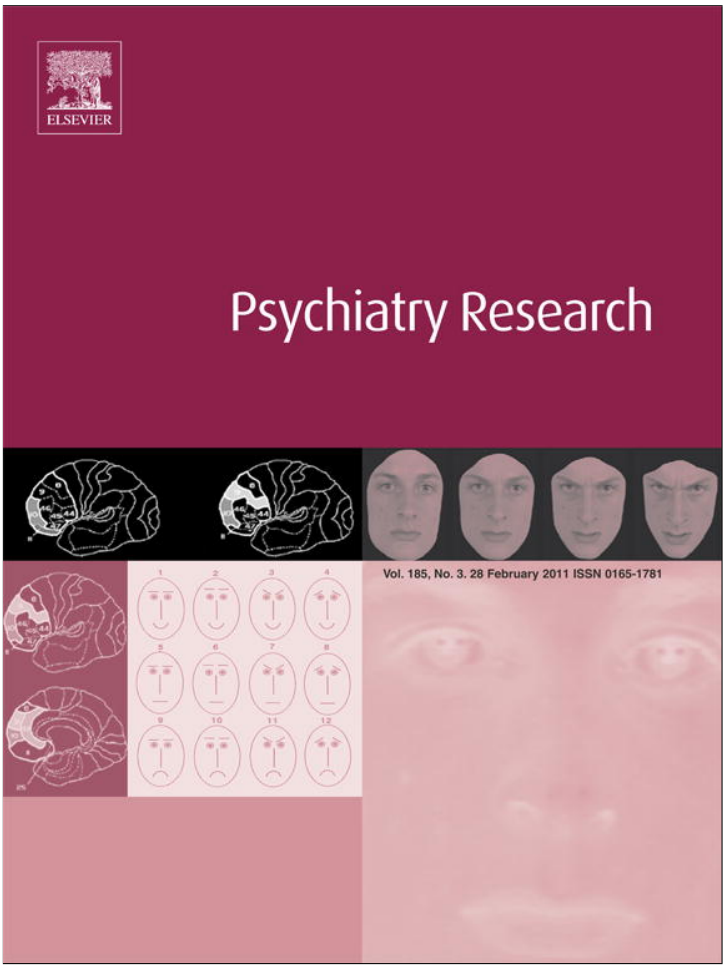

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Attentional bias in untreated panic disorder

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ABSTRACT

The role of attentional biases in panic disorder has been well characterised. However, recent studies suggest an important effect of antidepressant and anxiolytic drugs on cognitive bias and most studies have included medicated patients in their sample. This study therefore examined cognitive bias in an untreated sample of participants with panic disorder (PD). A sample of 23 untreated participants with panic disorder with or without agoraphobia (PPD) and 22 healthy controls (HC) were tested with a Facial Expression Recognition task featuring different emotional intensities, a Faces Dot Probe task, a Self Beliefs task and an Emotional Stroop task. PPD showed exaggerated attentional biases to negative face and word stimuli in two different paradigms and endorsed more panic-related and negative self-attributions. They also showed enhanced perception of facial expressions of sadness. These tasks are sensitive to cognitive bias in a community-based sample of untreated PD participants. Attentional biases in panic disorder cannot be explained by the use of medication in this group and may therefore play a critical role in the underlying pathogenesis of the disorder.

1. Introduction

Cognitive (Clark, 1986; Beck and Clark, 1997) and learning-theoretical models (Bouton et al., 2001) of panic support a role for biased information-processing to threat-related stimuli in the aetiology and maintenance of the disorder. Although patients with panic disorder (PD) show no deficits in general information processing (Kaplan et al., 2006) a large body of evidence suggests that they tend to selectively and automatically direct their attention towards threat stimuli, and that they tend to preferentially interpret ambiguous stimuli in a negative way (Ehlers et al., 1988; Clark et al., 1997; Lundh et al., 1999; Lim and Kim, 2005; Teachman et al., 2007). However, while a number of studies on PD, for instance, report vigilance for panic-related words in a verbal dot-probe task (Asmundson et al., 1992) or biased processing of facial expressions (Lundh et al., 1998), other studies using identical or similar paradigms have not been able to find panic-specific processing (Asmundson and Stein, 1994; Kessler et al., 2007).

