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Threat expectancy bias and treatment outcome in patients with panic disorder and agoraphobia

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ABSTRACT

Background and objectives: Previous studies suggest that patients with panic disorder and agoraphobia (PD/A) tend to overestimate the associations between fear-relevant stimuli and threat. This so-called threat expectancy bias is thought to play a role in the development and treatment of anxiety disorders. The current study tested 1) whether patients with PD/A ($N = 71$) show increased threat expectancy ratings to fear-relevant and fear-irrelevant stimuli relative to a comparison group without an axis I disorder ($N = 65$), and 2) whether threat expectancy bias before treatment predicts treatment outcome in a subset of these patients ($n = 51$).
Methods: In a computerized task, participants saw a series of panic-related and neutral words and rated for each word the likelihood that it would be followed by a loud, aversive sound.
Results: Results showed higher threat expectancy ratings to both panic-related and neutral words in patients with PD/A compared to the comparison group. Threat expectancy ratings did not predict treatment outcome.
Limitations: This study only used expectancy ratings and did not include physiological measures. Furthermore, no post-treatment expectancy bias task was added to shed further light on the possibility that expectancy bias might be attenuated by treatment.
Conclusions: Patients show higher expectancies of aversive outcome following both fear-relevant and fear-irrelevant stimuli relative to the comparison group, but this does not predict treatment outcome.

1. Introduction

Panic disorder with agoraphobia (PD/A) is characterized by recurrent and unexpected panic attacks and situational avoidance (American Psychiatric Association, 2013; Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Kessler et al., 2006). One model for the development and treatment of panic disorder (PD) is derived from Pavlovian fear conditioning and extinction (Mineka & Oehlberg, 2008; Pavlov, 1927). Meta-analyses have shown that patients with anxiety disorders demonstrate enhanced fear acquisition and reduced fear extinction relative to comparison groups without axis I disorder (Duits et al., 2015; Lissek et al., 2005). However, it is not clear whether these impaired fear conditioning processes are necessarily based on fear conditioning abnormalities or whether they involve more general biases towards threat expectancy. Indeed, studies that compared patients with PD to a comparison group without axis I disorder have found increased (subjective) threat expectancy ratings in patients to stimuli that were only verbally associated with a shock (Grillon et al., 2008) as well as to stimuli which were not explicitly associated with a shock (Lissek et al., 2009, 2010). These findings suggest a more general bias towards threat in patients with PD, which may be independent of fear conditioning processes.

The phenomenon of overestimating associations between fear-

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relevant stimuli and threat is known as 'threat expectancy bias'. Threat expectancy bias (i.e., overestimating the *forthcoming* stimulus-threat association) may play a causal role in the origin and maintenance of anxiety disorders (e.g., Beck & Clark, 1997). Interestingly, threat expectancy bias may originate from *pre-experimental* expectancies, rather than from learning threat contingencies in fear conditioning studies (e.g., Davey, 1992; McNally & Heatherton, 1993). An experimental study demonstrated that patients with PD, relative to a healthy comparison group, show a priori threat expectancy bias: they overestimate associations between fear-relevant stimuli and threat (Wiedemann, Pauli, & Dengler, 2001). One longitudinal study found that increased a priori threat expectancy ratings predict the persistence of PTSD symptoms in soldiers deployed to Iraq, even after controlling for earlier PTSD symptoms (Engelhard, de Jong, van den Hout, & van Overveld, 2009).

Threat expectancy bias may contribute to the development and maintenance of anxiety disorders by intensifying pre-existing anxiety and reducing extinction learning (e.g., Davey, 1997, 2006; McNally, 1990; Öhman & Mineka, 2001; Tomarken, Mineka, & Cook, 1989; Vroling & De Jong, 2013). Extinction learning is considered to be a core mechanism underlying exposure therapy (e.g. Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). Therefore, it could be hypothesized that threat expectancy bias before treatment predicts worse outcome of exposure therapy in patients with PD/A.

