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Impaired Retrieval Inhibition of Threat Material in Generalized Anxiety Disorder

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Abstract

Generalized anxiety disorder (GAD) is characterized by cognitive biases toward threat-relevant information, but the underlying mechanisms are unclear. We translated a retrieval-practice paradigm from cognitive science to investigate impaired inhibition of threat information as one such mechanism. Participants diagnosed with GAD and never-disordered control participants learned a series of cue–target pairs; whereas some cues were associated only with neutral targets, others were associated with both neutral and threat targets. Next, participants practiced retrieving neutral targets, which typically suppresses the subsequent recall of unpracticed associated targets (retrieval-induced forgetting; RIF). Finally, participants were tested on their recall of all targets. Despite showing intact RIF of neutral targets, the GAD group failed to exhibit RIF of threat targets. Furthermore, within the GAD group, less RIF of threat targets correlated with greater pervasiveness of worry. Deficits in inhibitory control over threat-relevant information may underlie the cognitive pathology of GAD, which has important treatment implications.

Keywords

generalized anxiety disorder, threat; cognitive bias, inhibition, retrieval-induced forgetting

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Generalized anxiety disorder (GAD) is a prevalent and chronic condition that involves pervasive, excessive, and uncontrollable worry about multiple sources of potential threat (American Psychiatric Association, 2013). In this context, GAD has been characterized empirically by the preferential cognitive processing of threat-relevant information (Mathews & MacLeod, 2005), such as attentional biases toward threat material (reviewed in Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). The mechanisms underlying the preferential processing of threat information in GAD, however, are not clear. Indeed, GAD is among the least studied of the anxiety disorders, particularly with respect to pathophysiological processes (Dugas, Anderson, Deschenes, & Donegan, 2010).

In the present study, we examined impaired retrieval inhibition of threat information as a mechanism that might underlie the pathology of GAD. In this framework, inhibitory control refers to a form of executive function that increases the difficulty of retrieving the information it targets. Inhibitory control is exercised regularly during the process of updating memory to make material that is retrieved more easily accessible by reducing the accessibility of associated but unretrieved material (Anderson, 2003). Experimental evidence for this formulation comes chiefly from studies that have used the retrieval-practice paradigm (Anderson, Bjork, & Bjork, 1994). In the original version of this paradigm, participants initially studied a series of cue–target pairs (e.g., fruit–banana, fruit–orange, leather–gloves, leather–saddle). They next practiced retrieving half of the targets associated with half of the cues by completing partial stems (e.g., fruit–ba_____). Finally, following a brief delay, participants were presented with each of the cues and asked to freely recall as many of that cue's associated targets as they could

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(Experiment 1) or were presented with stems such as fruit–b_____ and asked to recall the associated targets (Experiments 2 and 3).

It is not surprising that the highest rates of recall were for practiced targets (Rp+; e.g., fruit–banana). More interesting, however, is that unpracticed targets associated with the same cue (Rp–; e.g., fruit–orange) were recalled at lower rates than were unpracticed targets associated with unpracticed cues (Nrp; e.g., leather–gloves). Such below-baseline recall of Rp– targets is termed *retrieval-induced forgetting* (RIF). Anderson et al. (1994) postulated that the act of selecting Rp+ targets during the retrieval-practice phase requires selecting against corresponding Rp- targets, which is posited to inhibit the Rp- targets in a nonconscious manner, leading to their subsequently being recalled at a lower rate than Nrp targets. Since this investigation, RIF has been demonstrated to occur robustly with various types of neutral material in nonclinical populations. Noninhibitory accounts of RIF have advocates, but a substantial body of findings is consistent with the inhibitory explanation (see Storm & Levy, 2012).

The firm foundation of RIF in the cognitive science literature makes it an ideal translational paradigm with which to investigate inhibition of emotionally valenced information in clinical populations. With respect to GAD, impaired retrieval inhibition of threat material, as would be evidenced by a lack of RIF of threat targets, may underlie intrusive and pervasive worry about potential threats and memory biases for threat information. Indeed, some, but not all, models of information processing in anxiety disorders propose a central role for impairment in inhibitory control over threat stimuli (e.g., Bishop, 2007; Hirsch & Mathews, 2012). Despite burgeoning theoretical work in this domain, only one empirical study has directly examined inhibition of threat material in GAD: Inpatients diagnosed with GAD exhibited poorer intentional forgetting of anxiety-related than neutral words on a directed forgetting task (Albu, 2008). This effect, however, may have been an artifact of a general memory bias for anxiety-related words in the GAD participants, given that inhibitory bias was not distinguished from recall bias in the "remember" condition of the task.

