Cognitive-behavior therapy resolves implicit fear associations in generalized anxiety disorder

Andrea Reinecke a,*, Mike Rinck b, Eni S. Becker c, Jürgen Hoyer c

a University of Oxford, Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX, UK
b Behavioural Science Institute, Radboud University Nijmegen, The Netherlands
c Dresden University of Technology, Germany

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Abstract

Background: Cognitive schema theories postulate that anxiety disorders are associated with excessive fear associations in memory. For generalized anxiety disorder (GAD), it has been shown that patients not only exhibit negative implicit evaluations of clearly negative worry words (e.g., cancer), but also a generalization of this effect to neutral words (e.g., diagnosis). This study assessed the sensitivity of this bias, which has been interpreted as an indicator of a pathologically broadened fear structure, to cognitive-behavioral therapy (CBT).

Methods: An Extrinsic Affective Simon task was used to measure implicit associations with idiosyncratic neutral and negative worry words in 23 GAD patients and 25 healthy controls (HC). Patients were tested before and after CBT, and half of them were additionally tested while waiting for treatment. Clinical symptoms were measured before and after treatment, and at 6-months follow-up.

Results: CBT normalized bias for neutral words, and the extent of bias reduction during treatment predicted the extent of additional symptom improvement during the 6 months following intervention. Furthermore, the amplitude of pre-treatment bias predicted the onset of CBT response, with lower bias predicting immediate symptom improvement at the end of treatment, and higher bias predicting delayed treatment effects during the 6 months follow-up.

Conclusions: Biased implicit evaluation of neutral worry targets does not represent an enduring vulnerability factor for the development of GAD but is related to heightened levels of state worry. Furthermore, the normalization of this bias might be a crucial factor in the therapeutic action of CBT.

Generalized anxiety disorder (GAD) is characterized by excessive, seemingly uncontrollable worrying (DSM-IV-TR; American Psychological Association, 2000). Research has shown that GAD-specific worry is of a rather verbal, thought-related nature, instead of being perceptual (Borkovec & Inz, 1990). It is considered to play a key role in avoidant behavior, as it is believed to prevent the emotional processing of more aversive, image-based intrusions (Borkovec, Alcaine, & Behar, 2004). Thus, the occurrence of worry is negatively reinforced by the experience of immediate, although only temporary, fear reduction. However, it also prevents habituation to the fear trigger and therefore leads to an increase in the relevance and frequency of intrusions (Borkovec & Hu, 1990), a phenomenon which might explain the clinical observation that the fear reaction in GAD becomes more and more generalized to peripheral stimuli: a fear response is not only triggered by obvious stimuli such as a news report about an accident, but also by rather neutral or even positive stimuli, as for instance a text from the partner letting them know that they will be able to drive back home sooner than expected.

This stimulus generalization might be best explained by cognitive schema theories (Fo, Huppert, & Cahlill, 2006; Lang, Cuthbert, & Bradley, 1998), postulating that fear is encoded in memory as a network of fear-related situations (e.g., partner on their way home), fear triggers (e.g., news report of an accident, leading to image of the partner being in an accident), and fear responses (e.g., increased heartbeat, agitation). These different information units are thought to be interconnected, with any input at any level being able to activate the whole fear system. It is assumed that anxiety disorders are underpinned by particularly elaborate connections and strong activations within this fear network, which might for instance involve a higher number of fear trigger connections. Recent experimental research has
confirmed that in patients with GAD, the fear network is pathologically expanded, as even neutral stimuli can act as fear triggers (Reinecke, Becker, Hoyer, & Rinck, 2010). In this study, using a single-target implicit association task (STIAT), we had assessed automatic evaluation of worry-related stimuli in GAD patients and healthy control participants. Participants first categorized single black-printed valence words as positive or negative, thus implicitly giving a positive versus negative meaning to two response keys. In the main experiment, the same two keys were used to additionally react to red-printed words: in one of the blocks, participants were instructed to use the positive-key to respond to red-printed words, in the other block they were asked to use the negative-key. These words were GAD-specific targets, and implicit evaluation of these words can be measured by assessing the difference in reaction time when responding with the positive versus the negative key. Previous research has shown that a reaction is faster if the valence of the target matches the valence of the response key (Greenwald, McGhee, & Schwartz, 1998). To investigate the extent of stimulus generalization, two types of target words were used: words that were a direct source of worry, such as cancer or infidelity, and words that were neutral and only indirectly worry-related, as for instance diagnosis or marriage. Both patients and controls showed negative implicit evaluations of clearly negative worry words. However, only GAD patients also showed a similarly negative implicit evaluation of neutral worry words, although they explicitly rated these words as positive. These results mirror the clinical observation of stimulus generalization in GAD patients: fear becomes increasingly associated with more peripheral, not per se threatening stimuli, resulting in even neutral or positive stimuli being capable of triggering the worry process.