So far, the predictive value of threat expectancy bias on treatment outcome has not been investigated. One study investigated covariation bias, which is an overestimation of random associations between fear-relevant stimuli and *actual* aversive consequences (rather that an a priori bias), and demonstrated that high covariation bias measured directly after treatment predicted relapse after two years in patients with spider phobia (de Jong, Van Den Hout, & Merckelbach, 1995). In the current study, we tested whether high threat expectancy ratings before treatment predict poor treatment outcome in patients with PD/A using fear-relevant and fear-irrelevant stimuli. Although increased threat expectancies are most pronounced when fear-relevant (instead of fear-irrelevant) stimuli are used (e.g., Wiedemann et al., 2001), results from fear conditioning studies in patients with PD suggest that increased threat expectancy ratings may also be associated with fear-irrelevant stimuli. That is, patients with PD, relative to comparison groups, have demonstrated stronger fear responses to both threat cues and safety cues (Lissek et al., 2009, 2010).

In the current study, a threat expectancy task was administered in patients with PD/A and a comparison group without axis I disorder. Patients with PD/A completed the expectancy task before participating in exposure therapy. The aim of the current study was to replicate and extend previous findings by examining 1) whether patients with PD/A relative to the comparison group demonstrate higher threat expectancy ratings to panic-related as well as to neutral words before treatment, and 2) whether threat expectancy ratings measured before treatment would predict treatment outcome in patients with PD/A. We hypothesized that 1) the patient group would show a stronger threat expectancy bias to fear-relevant stimuli than the comparison group and that 2) higher threat expectancy ratings before treatment would be associated with worse treatment outcome in patients with PD/A. To extend earlier findings, we also explored whether the hypothesized increased threat expectancy ratings in patients with PD/A were not only related to fear-relevant stimuli but also to fear-irrelevant stimuli.

2. Method

2.1. Participants

Ninety-seven patients with PD/A were invited for the current study through three mental health care organizations in the Netherlands: Altrecht Academic Anxiety Centre (Utrecht), GGZ inGeest (Amsterdam), and GGZ Centraal (Ermelo). Twenty-six patients refused to participate. Seventy-one patients with PD/A (39% male) participated in the threat expectancy paradigm before they started exposure therapy with response prevention (ERP). The current study was part of a multi-center randomized controlled trial, in which the added value of D-cycloserine (DCS) administration in patients with PD/A was examined (Klein Hofmeijer-Sevink et al., in preparation). Sample size calculations were based on a power analysis comparing three groups (DCS before treatment versus DCS after treatment versus placebo), with a 0.05 significance level (two-tailed), power of 80% and Cohen's effect size of 1.1 (based on previous work by Otto et al., 2010). Calculations resulted in a recommended sample size of 20 patients per condition. To take into account the attrition rate (estimated to be approximately 20%), we included 71 patients. Exclusion criteria for the current study were 1) dependence and/or abuse of alcohol/drugs in the past three months; 2) current comorbid psychotic disorder; 3) current severe major depressive disorder; 4) current bipolar disorder; 5) mental deficiency (verbal IQ < 80 as assessed with the Dutch Adult Reading test; Schmand, Bakker, Saan, & Louman, 1991); and 6) insufficient ability to speak or read Dutch. Diagnosis of PD/A and any comorbid diagnoses were established with the Dutch version of the structured clinical interview for DSM-IV Axis-I disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1994; Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1998). Thirty-eight patients (54%) had no comorbid diagnosis, 15 patients (21%) were diagnosed with one comorbid other anxiety disorder, 10 patients (14%) with an additional mood disorder and 8 patients (11%) were diagnosed with both a comorbid other anxiety disorder and a mood disorder. Thirty-two patients (45%) used at least one psychotropic medicine at the time of participation, including the use of serotonin reuptake inhibitors ($N = 23$), benzodiazepines ($N = 13$) and tricyclic antidepressants ($N = 2$). Medication dosage was kept stable throughout the ERP.