In the present study, we examined RIF as an automatic inhibitory process and designed our task to isolate any impaired inhibition of threat information. The results of prior studies of RIF for valenced materials have been mixed. Amir, Coles, Brigidi, and Foa (2001), for example, found that individuals with social anxiety disorder exhibited RIF of neutral and positive social words, but not negative social words, indicating a deficit in retrieval inhibition specific to negative social information. Amir, Badour, and Freese (2009), however, found that participants who experienced trauma failed to show RIF for both neutral and threat information, suggesting a more general deficit in cognitive inhibition, and Jelinek, Rietschel, Kellner, Muhtz, and Moritz (2012) found a trend toward less RIF of disorder-relevant but not generally threat-relevant material in obsessive-compulsive disorder.

A major limitation of previous studies, and one possible reason for these inconsistent findings, involves their use of valenced words as both Rp+ and Rp– targets. This procedure is problematic because individuals with emotional disorders may overattend to, or even avoid rehearsing, threat-relevant Rp+ items (Bar-Haim et al., 2007; Williams, 1988). Furthermore, most previous studies have deviated from the canonical RIF paradigm in potentially critical ways. In particular, when introducing valenced material into the RIF task, investigators have altered the baseline associative strength between the cues and targets or the number of cues and targets presented, which likely affects participants' overall memory capacity for the stimuli and decreases the sensitivity to detect more subtle retrieval dynamics.

We addressed all of these issues in the present study. Specifically, we designed our task to closely follow the original RIF paradigm, but restricted threat targets to Rp– and Nrp conditions, and examined RIF by comparing recall of Rp– and Nrp threat targets to distinguish inhibitory impairment from general memory bias for threat. We hypothesized that the GAD group, versus a never-disordered (CTL) group, would uniquely exhibit less RIF of threat than of neutral targets, indexing a deficit in inhibitory control specific to threat information rather than a more general deficit in inhibition of both threat and neutral information. In addition, within the GAD group, we explored associations between RIF of threat targets and self-reported worry.

Method

Participants

A total of 52 participants (27 GAD, 25 CTL) between the ages of 18 and 60 years completed the study. Recruitment was conducted through local psychiatric clinics and online advertisements. Participants were screened for inclusion/exclusion criteria through a telephone interview. Exclusion criteria were not fluent in English, learning disabilities, history of severe head trauma, psychotic symptoms, bipolar disorder, and alcohol or substance abuse in the past 6 months as defined by the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR*; American Psychiatric Association, 2000). Participants identified as likely to meet inclusion criteria were invited to participate in a laboratory diagnostic evaluation based on *DSM-IV-TR* criteria using the Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I; First,

Spitzer, Gibbon, & Williams, 1996), administered by a trained interviewer. Participants in the GAD group met diagnostic criteria for current GAD.[1] Participants in the CTL group did not meet criteria for any current or lifetime Axis I disorder. The SCID-I diagnostic interviews were audio-recorded, and a randomly selected proportion of interviews (n = 14) were rerated by another interviewer blind to the original diagnoses. Interrater reliability was strong across the anxiety and unipolar depressive disorders (k = .9–1.0).

Measures

All participants completed the Generalized Anxiety Disorder Questionnaire–IV (GAD-Q-IV; Newman et al., 2002) and Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990). To assess related constructs, we administered the State-Trait Anxiety Inventory–Trait scale (STAI-T; Spielberger, Gorscuch, Lushene, Vagg, & Jacobs, 1983) as a measure of trait anxiety, the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) as a measure of depressive symptomatology, and the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) as a measure of state positive and negative affect. Finally, given our use of verbal stimuli, we administered the North American Adult Reading Test (NAART; Uttl, 2002) to use as a covariate in case of group differences.