One reason for these inconsistencies in results might be that the effects of medication or psychotherapy have been widely neglected in cognitive bias research in PD so far. Many of the previous studies in PD have explicitly included participants undergoing psychopharmacological treatment (Ehlers and Breuer, 1995; Lundh et al., 1998; Lundh et al., 1999; Lim and Kim, 2005; Kessler et al., 2007; Pillay et al., 2007) or do not provide information on subjects' medication status (Clark et al., 1997; Kroeze and van den Hout, 2000). Also, many studies have tested PD inpatients or outpatients as part of cognitive-behavioural treatment (CBT) outcome studies (Lundh et al., 1998; Kessler et al., 2007), leaving open whether they were already undergoing CBT. Following the consensus statements of the evidence-based NICE guidelines for the treatment of panic (NICE, 2007), both selective serotonin reuptake inhibitors SSRIs and CBT are first line treatments for the anxiety disorder, and recent studies indicate that completion of one or the other treatment also reduces disorder-specific emotional information-processing biases (Mogg et al., 1995; Mogg et al., 2004a; Reinecke et al., submitted) and neural responses to emotional stimuli (Prasko et al., 2004; Straube et al., 2006) in anxious patients.

A broad range of studies in healthy volunteers shows that even single-dose or short-term administrations of SSRIs or serotonin norepinephrine reuptake inhibitors (SNRIs) significantly modify cognitive-emotional processing. A 7-day administration of SSRIs was found to decrease the recognition of threatening facial expressions, reduce the emotion potentiated startle response and direct attention away from threat cues in a dot-probe task in healthy volunteers (Harmer et al., 2003b; Harmer et al., 2004; Murphy et al., 2009). By contrast, acute administration of SSRIs (Harmer et al., 2003a; Browning et al., 2007; Grillon et al., 2007) appears to increase threat relevant processing across a number of paradigms, consistent with reports of increased anxiety early on in treatment with SSRIs (Kent et al., 1998). Thus, if patients were tested early in the course of, or following a change in, antidepressant treatment, then performance on the cognitive-emotional bias tests may have been misleading.

The aim of this study was to assess emotional information processing in a less severely affected community-based sample of unmedicated and untreated participants with PD-specific panic attacks. We were interested in studying whether we would find similar cognitive biases as in commonly investigated outpatient or inpatient samples (Kessler et al.,

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2007) and which would help answer whether these biases are key to the disorder. We used a battery of tasks to capture biases in attention and interpretation believed to play a key role in panic disorder. Also, we assessed negative self-schemata (Beck et al., 1985) which already have been shown to play a key role in the pathogenesis of other disorders (Pringle et al., 2009), but have not yet been experimentally investigated in panic.