Sixty-five healthy control subjects (48% male) were recruited through advertisements (posters and flyers) and via contacts of the researchers. The comparison group was matched with the patient group on age, sex and highest attained educational level. Table 1 provides the demographics and clinical characteristics of the patient and comparison group. Absence of a lifetime DSM-IV Axis I disorder in the comparison group was confirmed by using the Mini International Neuropsychiatric Interview (Lecrubier et al., 1997; Sheehan et al., 1997). None of the subjects from the comparison group used psychotropic medication.

This study was approved by the Medical Research Ethics Committee of the University Medical Centre Utrecht. Subjects were first informed about the study, both orally and by written information, and then provided written informed consent.

2.2. Procedure

At baseline, prior to the first treatment session, the threat expectancy task was administered to patients with PD/A. The task was developed by Engelhard et al. (2009), and based on Davey, 1992; exp 2 and 4), and was adapted for the current study, i.e., the deployment-(un)related images used by Engelhard et al. (2009) were replaced by panic-related and neutral words for this study. Participants were seated in a quiet room and completed the threat

Table 1
Demographic and clinical characteristics of the participants.

	Patient group ($N = 71$)		Comparison group ($N = 65$)		Significance of group differences[a]
	N	%	N	%	
Male sex	28	39.4	31	47.7	$p = 0.332$
	Mean	*SD*	*Mean*	*SD*	
Age	34.8	10.2	37.9	13.6	$p = 0.145$
ACQ	2.19	0.56	1.13	0.41	$p < 0.001$
BSQ	2.64	0.66	1.28	0.19	$p < 0.001$
MI when alone	2.92	0.97	1.23	0.34	$p < 0.001$
MI when accompanied	2.18	0.71	1.10	0.21	$p < 0.001$
PDSS	14.8	4.6			*NA*

ACQ = Agoraphobic Cognition Questionnaire (Chambless, Caputo, Bright, & Gallagher, 1984); BSQ = Body Sensations Questionnaire (Chambless et al., 1984); MI = the Mobility Inventory (Chambless, Caputo, Jasin, Gracely, & Williams, 1985); PDSS = Panic Disorder Severity Scale (Shear et al., 1997).
[a] Two-tailed.

expectancy bias task on a laptop. To increase the probability that participants would answer truthfully during the task, they were told that the purpose of the study was to collect physiological responses to various words, and to link these with the participants' subjective ratings (cf. Engelhard et al., 2009). Subsequently, two fake electrodes were attached to two fingertips, and the expectancy task started. Verbal and written instructions were given to inform participants that words would be presented on the screen during the task, and that some of these words might be followed by the aversive, loud sound. Through headphones, participants then received a single presentation of a loud white noise (95 dB, 500 ms) that served as threat stimulus. Participants were asked to indicate their expectancy of the threat stimulus during each trial on an online Visual Analogue Scale (VAS; 0 = certain no noise, 100 = certain noise), to index the extent to which they expected the aversive sound to occur. VAS scales were continuously displayed during the task, and participants were asked to rate their threat expectancy at least once per presented word (cf. Engelhard et al., 2009). Threat expectancy ratings are commonly used in patients with PD (Grillon et al., 2008; Lissek et al., 2009, 2010) and are regarded as valid measures to study cognitive processes, for example in fear conditioning studies (Boddez et al., 2013). During the experiment, panic-related and neutral words were presented on the laptop screen in fixed random order. The task consisted of three panic words (in Dutch): “panic”, “fear”, “anxiety” and three neutral words “butter”, “carpet”, “sidewalk”; panic-related and neutral words were matched on word length and familiarity in the Dutch language. The panic-related words have been rated as more unpleasant than neutral words by 145 students in an earlier study (Hermans & De Houwer, 1994). General anxiety-related words (instead of more specific panic-related words) were used to address patients with different subtypes of panic symptoms (e.g., fear of fainting, going mad, or dying). The use of words was chosen over pictorial stimuli, because linguistic stimuli are less confined (i.e., they have less reality constraints) than pictorial stimuli (e.g., Lavy & Van den Hout, 1993). Within the threat expectancy task, each word was presented four times for 4–5 s, with inter-trial intervals (a black screen) varying between 5 and 9 s. Words from the same category (panic-related or neutral) were never presented more than twice consecutively. Halfway through the experiment (i.e., after 6 words of both categories had been presented), one single, unpaired threat stimulus was administered during the inter-trial interval, after presentation of a neutral word. Single presentation of the threat stimulus (presented without a panic-related or neutral word) was included to prevent the threat expectancy bias from disappearing over time (Davey, 1992; Engelhard et al., 2009). Contrary to previous studies investigating the covariation bias, we did not administer the threat stimulus (white noise) during presentation of a panic-related or neutral word, in order to prevent acquisition effects (Amrhein, Pauli, Dengler, & Wiedemann, 2005; Pauli, Montoya, & Martz, 1996; Pauli, Montoya, & Martz, 2001).