Materials

Table S1 in the Supplemental Material available online presents the full stimulus set used in our modified RIF paradigm. Following Anderson et al. (1994), the stimulus set consisted of 48 cue–target pairs: 8 cues with 6 targets for each cue. We selected the cues and targets using the University of South Florida Free Association Norms (Nelson, McEvoy, & Schreiber, 1998) to derive 8 cues that did not differ significantly with respect to the average degree of cue-to-target association or target word length, number of syllables, or frequency of use in the English language.[2] For 4 cues, all 6 targets were neutral (all-neutral cues; e.g., bowl–fruit, bowl–alley); for the other 4 cues, 3 of the targets were neutral and the other 3 were threat-relevant (neutral-threat cues; e.g., beat–drum, beat–abuse). These neutral and threat targets also did not differ significantly with respect to average degree of cue-to-target association or target length, number of syllables, or frequency of use. To balance the all-neutral cues with the neutral-threat cues on possible subcategorization, we ensured that for the all-neutral cues, 3 of the targets were associated with one meaning of the cue and the other 3 targets were associated with a different meaning of the cue (e.g., bowl–fruit, bowl–alley). Finally, to control for possible primacy and recency effects during each phase of the RIF task, we used one filler cue (tree) with 12 targets from the original RIF paradigm.

Procedure

Participants completed the diagnostic interview followed by the laboratory session approximately 1 week later. At the laboratory session, participants completed the GAD-Q-IV, PSWQ, STAI-T, CES-D, PANAS, and NAART. The RIF task was then presented using E-Prime software on an IBM-compatible computer and Dell 17-inch color monitor. Participants sat approximately 50 cm directly in front of the monitor.

RIF task

Learning phase. Participants were presented with the 48 cue–target pairs on a computer screen in block randomized order, according to one of six counterbalanced learning conditions to which participants were randomly assigned. Participants were shown each cue–target pair for 10 s and were asked to spend this entire time relating the target word to its cue. No cue was repeated in succession, and no two cues appeared in sequence more than once. Two filler pairs were presented at the start of the first block and the end of the last block. To ensure participants' sustained attention to the task, the experimenter was present in the laboratory room. Based on initial piloting of the task and to optimize initial learning of the cue–target pairs, participants completed the learning phase twice in immediate succession.

Practice phase. Participants completed a cued recall task in which they were presented with partial stems of 12 cue–target pairs (e.g., bowl–fr_____, beat–dr_____) on the computer screen for 10 s each, including 3 neutral targets from 2 all-neutral cues (bowl and panel, or card and wrap) and 3 neutral targets from 2 neutral-threat cues (beat and patient, or choke and will) in block randomized order, according to one of six counterbalanced practice conditions to which participants were randomly assigned. Participants were presented with each cue–target pair three times on an expanding schedule, with an average of 3.5 other pairs presented between the first and second presentation and 6.5 other pairs presented between the second and third presentation. For each cue–target pair, participants were asked to retrieve and say aloud the correct target. No cue was repeated in succession, and no two cues appeared in sequence more than once. Two filler pairs were presented at the beginning of the first block and the end of the last block. The experimenter was present in the laboratory room and recorded participants' responses.

Filler task. Participants completed a visual distractor task involving a complex figure (Rey, 1941) for 10 min. Participants were first instructed to copy the figure for 4 min, next to wait silently for 3 min, and finally to reproduce as much of the figure as possible from memory for 3 min.

Recall phase. Participants were presented with each cue for 30 s on the computer screen (e.g., bowl, beat) and were instructed to recall aloud as many of the targets as they were able. Cues were presented in counterbalanced order across participants, according to one of eight counterbalanced recall conditions to which participants were randomly assigned. The filler cue was presented at the start of the phase. The experimenter was present in the laboratory room and recorded participants' responses.

We used a category-cued free recall test given its relevance to the activation of threat representations in GAD (i.e., being presented with a particular cue and threat associations freely intrude in awareness; Hirsch & Mathews, 2012) and to provide comparison to prior studies with clinical samples that have all used this type of test (Amir et al., 2001; Amir et al., 2009; Jelinek et al., 2012). Notably, however, this type of test can elicit output interference effects, in which the initial retrieval of highly accessible Rp+ targets at test may interfere with the subsequent retrieval of Rp− targets (Storm & Levy, 2012). Therefore, as a supplementary analysis we examined output interference effects.

Following completion of the RIF task, participants were debriefed and compensated.

