

# Research Article

## GENERALIZED IMPLICIT FEAR ASSOCIATIONS IN GENERALIZED ANXIETY DISORDER

Andrea Reinecke, Ph.D.,<sup>1\*</sup> Eni S. Becker, Ph.D.,<sup>2</sup> Juergen Hoyer, Ph.D.,<sup>3</sup> and Mike Rinck, Ph.D.<sup>2</sup>

**Background:** Cognitive schema theories of anxiety postulate that higher-level cognitive processes such as attention and memory are guided by underlying distorted fear associations. While numerous studies investigated these disorder-specific, biased processes, hardly any research addressed the underlying schemata themselves. In particular, no study has ever addressed implicit fear associations in Generalized Anxiety Disorder (GAD). In addition, no study has ever experimentally investigated the clinical observation that in GAD, patients' worry processes seem to be triggered by a broad range of materials, even by neutral or positive stimuli. **Methods:** We used a Single Target Implicit Association Task (STIAT) to investigate implicit associations and stimulus generalization with clearly negative worry-related words (e.g., cancer, bankruptcy) and neutral words that are only indirectly related to worry topics (e.g., doctor, bank). Participants were 39 GAD patients and 23 healthy controls. **Results:** In line with our expectations, both groups showed negative implicit associations with negative target words, and only GAD patients also associated neutral words with negative attributes. **Conclusions:** These results support the hypothesis that GAD patients' fear associations generalize to stimuli that are only peripherally related to the core of their worries. *Depression and Anxiety* 27:252–259, 2010. © 2010 Wiley-Liss, Inc.

**Key words:** fear associations; implicit associations; generalized anxiety disorder; GAD; STIAT

Generalized Anxiety Disorder (GAD) is characterized by excessive worry concerning a broad range of topics. Although patients experience these worrying thoughts as highly aversive and uncontrollable,<sup>[1]</sup> they primarily seem to function as an avoidance strategy in emotional processing. More recent models of GAD<sup>[2–4]</sup> postulate that worry—a predominantly cognitive strategy—serves to avoid prolonged confrontation with intrusive images of feared catastrophes and to down-regulate high levels of physiological and emotional arousal caused by these images. This is confirmed by empirical studies showing that worrying reduces the somatic component of anxiety.<sup>[5,6]</sup> Therefore, worrying is directly negatively reinforced by an immediate successful suppression of negative arousal, which in turn leads to increased worrying. As worry compromises emotional processing and habituation, it is also related to an increase in the frequency of intrusions, leading more and more toward a GAD diagnosis. With a life-time prevalence of 5–6%,<sup>[7]</sup> the disorder not only occurs quite often, it also involves enormous human

and economic burden.<sup>[8]</sup> It is also estimated that more than 80% of GAD patients fulfil diagnostic criteria for at least one additional DSM diagnosis.<sup>[9,10]</sup>

<sup>1</sup>University of Oxford, Oxford, United Kingdom

<sup>2</sup>Behavioural Science Institute, Radboud University Nijmegen, The Netherlands

<sup>3</sup>Dresden University of Technology, Dresden, Germany

The authors disclose the following financial relationship within the past 3 years: Contract grant sponsor: Deutsche Forschungsgemeinschaft.

\*Correspondence to: Andrea Reinecke, University of Oxford, Department of Psychiatry, Warneford Hospital, OX3 7JX Oxford, United Kingdom. E-mail: andrea.reinecke@psych.ox.ac.uk

Received for publication 11 May 2009; Revised 14 December 2009; Accepted 15 December 2009

DOI 10.1002/da.20662

Published online 28 January 2010 in Wiley InterScience (www.interscience.wiley.com).

To date, the basic factors of successful treatment of generalized anxiety are poorly understood. Despite highly standardized and rationalized therapy approaches, not all patients benefit from treatment, and evidence shows that GAD is the least effectively treated anxiety disorder.<sup>[11,12]</sup> Recently, cognitive factors have been emphasized as an important key factor in the etiology and treatment of generalized anxiety and other anxiety disorders.<sup>[13–16]</sup> Cognitive models of anxiety assume that cognitive fear schemata guide anxiety-specific information processing. Thus, detailed knowledge of these processing biases and underlying schemata is important for the enhancement of diagnostic assessments and therapeutic approaches, as well as for predictions of disorder onset and relapse. Nevertheless, while a few studies addressed these basic schemata in analog social<sup>[17]</sup> and phobic anxiety<sup>[18,19]</sup> and patients with panic disorder,<sup>[20]</sup> no study ever investigated fear schemata in GAD patients.