2.3. Treatment outcome

Of 71 patients with PD/A who completed the threat expectancy bias task, 51 patients subsequently enrolled in the multicenter double-blind placebo-controlled trial (Klein Hofmeijer-Sevink et al., in preparation). The remaining 20 patients were not willing to participate in the randomized controlled trial. For those 51 patients who did participate in both the threat expectancy task and the randomized controlled trial, the average mean time between the threat expectancy bias task and the start of the treatment trial was 10 days ($SD = 35$). Within the treatment trial, patients were randomized to receive either placebo ($n = 19$) or fixed dosages of 125 mg DCS during ERP, given directly preceding ($n = 16$) or directly post ($n = 16$) session 2 to 7 of twelve 90-min sessions ERP.

The treatment outcome measures were the Mobility Inventory (MI; Chambless et al., 1985) and the Panic Disorder Severity Scale (PDSS; Shear et al., 1997). The MI measures self-reported avoidance, and contains two subscale scores: 1) mobility when a patient is alone and 2) when the person is accompanied by a trusted companion (Chambless et al., 2011). The PDSS encompasses an interview to rate the severity of panic symptoms in patients with established diagnoses. Both the MI and PDSS were assessed at baseline (pre-treatment), after sessions 3, 7 and 12 (post treatment), and at 3 and 6 months follow-up. For the current analyses, only baseline and post-treatment assessments were used. Treatment outcome was defined as the percentage of improvement = [(pre-treatment score − post-treatment score) * 100]/pre-treatment score. At group level, patients with PD/A demonstrated an average improvement of 27% ($SD = 22$) on MI scores and 68% ($SD = 37$) on the PDSS scores, indicating that at least half of the included patients could be classified as treatment responders, since these patients showed ≥ 25% improvement (Buchsbaum et al., 2006; Ho Pian et al., 2005; Saxena et al., 1999). Treatment outcome of DCS enhancement suggested no additional effect of DCS administration compared to placebo (results are reported elsewhere, Klein Hofmeijer-Sevink et al., in preparation).

2.4. Statistical analyses

Using IBM SPSS (version 22), a repeated measures ANOVA was conducted on the baseline measurements to investigate whether patients with PD/A showed higher threat expectancy ratings to panic-related and neutral words relative to the comparison group. Group (patients versus comparison group) was included as the between-subjects factor, and within-subjects factors were stimulus type (panic-related versus neutral words) and expectancy trial