Data reduction and statistical analyses

Data were included for the recall phase of the RIF task. For each participant, we computed proportions of correctly recalled targets as a function of cue type (all-neutral, neutral-threat) and target type (Rp+, Rp−, Nrp). Next, we computed RIF scores as a function of cue type by subtracting the proportion of correctly recalled Rp- targets from the proportion of correctly recalled Nrp targets; thus, a higher RIF score indexes greater inhibition (i.e., greater recall of Nrp targets than Rp− targets). To ensure that any enhanced recall of Rp− threat targets was due to impairment in inhibition during the practice phase rather than representing an artifact of a general memory bias for threat in individuals with GAD, we contrasted recall of Rp− threat targets with recall of Nrp threat targets from neutral-threat categories. That is, because recall of Nrp threat targets serves as an index of general memory for threat material, this comparison allowed us to isolate the recall of Rp− threat targets as an index specifically of inhibition of threat material. Finally, to index severity of worry, we calculated the number of worry topics endorsed on the GAD-Q-IV and PSWQ Worry Engagement score (Fresco, Heimberg, Mennin, & Turk, 2002; see Supplemental Material), respectively.

Results

Participant characteristics

Participants comprised a range of racial/ethnic backgrounds (non-Hispanic White: 65.4%; Asian: 15.4%; Hispanic/Latino: 5.8%; African American: 5.8%; American Indian/Alaska Native: 3.8%; Other: 1.9%) and education levels (M = 4.12 [some college], SD = 1.89). There were no group differences in education level, $t(49) = 0.62$, $p = .541$, age, $t(50) = 0.82$, $p = .415$, distribution by gender, $\chi^2(1, N = 52) = 0.63$, $p = .427$, or NAART score, $t(42.25) = -0.13$, $p = .895$. The GAD group had a higher proportion of non-Hispanic White participants than did the CTL group, $\chi^2(1, N = 51) = 5.67$, $p = .017$.[3] There were no significant main or interactive effects of non-Hispanic White racial status on RIF scores for neutral or threat words, and we did not have any hypotheses concerning effects of race on RIF scores; therefore, we did not covary race in subsequent analyses. As expected, the GAD group scored higher than did the CTL group on the GAD-Q-IV, $t(50) = -20.58$, $p < .001$, PSWQ, $t(41.69) = -10.61$, $p < .001$, STAI-T, $t(50) = -12.90$, $p < .001$, CES-D, $t(35.34) = -9.30$, $p < .001$, and PANAS–Negative Affect, $t(29.39) = -4.64$, $p < .001$, and the GAD group scored lower than did the CTL group on the PANAS–Positive Affect, $t(50) = 2.97$, $p = .005$.

Group differences in RIF

Recall data as a function of cue type and target type across the GAD and CTL groups are presented in Table 1. Recall data for all-neutral cues across the full sample indicated the typical trends, in which Rp+ targets were recalled at the highest rates (M = 62.50%, SE = 3.99%), followed by Nrp targets (M = 55.29%, SE = 3.17%), Rp+ versus Nrp $t(51) = 2.02$, $p = .049$, $d = 0.29$, and Rp− targets at the lowest rates (M = 50.00%, SE = 3.86%), Nrp versus Rp− $t(51) = 1.51$, $p = .137$, $d = 0.21$. In the full sample, the level of recall for one target (beat-strike) was >3 SD below the mean level of recall for targets, when examined both as an Rp- target and Nrp target. Therefore, we removed the recall data for this target from analysis.[4]

To examine the effect of GAD on RIF of threat targets, we conducted a 2 (group: GAD vs. CTL) × 2 (cue type: all-neutral vs. neutral-threat) repeated measures ANOVA on RIF scores. There was no significant main effect of group, $F(1, 50) = 0.26$, $p = .614$, $\eta^2_{partial} = .01$, or cue type, $F(1, 50) = 1.53$, $p = .222$, $\eta^2_{partial} = .03$. As predicted, the analysis yielded a significant interaction of group and cue

Table 1. Proportion of Correctly Recalled Targets for the GAD and CTL Groups

	GAD	CTL
	M (*SD*)	*M* (*SD*)
All-neutral cues		
Rp+ (neutral)	0.59 (0.30)	0.67 (0.27)
Rp– (neutral)	0.49 (0.31)	0.51 (0.25)
Nrp (neutral)	0.58 (0.20)	0.52 (0.26)
Neutral-threat cues		
Rp+ (neutral)	0.59 (0.25)	0.60 (0.27)
Rp– (threat)	0.59 (0.32)	0.51 (0.27)
Nrp (neutral)	0.60 (0.25)	0.54 (0.26)
Nrp (threat)	0.52 (0.28)	0.56 (0.30)

Note: CTL = never-disordered control participants; GAD = participants with current generalized anxiety disorder; Nrp = unpracticed cue–unpracticed target; Rp+ = practiced cue–practiced target; Rp– = practiced cue–unpracticed target.