For instance, the *bio-informational theory* of Lang et al.<sup>[21]</sup> postulates that fear is coded in memory as a network of mutually activating information units. These units include information about emotion-related situations (e.g., partner on a business trip), stimuli (e.g., news report of an accident) and responses (e.g., physiological, behavioral). Importantly, this fear network can be activated by any input that matches the stored representations at any of these levels and, thus, does not depend on a real existing stimulus.<sup>[21]</sup> As the amygdala is connected with the network, fear reactions can be triggered automatically and independently, even before a stimulus is consciously processed.<sup>[22]</sup>

In GAD, the fear network seems to be rather encompassing. As a result, even neutral or pleasant situations and stimuli are capable of activating the fear network. Clinical practice provides numerous examples that the fear networks in GAD patients are easily triggered, for instance by a news report (*Is it my partner who is involved in the accident on the M40?*), a phone call with a friend (*Will we always stay friends?*), or a routine health check (*Could I have cancer?*). It is assumed that excessive control behavior (one of which is worry) and, thus, failure to experience habituation,<sup>[23]</sup> create more and more generalized triggers of the worry process.<sup>[14]</sup> However, in contrast to these widely acknowledged experiences from clinical settings, no empirical study has ever addressed the proposed stimulus generalization in GAD experimentally. Instead, our knowledge of implicit GAD schemata is restricted to indirect conclusions from research on information processing biases: So far, most empirical studies addressed the consequences of cognitive fear schemata, for instance biases in attention, memory, or interpretation, instead of the schemata themselves.<sup>[24]</sup> A few of these studies do indeed point to the existence of a broad, generalized fear network in GAD, because they show biases for a wide range of emotional stimuli.<sup>[25]</sup>

The assessment of fear networks in GAD patients has become possible through the development of

performance-based reaction time (RT) tasks.<sup>[26]</sup> These tasks are designed to reflect affective associations with minimal influence of intentional processes. Frequently, these tasks measure how strongly a target category (e.g., spiders) is associated with an attribute category (e.g., unpleasant) relative to a second attribute category (e.g., pleasant). One of these tasks is the *Single Target Implicit Association Task* (STIAT),<sup>[27]</sup> which is highly similar to the *Single Category Implicit Association Test*.<sup>[28]</sup> In the STIAT, latencies of responses to three different stimulus types are measured, using only two response keys. Compared to the frequently used *Implicit Association Test* (IAT)<sup>[29]</sup> the STIAT is advantageous in that it allows to measure implicit associations with a single target category (e.g., spiders), without the need for a second target category.

In the first practice block of a STIAT, participants use the two keys to categorize attribute words (e.g., beauty, anxiety) into pleasant versus unpleasant words. In a second practice block, they learn to respond with one of the two keys whenever a target word is shown, for instance, words related to spiders such as “spider,” which might always require pressing the “unpleasant” key. Thus, these words do not require a categorization, just a simple reaction. In the two critical test blocks of the STIAT, the two tasks are combined: participants continue categorizing attribute words into pleasant versus unpleasant ones, and they continue responding to the target words. As targets, stimuli are used whose implicit evaluation is intended to be measured. In one of the two critical test blocks, participants always react to these target words with the “pleasant” key, in the other test block with the “unpleasant” key. Target words can be defined by a specific category (e.g., spider-related words<sup>[27]</sup>) or by surface characteristics (e.g., lowercase words<sup>[28]</sup>). Results of previous studies show that individuals react more quickly to negatively associated targets with the negative key compared to the positive key. Successful applications of the STIAT in the context of health behavior have already been reported.<sup>[30–32]</sup> To the best of our knowledge, however, no study ever used this task or another one to assess disorder-specific implicit fear associations in GAD.

In this article, we present data on the application of a STIAT to assess implicit fear associations in GAD. At the same time, this is the first study that taps into fear schemata in GAD at all. To disguise the stimulus feature of interest (i.e., the content of the target words) and, thus, make the task more indirect, the instructions defined targets by surface characteristics (i.e., “react to all red-printed words”) instead of meaning. These target words were particularly carefully selected. So far, research on cognitive biases in GAD usually employed unspecific stimulus materials, for instance emotional facial expressions or general fear-related words.<sup>[25,33–35]</sup> In this study, we particularly emphasized the presentation of individually selected, GAD-relevant words. Therefore, there were three versions of the experiment, each tailored to one of the typical main worry topics of

GAD patients: *relationships, health, and finances*. Each patient worked on the version that matched his or her main problem best. In addition, we designed the stimulus words so that they would allow for the investigation of stimulus generalization in GAD. Thus, the stimulus words for each topic consisted of clearly *negative* worry-related words from the content areas of relationships, health, and finances (e.g., divorced, cancer, bankruptcy) as well as *neutral* words from the same content areas (e.g., daughter, doctor, bank). We assume that the latter are indeed emotionally neutral for healthy controls (HCs), but negatively connoted for GAD patients. Therefore, we hypothesized that both patients and HCs would exhibit negative associations with the clearly negative, worry-related words, while only GAD patients would show negative associations with neutral, potentially worry-related words. The latter result would indicate that the fear network in GAD patients is indeed so elaborated that it includes also neutral worry-related words.