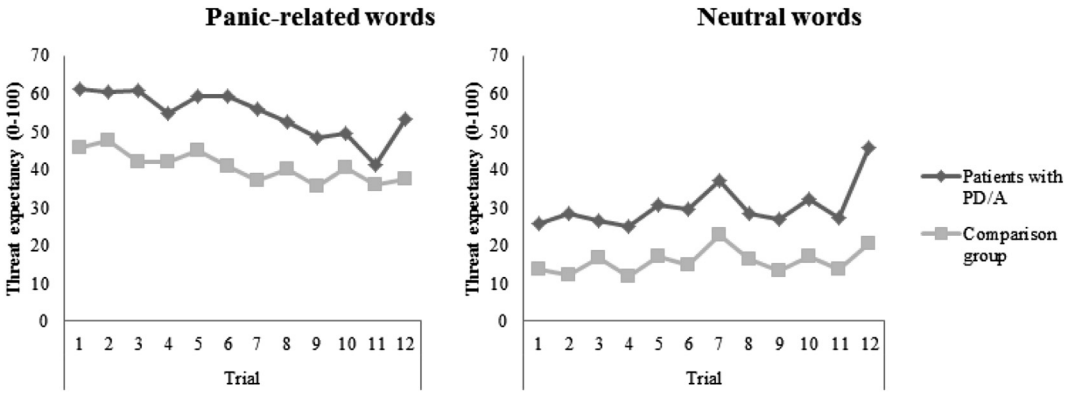

Fig. 1. Threat expectancy ratings regarding panic-related words (left graph) and neutral words (right graph) in patient and comparison group.

Table 2
Results of regression analyses predicting treatment outcome in patients with PD/A.

Model fits	MI when alone				MI when accompanied				PDSS			
	R^2	df	F	p	R^2	df	F	p	R^2	df	F	p
Panic word – stage 1	0.09	3, 40	1.2	0.315	0.04	3, 39	0.5	0.692	0.08	3, 49	1.3	0.281
Panic word – stage 2	0.07	3, 40	0.9	0.431	0.06	3, 39	0.7	0.541	0.06	3, 49	1.0	0.421
Neutral word – stage 1	0.10	3, 40	1.4	0.263	0.07	3, 39	0.9	0.447	0.10	3, 49	1.8	0.166
Neutral word – stage 2	0.17	3, 40	2.5	0.072	0.15	3, 39	2.1	0.121	0.07	3, 49	1.1	0.370

MI = Mobility Inventory; PDSS = Panic Disorder Severity Scale; Stage 1 = before presentation of the threat stimulus; Stage 2 = after presentation of the threat stimulus.

number (12 data points). Because participants were instructed to rate their expectancy at least once per presented word, data reduction was applied when there was more than one rating on one trial. In accordance with a previous similar study, the highest rating from each trial was selected for the analyses (Engelhard et al., 2009). When the assumption of sphericity was not met, Greenhouse-Geisser correction ($\varepsilon < 0.75$) or Huynh-Feldt correction ($\varepsilon > 0.75$) was applied to the F-ratio and degrees of freedom.

Linear regression analyses (enter method) were carried out to examine whether threat expectancy ratings predicted treatment outcome (MI and PDSS, as outlined above) in patients with PD/A.[1] Threat expectancy ratings were included separately for stimulus type (panic-related or neutral words) and stage (before or after presentation of the threat stimulus halfway through the experiment). Data from 10 patients could not be included in the regression analyses wherein MI served as outcome variable, because these patients did not complete the MI at both pre- and post-treatment measurement.

Finally, since a substantial proportion of patients ($N = 13$) used benzodiazepines at the time of testing, which might have influenced expectancy ratings in the current paradigm, analyses were repeated while excluding the patients who used benzodiazepines during participation. However, exclusion of these patients did not influence the results (data not shown) and therefore results are reported including the whole group.

3. Results

Repeated measures ANOVA demonstrated overall increased expectancy ratings in the patient group relative to the comparison group, as indicated by a significant main effect of group, $F(1,132) = 24.0$, $p < 0.001$, $\eta_p^2 = 0.15$. Fig. 1 displays the baseline expectancy ratings in patient and comparison groups; ratings are shown separately for panic-related words (left graph) and neutral words (right graph). The (crucial) group by stimulus interaction, $F(1, 132) = 0.03$, $p = 0.81$, $\eta_p^2 < 0.01$, group by trial interaction, $F(7.9, 1040.0) = 0.94$, $p = 0.50$, $\eta_p^2 = 0.01$, and group by stimulus type by trial interaction, $F(11, 1452) = 1.13$, $p = 0.33$, $\eta_p^2 = 0.01$, were not significant. Furthermore, a significant interaction between stimulus type and trial was found across groups between trial 6 and 7, reflecting an increase in threat expectancy ratings towards neutral words and a decrease in threat expectancy towards panic-related words as a consequence of the single presentation of the threat stimulus preceding trial 7, $F(1, 132) = 8.6$, $p = 0.004$, $\eta_p^2 = 0.06$.