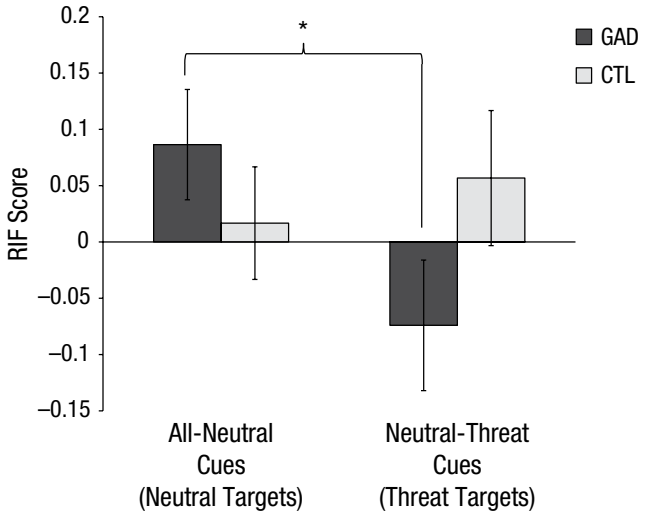

Fig. 1. RIF scores as a function of cue type across the GAD and CTL groups. CTL = never-disordered control participants; GAD = participants with current generalized anxiety disorder. Error bars = ±1 standard error. *Significant pairwise comparison, $p = .021$.

type, $F(1, 50) = 4.23$, $p = .045$, $\eta^2_{partial} = .08$. Planned pairwise comparisons indicated that the GAD group exhibited less RIF of threat targets ($M = -0.07$, $SE = 0.06$) than of neutral targets ($M = 0.09$, $SE = 0.05$), $p = .021$, $d = .48$. In contrast, the CTL group did not exhibit this pattern (RIF of threat targets: $M = 0.06$, $SE = 0.06$; RIF of neutral targets: $M = 0.02$, $SE = 0.05$), $p = .572$, $d = 0.11$. The significant interaction of group and cue type on RIF scores is presented in Figure 1.

In a follow-up analysis, we conducted a 2 (group: GAD vs. CTL) × 2 (cue type: all-neutral vs. neutral-threat) repeated measures ANCOVA on RIF scores, with STAI-T, CES-D, PANAS–Positive Affect, and PANAS–Negative Affect scores as covariates. The significance levels for all effects were identical to those reported earlier, and there were no significant main or interaction effects of STAI-T, CES-D, PANAS–Positive Affect, and PANAS–Negative Affect scores on RIF scores, all *p*s > .220.

Associations with RIF in the GAD group

Within the GAD group, we examined correlations between RIF scores for threat targets and (a) number of worry topics endorsed on the GAD-Q-IV and (b) PSWQ Worry Engagement score, partialing the effects of STAI-T, CES-D, PANAS–Positive Affect, and PANAS–Negative Affect scores. Less RIF of threat targets was significantly correlated with greater number of worry topics, $r(21) = -.42$, $p = .046$, medium to large effect size (ES), but was not significantly correlated with PSWQ Worry Engagement, $r(21) = -.31$, $p = .151$, medium ES. There was no significant association between RIF scores for neutral targets and either GAD-Q-IV number of worry topics, $r(21) = .02$, $p = .913$, or PSWQ Worry Engagement, $r(21) = .02$, $p = .934$. To ensure that this association was unique to a GAD-specific construct, we examined correlations between RIF scores for threat targets and STAI-T, CES-D, PANAS–Positive Affect, and PANAS–Negative Affect scores, partialing the effects of number of worry topics and PSWQ Worry Engagement. None of these correlations was significant, *r* range = –.03 to .39, all *p*s > .053; the one correlation that was marginally significant indicated that more RIF of threat targets was marginally correlated with higher STAI-T score, $r(23) = .39$, $p = .053$, medium to large ES.

Discussion

This is the first study to investigate the automatic inhibition of threat-relevant information in GAD. As hypothesized, individuals diagnosed with GAD uniquely failed to exhibit RIF of threat targets and exhibited less RIF of threat targets than neutral targets, indicating impaired inhibitory control over threat information. This pattern of findings was significantly different from that in CTL participants, who did not exhibit disproportionate RIF of threat versus neutral targets.