## METHODS

### PARTICIPANTS

Thirty-nine patients with GAD (GADs) and 23 HCs participated. Patients were recruited from the waiting list of the Dresden University of Technology outpatient clinic for psychotherapy. DSM-IV diagnoses were assessed using the Composite International Diagnostic Interview (CIDI).<sup>[36]</sup> Nine patients additionally fulfilled DSM-IV criteria for major depression, one for dysthymia, two for specific phobia, and one each for social phobia and panic disorder. On an average, patients scored  $M = 59.7$  ( $SD = 8.8$ ) on the Penn State Worry Questionnaire (PSWQ),<sup>[37,38]</sup>  $M = 14.3$  ( $SD = 7.0$ ) on the Beck Depression Inventory (BDI),<sup>[39,40]</sup> and  $M = 136.7$  ( $SD = 23.9$ ) on the Meta Cognition Questionnaire (MCQ).<sup>[41,42]</sup> HCs were recruited via newspaper ads. They were screened for psychiatric diagnoses using the “Diagnostisches Interview bei psychischen Störungen” (F-DIPS),<sup>[43]</sup> which is the German version of the Anxiety Disorders Interview Schedule for DSM-IV (ADIS).<sup>[44]</sup> They were required not to clinically or subclinically fulfil the criteria of any DSM-IV diagnosis, and not to fulfil any of the criteria for a GAD diagnosis. The two groups were matched with respect to educational level, age, and gender (*years of education*: GADs  $M = 14.4$ ,  $SD = 2.2$ ; HCs  $M = 14.4$ ,  $SD = 1.9$ ,  $t(60) = 0.07$ ,  $P = .948$ ; *age*: GADs  $M = 46.2$ ,  $SD = 13.4$ ; HCs  $M = 40.7$ ,  $SD = 13.8$ ,  $t(60) = 1.54$ ,  $P = .128$ ; *gender*: GADs 74% female; HCs 61% female,  $\chi^2(1) = 0.27$ ,  $P = .393$ ).

### MATERIALS AND APPARATUS

In this task, attribute words and target words were used. The *attribute words* consisted of two sets of eight generally pleasant words (*set 1*: cheery, fabulous, fascinating, joy, nature, pleasure, spectacular, sunrise/ *set 2*: beauty, coziness, flowerage, gorgeous, gratifying, marvellous, miracle, springlike, wonder) and eight unpleasant, fear-related words (*set 1*: agitated, anxiety, dizziness, jumpy, nervous, palpitation, strain, weary/ *set 2*: anxious, concerned, fear, nervousness, numb, stroke, tense, tired) each. The presentation of the two sets was counterbalanced across participants. All attribute words were presented in black color and font size 24. As *target words*, three different sets of word stimuli were used, related to the worry topics of *relationships, health, or finances*. These specific worry domains were selected based on earlier research showing that they are—although to

a stronger degree in GAD patients—the most frequent areas of worry among both GADs and controls.<sup>[4,45,46]</sup> Before an experimental session, participants were presented with these three topics and instructed to choose their individual main worry with respect to its frequency and intensity, or indicate if none of the areas were subject to worries. All participants were able to choose a main worry domain. Each patient worked with only one word set, selected to match his or her main worry topic. This way, the relationship words were used for 51% ( $N = 20$ ) of GADs and 48% ( $N = 11$ ) of HCs, health words for 39% ( $N = 15$ ) of GADs and 22% ( $N = 5$ ) of HCs, and finance words for 10% ( $N = 4$ ) of patients and 30% ( $N = 7$ ) of controls. For each of the three worry topics, two target word sets existed, and their presentation was counterbalanced across participants. Each target word set consisted of eight neutral words (*relationship set 1*: appointment, granny, kinship, marriage, neighbors, relatives, siblings, son/ *set 2*: chumminess, daughter, father, friend, grandchild, grandpa, matrimony, upbringing; *health set 1*: doctor, examination, medic, pharmacy, pulse, sickness certificate, tablet, vaccination/ *set 2*: blood pressure, check-up, diagnosis, doctor, doctor’s appointment, health insurance, medication, nurse; *finances set 1*: bank assistant, cash payment, check, direct debit, interest, pension, savings, stock market/ *set 2*: cash machine, bank, bank account, interest rate, loan contract, money, payment, savings) and eight negative words (*relationship set 1*: deserted, dispute, divorced, indignity, infidelity, lonesome, outsider, parting/ *set 2*: alone, argument, ingratitude, loneliness, offended, reject, separated, widowed; *health set 1*: cancer, emergency doctor, death, incurable, intensive care, nursing case, pain, sick/ *set 2*: accident, die, disability, disease, emergency room, fatal, high-maintenance, melanoma; *finances set 1*: bust, debts, demand note, execution, impoverished, market crisis, moneyless, welfare case/ *set 2*: bankruptcy, indebted, marshal, order to pay, rent increase, ruin, social benefits, poverty). They were printed in red color and font size 24. The valence and topic-relatedness of all stimulus words was established in a pilot study with a group of healthy participants who did not participate in the experiment reported here.

### PROCEDURE

At the beginning of the experimental session participants completed the *Inventory to Diagnose Depression* questionnaire (IDD)<sup>[47]</sup> and the trait form of the *State-Trait Anxiety Inventory* (STAIT).<sup>[48]</sup> The state form (STAIS) was given before and after the experimental task. The STAIT experiment involved a sequence of five blocks: (a) one attribute categorization block, and (b) four combined blocks that required simultaneous categorization of attributes and targets. Each word stimulus was preceded by a fixation cross for 500 msec and was shown until a response was made. At the beginning of the experiment, all subjects performed the *attribute block*. Participants had to categorize the attribute words according to their valence. They were asked to press one of two keys in response to pleasant words (“pleasant key”) and the other key in response to unpleasant words (“unpleasant key”). The general term “unpleasant” was used in the instructions, although all unpleasant words were specific in that they were fear related (rather than, e.g., related to sadness or disgust). The assignment of the left and the right key to “pleasant” and “unpleasant” was counterbalanced across participants. Stimuli in this block were eight positive and eight fear-related attribute words, each one presented twice in pseudo-randomized order.

