Causes Anxiety Reduction**	**Criterion 4: Specificity of Threat Reappraisal- Anxiety Reduction Relation**
Vogële et al. (2010)	Social Anxiety Disorder	+	-	-	+
Wilson & Rapee (2005)	Social Anxiety Disorder	-	-	-	-
Woody et al. (2011)	OCD	+	+*	-##	+§

Note.

* = involved comparison with credible treatment and demonstrated specificity of CBT

** = involved comparison with credible treatment and showed no between-group differences on threat reappraisal

ǂ = demonstrated bi-directional effects

= demonstrated that anxiety reduction causes threat reappraisal

§ = also reported a significant relation between change in alternative mediator and anxiety reduction

§§ = only reported a significant relation between change in the alternative mediator and anxiety reduction.