The formulation that impaired inhibitory control over threat-relevant information is central to GAD is further supported by the unique association of poorer inhibition of threat words to greater self-reported number of worry topics within the GAD group. This finding suggests that impaired inhibitory mechanisms are involved in the pervasiveness of worry in GAD. The correlation between inhibition of threat words and worry engagement as

assessed using the PSWQ was slightly weaker and not statistically significant, but represented a medium ES. In addition, there was no significant association between poorer inhibition of threat targets and trait anxiety, depressive symptoms, or positive or negative affect, indicating that only GAD-specific pathology was significantly associated with the observed effects. In the one marginally significant partial correlation with trait anxiety, better inhibition of threat words was associated with higher trait anxiety. Thus, once the influence of worry is partialed, higher trait anxiety levels in GAD may have an opposing relation with stronger inhibition of threat material. Later, we discuss the theoretical and clinical implications of these findings.

Supporting the validity of our modified RIF paradigm, in the full sample we found numerically that Rp+ neutral targets were recalled at the highest rates, followed by Nrp neutral targets, and then by Rp− neutral targets. The difference in recall rates between Nrp and Rp− neutral targets (5.29%) was similar to the difference in recall rates that were reported for Nrp and Rp− weak associates in the original RIF paradigm (6.3%; Anderson et al., 1994, Experiment 1), and in this study was not statistically significant and represented a small ES. In considering this finding, we utilized a novel stimulus selection method to derive a set of cues that were associated with neutral and threatening targets to the same degree. This balancing as a function of target valence likely resulted in a weaker overall associative strength between cues and targets than would have occurred had we not needed to manipulate target valence. This weaker associative strength, in turn, may have served to slightly reduce overall RIF in this study.

Impaired inhibitory control over threat information, combined with intact inhibitory control over neutral information, may contribute to pathological worry and memory biases in GAD. For example, these results suggest that following everyday situations that involve both neutral and threatening representations (e.g., meeting with one's boss at work, reviewing one's finances), individuals with GAD disproportionately bring to mind the threatening content, even (or especially) when they attempt to retrieve the neutral content (see Amir et al., 2001, for a different interpretation in social anxiety disorder). This implication is intriguing given theory that persons with GAD engage in worry in an attempt to avoid or neutralize aversive images (Borkovec, 1994); even when they occur at an automatic level, repeated attempts to inhibit the retrieval of threat material apparently fail and may inadvertently give rise to increasingly anxious thinking. This notion is consistent with recent theoretical work on pathological worry and impairments in executive control over threat-relevant intrusions in working memory (Hirsch & Mathews, 2012). Furthermore, impaired inhibitory control may underlie perseverative thought in psychopathology more broadly. For instance, in major depressive disorder (MDD), deficient ability to remove negative material from working memory has been found to be associated with rumination (Joormann & Gotlib, 2008), another form of perseverative thinking that shares properties with worry. Given the high comorbidity of GAD and MDD (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), it will be particularly informative to conduct a transdiagnostic investigation of inhibitory processing of different types of emotional stimuli (e.g., threat, loss) across both disorders and in relation to both forms of repetitive thought. Such a study would integrate the literatures on inhibitory control in GAD and MDD and potentially pinpoint targets for transdiagnostic intervention.

With respect to current implications for intervention, these results indicate that targeting a deficit in inhibition of threat material may be an important component of treatment for GAD. For example, mindfulness-based interventions may help individuals to disengage from worry and facilitate the development of adaptive executive control processes (e.g., Jha, Stanley, Kiyonaga, Wong, & Gelfand, 2010). In addition, as has been the case with emotional working memory training programs (e.g., Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013), the current retrieval-practice paradigm could be modified and conducted repeatedly to train individuals to automatically inhibit threat material, and the effects on worry and other symptoms could be examined. This not only would interrogate the causal influence of automatic inhibitory impairments on worry, the core cognitive pathology of GAD, but also may ultimately curtail this pernicious thought process. Promising data have been reported by Daches and Mor (2014), who found that training individuals with high levels of trait rumination to repeatedly inhibit negative words in working memory reduced their subsequent levels of rumination, and by Cohen, Mor, and Henik (2015), who reported similar beneficial effects on rumination when individuals received training in executive control processes prior to viewing negative images.