Afterwards, subjects were presented with four *attribute-target-combination blocks*. In these blocks, attribute words and target words appeared in a mixed random order. In each of these blocks, attribute words were presented in 48 out of the 64 trials, and participants continued to classify these words according to their valence by pressing either the pleasant key or the unpleasant key. The remaining one quarter of trials were target trials. Targets were distinguishable

from attributes by their red print color. Participants did not categorize these words, instead they always responded to them by pressing the same key. In two out of the four combination blocks, they were asked to always respond by pressing the left key, in the other two blocks by pressing the right key. Moreover, in two of the four combination blocks, the negative worry words (e.g., *accident*) were used as target words. In the other two blocks, the neutral worry words (e.g., *doctor*) were shown. Thus, two of the combined blocks allowed a GAD-compatible reaction to the targets (negative targets and fear-unpleasant key, neutral targets and fear-unpleasant key), and two blocks required a GAD-incompatible response (negative targets and pleasant key, neutral targets and pleasant key). In each block, half of the trials required responding with the pleasant key and half required the unpleasant key. To this end, each block contained 16 attribute words that required the same response as the 16 target words, while 32 attribute words required the opposite response. The order of the four blocks was counterbalanced across participants, such that each of four possible orders was used equally often: they started with either the two blocks containing the negative targets or the two blocks containing the neutral targets. Within each half, they encountered the compatible or the incompatible block first. The experiment was conducted on an Apple Macintosh computer with a 17 in screen and a resolution of 1024 × 768 pixels.

After the STIAT task, participants gave explicit valence ratings for the target words of all three domains on a 7-point scale ranging from -3 (very unpleasant) to +3 (very pleasant).

## RESULTS

### QUESTIONNAIRES

The mean questionnaire scores for the two groups of participants are presented in Table 1. While depression (IDD), trait anxiety (STAIT) and state anxiety (STAIS) scores fell within normal range in the HC group, GADs showed significantly higher depression and trait anxiety scores than HCs.

### EXPLICIT TARGET VALENCE RATINGS

Mean valence ratings were calculated for neutral and negative targets in each of the three worry domains *relationships*, *health*, and *finances*, see Table 2A. These means were subjected to one-sample *t*-tests using the mean valence category 0 as the test value, separately for

**TABLE 1. Questionnaire scores (means, standard deviations) in the GAD group versus the HC group**

	GADs	HCs	sign. of <i>t</i> -test
IDD	13.5 (7.4)	2.9 (2.4)	.000
STAIT	54.6 (5.1)	34.2 (5.1)	.000
STAIS pre	45.7 (3.3)	45.5 (5.5)	n.s.
STAIS post	45.5 (2.4)	45.4 (2.4)	n.s.

IDD, Inventory to Diagnose Depression, STAIT, State Trait Anxiety Inventory—Trait form, STAIS, State Trait Anxiety Inventory—State form.

each group, to classify them as positive, neutral, or negative. In both groups, negative targets were rated as negative in all three worry domains, GADs: all  $t(37) > 14.66$ , all  $P < .001$ , HCs: all  $t(22) > 10.12$ , all  $P < .001$ , and neutral targets were rated as positive in all three domains, GADs: all  $t(37) > 2.74$ , all  $P < .05$ , HCs:  $t_{\text{health}}(22) = 1.98$ ,  $P = .060$ , other two  $t(22) > 3.77$ , both  $P < .001$ . GADs rated negative targets in the domain *relationships* as significantly more negative than HCs,  $t(60) = 2.03$ ,  $P = .048$ . In contrast, the groups did not differ with respect to their ratings for negative targets in the health and finances domain, both  $t(60) < 1.31$ , both  $P > .197$ , nor for any of the three neutral categories, all  $t(60) < 1.54$ , all  $P > .129$ .

Results were similar when only the participants' main worry domains were considered in the comparison of negative versus neutral target ratings in the two groups, see Table 2B. Negative targets were evaluated as negative by both groups, whereas neutral targets were categorized as positive, all  $t(37/22) > 2.63$ , all  $P < .05$ . While the groups did not differ in their ratings of neutral targets,  $t(60) = 0.55$ ,  $P = .588$ , there was a non-significant trend of GADs to perceive negative targets of their main worry domain as more negative than HCs,  $t(60) = 1.93$ ,  $P = .059$ .