Regression analyses demonstrated no significant predictive value of threat expectancy ratings on treatment outcome. That is, threat expectancy did not account significantly for the variability in treatment outcome measured with the two subscales of the MI (i.e., mobility when a patient is alone and when the patient is accompanied by a trusted companion) or the PDSS. Table 2 provides an overview of the model fits, displayed for each treatment outcome per stimulus type (panic-related versus neutral words) and stage (before versus after presentation of the threat stimulus halfway the experiment).[2]

4. Discussion

In this study, we examined 1) differences in threat expectancy ratings between patients with PD/A and a comparison group, and 2) the predictive value of threat expectancy on treatment outcome in patients. Results demonstrated higher threat expectancy ratings to both panic-related and neutral words in patients with PD/A relative to the comparison group. The observed threat expectancy bias in patients with PD/A persisted throughout the task, despite the fact

[1] For exploratory purposes, DCS was also included as predictor in the regression model. However, neither administration of DCS nor the interaction between threat expectancy ratings and DCS was associated with treatment outcome.

[2] Additional exploratory analyses demonstrated no significant association between threat expectancy ratings and treatment outcome (MI when alone, MI when accompanied, PDSS) at 3 or 6 months follow-up.

that the threat stimulus was never paired with a panic-related or neutral word. The increased expectancy ratings to fear-relevant stimuli in patients with PD/A relative to the comparison group are in line with previous findings (Wiedemann et al., 2001). This study also found increased expectancy ratings to fear-*irrelevant* stimuli in patients with PD/A versus the comparison group. This is in line with the earlier study in soldiers deployed to Iraq that used the same paradigm (Engelhard et al., 2009). It found that PTSD symptoms were associated with threat expectancy ratings to both fear-relevant and fear-irrelevant stimuli, but only the former predicted the persistence of symptoms over time. An earlier study in patients with PD/A versus a healthy comparison group did not find higher a priori expectancy ratings to fear-irrelevant stimuli (Wiedemann et al., 2001). Methodological differences between these studies (such as the use of online ratings versus a priori ratings, verbal versus pictorial stimuli) hamper the drawing of a general conclusion regarding expectancy ratings to fear-irrelevant stimuli in patients with PD/A.

The increased expectancy ratings towards both fear-relevant and fear-irrelevant stimuli in patients with PD/A might be interpreted as context anxiety. Context anxiety comprises enhanced fear responses within a threatening context (irrespective of the stimulus that is presented), and has previously been demonstrated in patients with PD, relative to a healthy comparison group (Grillon et al., 2008). In addition, the current findings are in line with the results from our meta-analysis on classical fear conditioning (Duits et al., 2015), in which we found increased fear responses to safety cues (which resemble fear-irrelevant stimuli) in patients with anxiety disorders relative to comparison groups during acquisition phases. Taken together, these findings suggest that impaired inhibition of fear and/or increased generalization of fear in patients with anxiety disorders may already exist prior to (fear conditioning) experiments. The current findings suggest that patients with PD/A tend to (persistently) overestimate forthcoming stimuli-threat contingencies, which has been associated with an increased risk of developing anxiety symptoms (Engelhard et al., 2009).