There are four noteworthy limitations of the present study. First, although these findings implicate impaired retrieval inhibition of threat as one maintaining mechanism in GAD, we did not assess threat appraisal biases, which likely are a synergistic mechanism underlying preferential processing of threat (Mogg & Bradley, 1998). This limitation is mitigated by the fact that RIF was calculated relative to Nrp threat targets, such that elevated salience or appraisal of threat material alone is insufficient to explain the current findings, and an inhibitory account is necessary. Nevertheless, future studies should include an assessment of participants' subjective appraisal of threat targets. Second, we only assessed retrieval

inhibition of threat material in this study. Future studies should examine whether deficits in retrieval inhibition in GAD extend to other types of emotional information, and should explore other inhibitory processes, such as executive control over threat distractors, which may be associated with attentional biases in GAD (Hirsch & Mathews, 2012). Third, we carefully selected a standardized set of cue–target pairs to maximize the internal validity of our paradigm. Because sources of worry in GAD are variable across individuals, it is possible that these tightly controlled threat targets were not maximally relevant to all participants. Follow-up studies should develop stimuli that capture additional worry themes (e.g., interpersonal concerns). Fourth, we used a category-cued recall test for both theoretical and empirical reasons; this type of test, however, combines effects that occur at the levels of cue–target association and of target representation. Further work should build on this translational RIF paradigm by developing independent cues for the test phase that would help to disambiguate these effects.

In summary, the current results demonstrate that GAD is characterized by impaired retrieval inhibition of threat-relevant material, a finding that has important implications for the understanding and treatment of this disorder. Future translational research linking inhibitory mechanisms to cognitive pathology in GAD will facilitate the development of novel interventions that are grounded in basic cognitive science.

Author Contributions

K. Kircanski developed the study concept. K. Kircanski, D. C. Johnson, R. A. Bjork, and I. H. Gotlib contributed to the study design. M. Mateen performed data collection. K. Kircanski and M. Mateen performed the analysis and interpretation under the supervision of I. H. Gotlib. K. Kircanski drafted the manuscript. D. C. Johnson, R. A. Bjork, and I. H. Gotlib. provided critical revisions. All authors approved the final version of the manuscript for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Supplemental Material

Additional supporting information may be found at http://cpx.sagepub.com/content/by/supplemental-data.

Notes

1. In the GAD group, 22 participants met criteria for a comorbid anxiety or depressive disorder, and there were no significant differences between GAD participants with and without a comorbid anxiety or depressive disorder in RIF of threat or neutral targets.
2. The stimulus "choke-engine" was not in the Free Association Norms; we added it to balance the cues on possible subcategorization. In addition, four cues each had one target with no frequency data.
3. One CTL participant did not provide race/ethnicity or education level.
4. The inclusion of data for "beat-strike" did not diminish the primary findings. With respect to the 2 (group) × 2 (cue type) ANOVA on RIF scores, there was no significant main effect of group, $F(1, 50) = 0.15$, $p = .700$, $\eta^2_{partial} = .00$, or cue type, $F(1, 50) = 1.63$, $p = .207$, $\eta^2_{partial} = .03$. As predicted, the analysis yielded a significant interaction of group and cue type, $F(1, 50) = 4.49$, $p = .039$, $\eta^2_{partial} = .08$. Planned pairwise comparisons indicated that the GAD group exhibited less RIF of threat targets ($M = -0.06$, $SE = 0.05$) than of neutral targets ($M = 0.09$, $SE = 0.05$; $p = .018$, $d = .45$), whereas the CTL group did not exhibit this pattern (RIF of threat targets: $M = 0.05$, $SE = 0.06$; RIF of neutral targets: $M = 0.02$, $SE = 0.05$; $p = .562$, $d = 0.12$). With respect to correlations with RIF scores in the GAD group, less RIF of threat targets was significantly correlated with greater number of worry topics, $r(21) = -.49$, $p = .017$, medium to large effect size (ES), and was marginally correlated with PSWQ Worry Engagement score, $r(21) = -.39$, $p = .068$, medium to large ES.

References

Albu, M. (2008). Automatic and intentional inhibition in patients with generalized anxiety disorder. *Cognition, Brain, Behavior*, *12*, 233–249.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Amir, N., Badour, C. L., & Freese, B. (2009). The effect of retrieval on recall of information in individuals with posttraumatic stress disorder. *Journal of Anxiety Disorders*, *23*, 535–540.