Cognitive theories of anxiety (e.g., Foa et al., 2006; Williams, Watts, MacLeod, & Mathews, 1997) consider such biases in emotional processing as key agents in the development and maintenance of anxiety disorders such as GAD. These theories ultimately have important implications for clinical practice and treatment targets, and are informed by experimental evidence. To refine current theoretical assumptions regarding the functional relationship between pathological states and cognitive biases, it is essential to investigate whether the bias is susceptible to treatment or whether it instead reflects an enduring vulnerability factor. Moreover, investigating the relationship between pre-treatment bias and treatment response potentially has important implications for patient-tailored stratification decisions regarding treatment type and duration, prior to the cost-intensive application of an intervention.

Cognitive-behavioral treatment (CBT) is recommended as a first-line treatment for GAD (National Institute for Health and Clinical Excellence, 2007). Research has shown that therapy reduces attentional bias for threat (Mathews, Mogg, Kentsish, & Eysenck, 1995; Mogg, Bradley, Millar, & White, 1995), suggesting that the bias might play a key role in the maintenance of the disorder but does not represent a stable vulnerability factor for the development of GAD. However, these studies have not included waiting-list patient groups to be able to evaluate to what extent bias changes are significantly different from mere retest effects. Thus, reliable conclusions regarding the role of this bias in the pathogenesis of GAD cannot be drawn yet. Also, no research has yet addressed whether CBT modifies implicit threat evaluations in GAD into a more benign direction. Can CBT reverse the expansion of the fear network in memory, seen in the formation of more negative implicit evaluations of even neutral words in GAD, and narrow down stimulus generalization? Or is this biased implicit evaluation a more chronic vulnerability factor for the development of GAD and, thus, resistant to treatment? Recent studies addressing changes in implicit fear bias in patients with other anxiety disorders following CBT provide mixed evidence with respect to whether these biases are sensitive to treatment. Some studies do report malleability of bias in spider phobia (Teachman & Woody, 2003), and a correlation between change in implicit fear associations and symptom severity in panic disorder (Teachman, Marker, & Smith-Janik, 2008). However, no patient waiting groups had been included in these studies, making it difficult to disentangle real treatment effects from mere test-retest effects. Another study including such a patient waiting group failed to find an effect of a single-block session of CBT on implicit bias over and above retest effects (Huijing & de Jong, 2009). However, experimental post-assessment took place immediately after treatment, although bias change might require a more thorough consolidation of treatment effects. Follow-up research into treatment sensitivity of implicit fear bias needs to take these limitations into account.

Regarding the prediction of treatment success by the magnitude of cognitive bias before treatment, similarly little research exists to date. However, if it were possible to identify in advance patients who are less likely to respond to a certain treatment, this would allow earlier application of an individually more auspicious, alternative form of therapy. This seems particularly relevant in GAD, where only 50–70% of patients benefit from CBT interventions, and a subgroup of those relapse during follow-up (for a review, see Hoyer & Gloster, 2009). One previous study has shown that patients with a particularly pronounced negative interpretation bias before treatment showed higher levels of residual symptoms at the end of therapy (Butler, 1993). Although this study is unique and progressive in that it investigates the potential of cognitive bias as a predictor of treatment success, the interpretability of results is limited: the applied measure of interpretation bias might have allowed for strategic response bias, and no follow-up data on symptom severity is available to estimate to which degree treatment-induced bias change predicts symptom stability after the end of treatment.

In this study, we examined whether negative implicit evaluation of neutral worry-words in GAD, shown in our earlier study (Reinecke et al., 2010), is sensitive to CBT, and whether the magnitude of pre-treatment bias and of bias change predicts treatment response. Cognitive bias and clinical symptoms of worry and thought suppression were assessed before and after CBT treatment in a group of GAD patients and compared to a group of healthy controls at matching time points. In addition, in order to overcome the methodological limitations described above, the study design incorporated a patient waiting list group tested twice before treatment to be able to distinguish treatment effects from mere retest effects. Moreover, subjective symptoms of worry and anxiety were also assessed at 6-month follow-up to establish whether the magnitude of pre-treatment bias and the degree of bias change during treatment are associated with symptom stability after treatment discontinuation. As in our earlier study (Reinecke et al., 2010), idiosyncratic stimulus materials were used in the experimental task to ensure that participants worked with words relating to their main worry topic.

We examined the main hypothesis that GAD-specific biased implicit evaluations of neutral worry words (e.g., marriage as opposed to the negative worry word infidelity) are susceptible to CBT treatment, over and above mere retest effects. In addition, post-hoc exploratory analyses aimed at determining the relationships between i) the magnitude of implicit bias at baseline and the magnitude of treatment response, and ii) pre-treatment bias and bias change during treatment with symptom development during the 6 months following treatment.
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