### IMPLICIT ASSOCIATION EFFECTS

Error rates were low (total 3%), and did not differ between groups or conditions. Therefore, only RTs of

**TABLE 2. Explicit valence ratings (means and standard deviations) in the two groups for A) all negative versus neutral target words used in the three experimental conditions, and B) for individuals' main worry topic only**

	GADs	HCs	sign. of <i>t</i> -test
(A)			
<i>Relationships</i>			
Negative	-2.0 (0.7)	-1.5 (0.7)	.048
Neutral	1.5 (0.7)	1.2 (0.8)	n.s.
<i>Health</i>			
Negative	-2.1 (0.6)	-1.9 (0.8)	n.s.
Neutral	0.5 (0.7)	0.4 (0.5)	n.s.
<i>Finances</i>			
Negative	-2.4 (0.7)	-2.2 (0.7)	n.s.
Neutral	0.4 (0.7)	0.3 (0.7)	n.s.
(B)			
<i>Main worry</i>			
Negative	-2.2 (0.7)	-1.8 (0.9)	.059
Neutral	0.7 (1.1)	0.6 (1.0)	n.s.

correct responses to target trials were used. All incorrect responses and attribute trials were discarded from the data set before the analyses. Previous STIAT studies varied in whether attribute trials were analyzed or not, and which scores were computed from them. Here, attribute trials were not analyzed because their number was confounded with the experimental conditions: To ensure that both responses always occurred equally often, the attributes which did not require the same response key as the targets always appeared twice as often as the attributes which did. In contrast, when analyzing only the target trials, responses to identical stimuli can be measured in all experimental conditions. Therefore, we decided to use the “cleanest” analysis, which is limited to the target trials. For each participant, we calculated four median RT scores, one score each for each combination of target word (neutral versus negative words) and response key (pleasant versus unpleasant). STIAT scores were then calculated for each word type by subtracting the median RT yielded with the pleasant key from the median RT yielded with the unpleasant key. This way, negative STIAT scores indicate that responses with the unpleasant key were faster than responses with the pleasant key, suggesting the predicted negative association of target words with fear. The internal consistency of these STIAT scores was computed by treating target stimuli as items, yielding Cronbach’s  $\alpha = .34$ , a value not unusually low for indirect measures of associations. The STIAT scores were then subjected to a 2 (neutral versus negative targets)  $\times$  2 (start block neutral versus negative)  $\times$  2 (GADs, HCs) ANOVA and follow-up  $t$ -tests. Means and standard deviations of the RTs per

**TABLE 3. (A) Reaction times in ms (means and standard deviations) in the two groups to negative and neutral targets with the pleasant versus unpleasant response key, and (B) STIAT scores (means and standard deviations) for negative and neutral target words**

	GADs	HCs
<i>(A) Reaction times</i>		
<i>Negative</i>		
Pleasant key	844 (170)	763 (122)
Unpleasant key	784 (139)	699 (114)
<i>Neutral</i>		
Pleasant key	803 (166)	713 (133)
Unpleasant key	855 (208)	707 (131)
<i>(B) STIAT effects</i>		
<i>Negative</i>		
	-60 (91)	-63 (90)
<i>Neutral</i>		
	-52 (86)	6 (55)

A positive score indicates a positive association with the target word; a negative score indicates a negative fear association.

group, target type and response key as well as the STIAT effects are shown in Table 3.

The results of the analyses revealed that as predicted, the participants showed a negative association with negative target words. This was true for GADs:  $t(38) = 4.07$ ,  $P < .001$ ,  $d = 0.93$ , and for HCs as well:  $t(22) = 3.37$ ,  $P < .01$ ,  $d = 1.0$ . In contrast, and also as predicted, neutral target words were negatively associated in GADs,  $t(38) = 3.80$ ,  $P = .001$ ,  $d = 0.86$ , but not in HCs,  $t(22) = 0.57$ , n.s.,  $d = 0.17$ , yielding a significant interaction of target type and group,  $F(1,60) = 5.17$ ,  $P < .05$ ,  $\eta^2 = .08$ . As predicted, for HCs the STIAT score was significantly more negative for negative targets than for neutral ones,  $t(22) = 4.06$ ,  $P = .001$ ,  $d = 0.94$ . For GADs, the STIAT scores for negative and neutral targets did not differ from each other,  $t(38) = 0.41$ , n.s.,  $d = 0.09$ . Accordingly, HCs and GADs showed similarly negative associations with negative targets,  $t(60) = 0.16$ , n.s.,  $d = 0.04$ , while the GADs’ associations with neutral targets were significantly more negative than those of HCs,  $t(60) = 2.94$ ,  $P < .01$ ,  $d = 0.81$ . These results did not depend on whether participants started with a block of neutral or negative targets. There was no significant main effect of the variable *start block*,  $F(1,58) = 0.06$ ,  $P = .802$ ,  $\eta^2 = .00$ , nor did any interactions with this factor reach significance, all  $F(1,58) < 1.93$ , all  $P > .171$ , all  $\eta^2 < .03$ .

## DISCUSSION

To our knowledge, this study is the first to show that GAD is characterized by biased associations related to normatively neutral stimuli. The STIAT used in this study showed that both GAD patients and HCs associate negative target words (e.g., *cancer*, *accident*) more strongly with negative, fear-related attributes than with positive attributes. This finding is hardly surprising, and it may be taken as validation of the STIAT. The more important finding for theoretical models of GAD is that only the GAD patients exhibited a similarly strong negative association for neutral words related to their main worry topic (e.g., *diagnosis* or *doctor*), although they explicitly rated these words as positive.