Amir, N., Coles, M. E., Brigidi, B., & Foa, E. B. (2001). The effect of practice on recall of emotional information in individuals with generalized social phobia. *Journal of Abnormal Psychology*, *110*, 76–82.

Anderson, M. C. (2003). Rethinking interference theory: Executive control and the mechanisms of forgetting. *Journal of Memory and Language*, *49*, 415–445.

Anderson, M. C., Bjork, R. A., & Bjork, E. L. (1994). Remembering can cause forgetting: Retrieval dynamics in long-term

memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *20*, 1063–1087.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin*, *133*, 1–24.

Bishop, S. J. (2007). Neurocognitive mechanisms of anxiety: An integrative account. *Trends in Cognitive Sciences*, *11*, 307–316.

Borkovec, T. D. (1994). The nature, functions, and origins of worry. In G. Davey & F. Tallis (Eds.), *Worrying: Perspectives on theory, assessment and treatment* (pp. 5–33). Oxford, England: Wiley.

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clinical Psychological Science*, *3*, 15–25.

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research*, *38*, 160–171.

Dugas, M. J., Anderson, K. G., Deschenes, S. S., & Donegan, E. (2010). Generalized anxiety disorder publications: Where do we stand a decade later? *Journal of Anxiety Disorders*, *24*, 780–784.

First, M. B., Spitzer, R., Gibbon, M., & Williams, J. (1996). *Structured Clinical Interview for DSM-IV Axis I Disorders–Clinician Version (SCID-CV)*. Washington, DC: American Psychiatric Press.

Fresco, D. M., Heimberg, R. G., Mennin, D. S., & Turk, C. L. (2002). Confirmatory factor analysis of the Penn State Worry Questionnaire. *Behaviour Research and Therapy*, *40*, 313–323.

Hirsch, C. R., & Mathews, A. (2012). A cognitive model of pathological worry. *Behaviour Research and Therapy*, *50*, 636–646.

Jelinek, L., Rietschel, L., Kellner, M., Muhtz, C., & Moritz, S. (2012). The effect of practice on the recall of salient information in obsessive-compulsive disorder. *Psychiatry Research*, *198*, 89–93.

Jha, A. P., Stanley, E. A., Kiyonaga, A., Wong, L., & Gelfand, L. (2010). Examining the protective effects of mindfulness training on working memory capacity and affective experience. *Emotion*, *10*, 54–64.

Joormann, J., & Gotlib, I. H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *Journal of Abnormal Psychology*, *117*, 182–192.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*, 617–627.

Mathews, A., & MacLeod, C. (2005). Cognitive vulnerability to emotional disorders. *Annual Review of Clinical Psychology*, *1*, 167–195.

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy*, *28*, 487–495.

Mogg, K., & Bradley, B. P. (1998). A cognitive-motivational analysis of anxiety. *Behaviour Research and Therapy*, *36*, 809–848.

Nelson, D. L., McEvoy, C. L., & Schreiber, T. A. (1998). *The University of South Florida word association, rhyme, and word fragment norms*. Retrieved from http://web.usf.edu/FreeAssociation/

Newman, M. G., Zuellig, A. R., Kachin, K. E., Constantino, M. J., Przeworski, A., Erickson, T., & Cashman-McGrath, L. (2002). Preliminary reliability and validity of the Generalized Anxiety Disorder Questionnaire–IV: A revised self-report diagnostic measure of generalized anxiety disorder. *Behavior Therapy*, *33*, 215–233.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*, 385–401.

Rey, A. (1941). The psychological examination in cases of traumatic encepholopathy. *Archives de Psychologie*, *28*, 215–285.

Schweizer, S., Grahn, J., Hampshire, A., Mobbs, D., & Dalgleish, T. (2013). Training the emotional brain: Improving affective control through emotional working memory training. *Journal of Neuroscience*, *33*, 5301–5311.

Spielberger, C. D., Gorscuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologist Press.

Storm, B. C., & Levy, B. J. (2012). A progress report on the inhibitory account of retrieval-induced forgetting. *Memory & Cognition*, *40*, 827–843.

Uttl, B. (2002). North American Adult Reading Test: Age norms, reliability, and validity. *Journal of Clinical and Experimental Neuropsychology*, *24*, 1123–1137.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063–1070.

Williams, J. M. G. (1988). *Cognitive psychology and emotional disorders*. Chichester, England: Wiley.