This is the first study in which the predictive value of a priori threat expectancy ratings on treatment outcome was investigated in patients with PD/A. Based on previous findings regarding covariation bias (de Jong et al., 1995) and the idea that increased threat expectancy would result in delayed or reduced extinction of fear, we hypothesized that higher threat expectancy ratings before treatment would be associated with worse treatment outcome in patients with PD/A. However, results demonstrated no significant predictive value of threat expectancy ratings on treatment outcome. This suggests that pre-treatment expectancy ratings are not related to treatment outcome, and we should focus on other predictors for treatment outcome instead. An example of such a potential predictor is individual differences in fear extinction, which might serve as an underlying factor of the development of anxiety disorders (e.g., Engelhard et al., 2009; Guthrie & Bryant, 2006; Lommen, Engelhard, Sijbrandij, van den Hout, & Hermans, 2013), and exposure therapy (Hofmann, 2008; Massad & Hulsey, 2006; Myers & Davis, 2008). Support for the predictive value of fear extinction on treatment outcome was found in recent studies conducted in patients with PD/A (Hahn et al., 2014; Kircher et al., 2012; Lueken et al., 2013). Treatment non-responders displayed enhanced activation of threat-related brain systems in response to safety cues during extinction when compared to responders (Lueken et al., 2013). Another explanation for the current findings may be that the expectancy bias task was not sensitive enough to examine the relationship between expectancy ratings and treatment outcome. The study was limited by exclusively using subjective threat expectancy ratings, which reflect more cognitive based processes that might be susceptible to experimental demands, such as participants trying to determine the purpose of the experiment (Boddez et al., 2013). Physiological outcome measurements (such as startle potentiation) might on the other hand represent a different aspect of anxiety; it has been suggested that physiological measurements reflect the emotional instead of cognitive component of anxiety (Sevenster, Beckers, & Kindt, 2012). Therefore, we recommend that future studies add physiological outcome measures to measure both emotional and cognitive aspects of anxiety.

The apparent discrepancy between previous findings by de Jong et al. (1995) who found an increased return of fear after two years in spider phobics who had demonstrated increased covariation bias directly after treatment- and the current findings may be explained by conceptual and methodological differences between the studies. First, de Jong et al. investigated covariation bias by partly reinforcing pictorial stimuli by a threat stimulus, while the current study focused on the expectancy bias, in which verbal stimuli were never paired with a threat stimulus (cf. Engelhard et al., 2009; Davey, 1992; exp 2 and 4). As a consequence, the outcomes of de Jong and colleagues may have been more related to contingency learning, while the current study focused specifically on a priori threat expectancy bias. Nevertheless, in the present study some reinforcement effect halfway through the experiment cannot be ruled out, because an increase in expectancy ratings towards neutral words and a decrease in threat expectancy towards panic-related words was demonstrated after the single (unpaired) white noise presentation halfway through the experiment. Second, de Jong and colleagues assessed covariation bias shortly *after* treatment, while the current study examined expectancy bias *before* treatment. For future studies, we recommend the use of both pre- and post-treatment measurements within one experiment to extend our knowledge about the course of the threat expectancy bias as a function of treatment outcome. Other differences between the previous versus current study that may explain the discrepancy in findings are: differences between study populations (patients with spider phobia versus patients with PD/A), sample sizes (19 patients versus 51 patients), stimulus type (visual versus verbal stimuli), duration of treatment (one 2.5-hr exposure session versus twelve 1.5-hr exposure sessions) and timing of treatment outcome measurements (two years after treatment versus measurement after twelve therapy sessions). In addition, we also found no support for an association between threat expectancy and treatment outcome at 3 or 6 months after treatment.

To conclude, higher threat expectancy ratings to both panic-related and neutral words were demonstrated in patients with PD/A compared to the comparison group, but these increased ratings did not predict treatment outcome in patients with PD/A. Future research should add both physiological and subjective outcome measurements. In addition, we recommend the use of a pre- and post-treatment expectancy bias task to shed further light on the possibility that the expectancy bias is down-regulated as a result of treatment. By learning more about potential changes in the expectancy bias as a result of treatment, we may extend our knowledge about the effective components of exposure treatment and eventually improve treatment outcome.

Conflicts of interest

The authors declare no conflict of interest.

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