These results support the hypothesis that GAD patients extend their fear associations to stimuli that are only indirectly related to the originally feared situations or objects. The striking dissociation between explicit and implicit evaluations of these stimuli thereby indicates a highly automatic nature of the generalization process. For instance, a patient might be afraid of a family member being diagnosed with a fatal disease. Not only does the name of the disease, for instance *cancer*, trigger worrying, but also the thought of any health-related topic, for instance the explicitly positively evaluated word *health* itself. Thus, fear becomes increasingly connected with more peripheral stimuli, and this generalization process explains why even neutral or positive stimuli can provoke worry and fear in GADs. As postulated by cognitive models of

anxiety,<sup>[9]</sup> this generalization is supported by a lack of habituation: patients cancel emotional processing before a problem is solved or the fear has decreased.<sup>[49]</sup> This forceful emotional suppression may relieve the patient for a short time, but in the long run, it will lead to stimulus generalization and an increase of intrusions and worry.<sup>[50,51]</sup> As far as we know, the current study is the first to demonstrate this generalization effect in GAD experimentally.

It has been postulated that activation of the fear network is a necessary prerequisite for the occurrence of processing biases.<sup>[52]</sup> Therefore, it could have been argued that we should have found negative associations for neutral worry-related words in GADs only after the previous presentation of clearly negative, worry-related words. However, this was not the case: participants who started with a negative target block did not show larger STIAT effects than those who started with a neutral block. This might indicate that the neutral target words themselves are capable of activating the GADs' fear network, although one has to keep in mind that this analysis may suffer from a lack of power.

These current results add to our knowledge of fear associations underlying biased cognitive processes such as attention, memory, and interpretation in anxiety disorders.<sup>[34]</sup> Moreover, they might open up new ways for the treatment of these disorders. Recently, many researchers have begun to develop re-trainings of biased cognitive processes such as attention<sup>[53]</sup> or interpretation,<sup>[54]</sup> in an attempt to identify the causal role of these processes as well as to augment existing therapies. The results reported here suggest that it might be worthwhile to also use indirect measures of fear associations such as the STIAT to train positive implicit associations towards fear-related stimuli, employing basic mechanisms of evaluative conditioning.<sup>[55]</sup> To this end, modified versions of the tasks have to be developed, which are suitable for changing rather than measuring implicit associations. The STIAT, for instance, could be modified such that neutral, worry-related words always require a positive response. Future studies will have to explore the utility of this approach.

Some limitations and unanswered questions need to be addressed as well. Given that negative target words directly represented the patients' core worry, one might wonder why we failed to find more negative evaluations in patients than in HCs. Also, it might seem surprising that there was no difference between negative and neutral target words in the patient group. The latter result might suggest that the implicit fear network in GAD is indeed so elaborated that neutral, only indirectly worry-related words are as negatively associated as negative words. On the other hand, both results might indicate that the STIAT is not sensitive enough to capture subtle differences between negatively associated stimuli. The low internal consistency of the current STIAT (which it shares with many RT tasks in which stimulus contents is task-irrelevant) may contribute to this lack of sensitivity. Therefore, the lack of differences needs to be interpreted with caution.

Despite our attempt to tailor the relevance of the stimulus materials to the participants' individual concerns, one might argue that the choice of only three worry domains might have been too limited. Indeed, it might have been the case that, for some participants, another domain might have been the most central one. However, at least one domain was important for all GADs and HCs who participated in this study. Therefore, we can be sure that all participants received a domain that was relevant to him or her.

Although the present study confirms differences between GADs and HCs in automatic implicit evaluations of neutral targets, it is possible that the results reflect a more basic element of anxiety that is necessary, but not sufficient for a GAD diagnosis, such as dysfunctional emotion regulation. Therefore, it would be premature to conclude that the effect found here is exclusive to GAD. Follow-up studies that assess implicit associations in different anxiety disorders should shed more light on this question of disorder-specificity. Moreover, strictly speaking, RT measures like the STIAT cannot tell us whether the GADs' fear network is more elaborated, whether it is more strongly activated, or both. Fortunately, these are only different theoretical conceptualizations of the same important clinical phenomenon, which our study demonstrated. Finally, the STIAT used here was effective in measuring biased implicit fear associations in GAD. However, this does not necessarily mean that the observed STIAT scores are also useful for measuring treatment effects, predicting treatment success, or predicting relapse after treatment of GAD. Additional research is essential to determine the usefulness of indirect measures of fear associations in these contexts. Previous results of pre-post treatment studies with phobic patients are highly encouraging in this respect.<sup>[56-58]</sup>

Despite the limitations just mentioned, the current study adds to our understanding of the relation between clinical symptoms and cognitive processes. It supports the assumption of cognitive schema models of anxiety that distorted information processing is based on disorder-specific fear networks. Thus, this approach allows for a closer look into the "affective black box," and it encourages further research into its relevance for improved treatments of anxiety.

**Acknowledgments.** This research was supported by a grant from the Deutsche Forschungsgemeinschaft (DFG) awarded to Eni S. Becker and Juergen Hoyer, and by the Behavioural Science Institute of Radboud University Nijmegen. We are grateful to Kristin Grundl, Samia Chaker, Juliane Runge, and Katja Beesdo who helped in recruiting and testing the participants, to Birgit Nündel for helpful discussions on the study design, and to the reviewers for helpful comments.

## REFERENCES

1. Hoyer J, Becker ES, Roth WT. Subjective features of worry in GAD patients, social phobics and controls. *Depress Anxiety* 2001;13:89-96.

2. Borkovec TD, Alcaine O, Behar E. Avoidance theory of worry and generalized anxiety disorder. In: Heimberg RG, Turk CL, Mennin DS, editors. *Generalized Anxiety Disorder: Advances in Research and Practice*. New York: Guilford Press; 2004:77–108.
3. Mennin DS, Turk CL, Heimberg RG, Carmin CN. Focusing on the regulation of emotion: a new direction for conceptualizing and treating generalized anxiety disorder. In: Reinecke MA, Clark DA, editors. *Cognitive Therapy Over the Lifespan: Theory, Research and Practice*. New York: Wiley; 2004:60–89.
4. Roemer L, Molina S, Borkovec TD. An investigation of worry content among generally anxious individuals. *J Nerv Ment Dis* 1997;185:314–319.
5. Borkovec TD, Hu S. The effect of worry on cardiovascular response to phobic imagery. *Behav Res Ther* 1990;28:69–73.
6. Borkovec TD, Inz J. The nature of worry in generalized anxiety disorder: a predominance of thought activity. *Behav Res Ther* 1990;28:153–158.
7. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005;62:617–627.
8. Hoffman D, Dukes E, Wittchen HU. Human and economic burden of generalized anxiety disorder. *Depress Anxiety* 2008;25:72–90.
9. Brown TA, Moras K, Zinbarg RE, Barlow DH. Diagnostic and symptom distinguishability of generalized anxiety disorder and obsessive-compulsive disorder. *Behav Ther* 1993;24:227–240.
10. Sanderson WC, Barlow DH. A description of patients diagnosed with DSM-III-R generalized anxiety disorder. *J Nerv Ment Dis* 1990;178:588–591.
11. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder (Review). *Cochrane Database Systematic Review*; 1(CD001848), 2007.
12. Ladouceur R, Dugas MJ, Freeston MH, et al. Efficacy of a cognitive-behavioral treatment for generalized anxiety disorder: evaluation in a controlled clinical trial. *J Consult and Clin Psychol* 2000;68:957–964.
13. Beck AT, Emery G, Greenberg RI. *Anxiety Disorders and Phobias*. New York: Basic Books; 1985.
14. Becker ES, Margraf J. *Generalisierte Angststoerung. Ein Therapieprogramm*. Berlin: Beltz Verlag; 2002.
15. Mansell W. Conscious appraisal and the modification of automatic processes in anxiety. *Behav Cogn Psychother* 2000;28:99–120.
16. Wells A. A metacognitive model and therapy for Generalized Anxiety Disorder. *Clin Psychol Psychother* 1999;6:86–95.
17. De Jong PJ, Pasman W, Kindt M, van den Hout MA. A reaction time paradigm to assess (implicit) complaint-specific dysfunctional beliefs. *Behav Res Ther* 2001;39:101–113.
18. Ellwart T, Rinck M, Becker E. Fear to love: implicit and explicit associations towards spiders. *Emotion* 2006;6:18–27.
19. Teachman BA, Gregg AP, Woody SR. Implicit associations for fear-relevant stimuli among individuals with snake and spider fears. *J Abnorm Psychol* 2001;110:226–235.
20. Teachman BA, Smith-Janik SB, Saporito J. Information processing biases and panic disorder: relationships among cognitive and symptom measures. *Behav Res Ther* 2007;45:1791–1811.
21. Lang PJ, Cuthbert BN, Bradley MM. Measuring emotion in therapy: imagery, activation, and feeling. *Behav Ther* 1998;29:655–674.
22. LeDoux JE, Phelps EA. Emotional networks in the brain. In: Lewis M, Haviland-Jones J, editors. *Handbook of Emotion*. New York: Guilford Press; 2000:157–172.
23. Borkovec TD, Ray WJ, Stoeber J. Worry: a cognitive phenomenon intimately linked to affective, physiological, and interpersonal behavioral processes. *Cogn Ther Res* 1998;22:561–576.
24. Teachman BA, Woody SR. Staying tuned to research in implicit cognition: relevance for clinical practice with anxiety disorders. *Cogn Behav Pract* 2004;11:149–159.
25. Mogg K, Bradley BP. Attentional bias in generalized anxiety disorder versus depressive disorder. *Cogn Ther Res* 2005;29:29–45.
26. Fazio RH, Olson MA. Implicit measures in social cognition research: their meaning and use. *Annu Rev Psychol* 2002;54:297–327.
27. Wigboldus DHJ, Holland RW, van Knippenberg A. 2009. Single target implicit associations. Manuscript submitted.
28. Karpinski A, Steinman RB. The Single Category Implicit Association Test as a measure of implicit social cognition. *J Pers Soc Psychol* 2006;91:16–32.
29. Greenwald AG, McGhee D, Schwartz J. Measuring individual differences in implicit cognition: the implicit association test. *J Pers Soc Psychol* 1998;74:1464–1480.
30. Huijding J, de Jong PJ. Automatic associations with the sensory aspects of smoking: positive in habitual smokers but negative in non-smokers. *Addict Behav* 2006;31:182–186.
31. Penke L, Eichstaedt J, Asendorpf JB. Single-Attribute Implicit Association Tests (SA-IAT) for the assessment of unipolar constructs—the case of sociosexuality. *Exp Psychol* 2006;53:283–291.
32. Thush C, Wiers RW. Explicit and implicit alcohol-related cognitions and the prediction of future drinking in adolescents. *Addict Behav* 2007;7:1367–1383.
33. Coles ME, Heimberg RG. Memory biases in the anxiety disorders: current status. *Clin Psychol Rev* 2002;22:587–627.
34. Mathews A, MacLeod C. Cognitive vulnerability to emotional disorders. *Annu Rev Clin Psychol* 2005;1:167–195.
35. Williams JMG, Watts FN, MacLeod C, Mathews A. *Cognitive Psychology and Emotional Disorders*. Chichester, England: Wiley; 1997.
36. Wittchen HU, Pfister H. *DIA-X Interviews: Manual Fuer Screening-Verfahren und Interview*. Frankfurt: Swets & Zeitlinger; 1997.
37. Meyer TE, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. *Behav Res Ther* 1990;28:487–495.
38. Stoeber J. Besorgnis: ein vergleich dreier inventare zur erfassung allgemeiner sorgen. *Zeitschrift für Differentielle und Diagnostische Psychologie* 1995;16:50–63.
39. Beck AT, Steer RA. *Manual for the Revised Beck Depression Inventory*. San Antonio, TX: The Psychological Corporation; 1987.
40. Hautzinger M, Bailer M, Worall H, Keller F. *Beck-Depressions-Inventar (BDI)*. Bearbeitung der deutschen Ausgabe. Testhandbuch. Goettingen, Germany: Huber; 1994.
41. Cartwright-Hatton S, Wells A. Beliefs about worry and intrusions: The Meta-Cognitions Questionnaire and its correlates. *J Anxiety Disord* 1997;11:279–296.
42. Hoyer J, Graefe K. *Meta-Kognitions-Fragebogen*. Unpublished manuscript, Technische Universitaet Dresden, 1999.
43. Margraf J, Schneider S, Soeder U, et al. *Diagnostisches Interview bei psychischen Stoerungen [Diagnostive Interview for Mental Disorders]*. Unpublished manual, Technische Universitaet Dresden, 1996.
44. DiNardo PA, Brown TA, Barlow DH. *Anxiety Disorders Interview Schedule for DSM-IV: Lifetime Version (ADIS-IV-L)*. Albany, NY: Graywind; 1994.
45. Becker ES, Goodwin R, Hoelting C, Hoyer J, Margraf M. Content of worry in the community: what do people with generalized anxiety disorder or other disorders worry about? *J Nerv Ment Dis* 2003;191:688–691.

46. Hoyer J, Becker ES, Roth WT. Characteristics of worry in GAD patients, social phobics, and controls. *Depress Anxiety* 2001;13:89–96.
47. Zimmermann M, Coryell W, Wilson S, Corenthal C. A self-report scale to diagnose Major Depressive Disorder. *Arch Gen Psych* 1986;43:1076–1081.
48. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *Manual for State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press; 1983.
49. Hoyer J, Beesdo K, Gloster A, et al. Worry exposure versus applied relaxation in the treatment of generalized anxiety disorder. *Psychother Psychosom* 2009;78:106–115.
50. Wegner DM. Ironic processes of mental control. *Psychol Rev* 1994;10:34–52.
51. Becker ES, Rinck M, Roth WT, Margraf J. Don't worry and beware of white bears: thought suppression in anxiety patients. *J Anxiety Disord* 1998;12:39–55.
52. Foa EB, Kozak MJ. Emotional processing of fear: exposure to corrective information. *Psychol Bull* 1986;99:20–35.
53. MacLeod C, Rutherford E, Campbell L, et al. Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *J Abnorm Psychol* 2002;111:107–123.
54. Mathews A, Mackintosh B. Induced emotional interpretation bias and anxiety. *J Abnorm Psychol* 2000;109:602–615.
55. De Houwer J, Thomas S, Baeyens F. Associative learning of likes and dislikes: a review of 25 years of research on human evaluative conditioning. *Psychol Bull* 2001;127:853–869.
56. Huijding J, de Jong PJ. Implicit and explicit attitudes toward spiders: sensitivity to treatment and predictive value for generalization of treatment effects. *Cogn Ther Res* 2009;33:211–220.
57. Reinecke A, Becker ES, Rinck M. Test–retest reliability and validity of three indirect tasks assessing implicit threat associations and behavioural response tendencies. *J Psychol* 2009.
58. Teachman BA, Woody SR. Automatic Processing in spider phobia: implicit fear associations over the course of treatment. *J Abnorm Psychol* 2003;112:100–109.