2. Methods

2.1. Participants

Twenty-three participants with panic disorder and 22 healthy controls participated in the study. They were recruited via online advertisements and posters at Oxford Universities. General exclusion criteria were lack of fluency in English language (native speaker panic group: 19, control group: 20), current psychotropic or psychotherapeutic treatment, epilepsy, psychotic disorders, and substance abuse. Also, all participants were required to not have been on antidepressant medication or under psychotherapeutic treatment for the last 3 months. Volunteers were first pre-screened via an online-version of the Panic Disorder Severity Scale PDSS (Houck et al., 2002) to assess the severity of panic symptoms during the last 3 months. In addition, medication status was assessed. For the group of participants with panic disorder (PPD), only unmedicated volunteers with a PDSS score of at least 5 were invited to answer a range of additional screening questions (e.g. description of the anxiety symptoms). Ninety-three participants were interviewed this way, out of which 70 were excluded. The most common reasons were: the panic attacks were not panic disorder specific but reflected another anxiety problem (e.g., social or generalised anxiety), intermittent start of antidepressant or CBT treatment, epilepsy or insufficient English. The healthy control subjects (HC) were selected to have PDSS scores of <3 and an absence of any panic related symptoms in the follow-up screening. Those volunteers meeting these initial criteria were invited to attend an appointment for a face to face meeting and were screened using the Structured Clinical Interview for DSM-IV Axis I Disorders SCID-CV (First et al., 1997). To be included in the control group, volunteers were required to not fulfil diagnostic criteria for any axis-1 disorder (current or past). Volunteers of the panic group were required to fulfil all criteria for current panic disorder. In case of comorbidity, the panic disorder had to be the primary diagnosis. Fifteen of the 23 panic group volunteers fulfilled all criteria for a panic disorder without agoraphobia (13 with panic attacks during the last 3 months, 2 with only limited symptom attacks during last 3 months but with panic attacks in the preceding 3 months). Eight participants were diagnosed with full panic disorder with agoraphobia. For 9 subjects, a comorbid diagnosis was determined (generalized anxiety disorder: 3, obsessive–compulsive disorder: 2, social phobia/anorexia nervosa/major depression/dysthymia: 1 each). The groups did not differ with respect to gender, age, years of education and verbal IQ, see Table 1.

Table 1
Mean questionnaire scores, standard deviations and significance of *t*-tests, separated for the panic group vs. healthy control group.

Measure	Panic group ($N=23$)		Control group ($N=22$)		Statistical significance
	M	S.D.	*M*	S.D.	
Gender	70% ♀		73% ♀		0.815
Age	28.6	8.1	26.2	6.9	0.297
Years of education	17.7	2.5	17.4	2.6	0.625
NART	114.3	4.9	116.5	4.9	0.148
PDSS	8.8	5.5	0.2	0.5	0.000
HADS anxiety	13.1	3.8	5.2	3.6	0.000
HADS depression	6.2	3.0	1.6	2.3	0.000
STAI-T	55.1	11.2	37.1	9.7	0.000
EPQ neuroticism	18.2	4.6	9.9	6.3	0.000
EPQ extraversion	12.1	5.3	13.2	6.0	0.551
EPQ psychoticism	3.9	2.8	3.7	2.8	0.754
EPQ lie	10.00	9.1	6.8	3.9	0.140
FQ agoraphobia	33.0	18.4	21.1	14.7	0.021
FQ blood–injury phobia	10.6	7.1	8.5	7.5	0.336
FQ social phobia	14.1	7.8	10.4	7.0	0.109
SBQ	27.9	5.9	18.3	6.4	0.000
ACQ total	2.1	0.5	1.4	0.3	0.000
ACQ loss of control	2.0	0.5	1.7	0.4	0.026
ACQ physical concerns	2.1	0.7	1.2	0.2	0.000
ACQ belief total	27.9	13.3	15.8	17.5	0.012
ACQ belief loss of control	27.0	13.9	22.5	18.5	0.355
ACQ belief physical concerns	28.8	17.5	9.2	19.2	0.001
BBSIQ panic body sensation	1.8	0.6	1.1	0.2	0.000
BBSIQ external events	1.7	0.5	1.2	0.2	0.000

Note: NART = National Adult Reading Test, PDSS = Panic Disorder Severity Scale, HADS = Hospital Anxiety and Depression Scale, STAI = State-Trait Anxiety Inventory, EPQ = Eysenck Personality Inventory, FQ = Fear Questionnaire, SBQ = Safety Behaviours Questionnaire, ACQ = Agoraphobic Cognitions Questionnaire, BBSIQ = Brief Body Sensations Interpretation Questionnaire.

2.2. General procedure

Volunteers were sent the Agoraphobic Cognitions Questionnaire ACQ (Chambless et al., 1984), the Fear Questionnaire FQ (Marks and Mathews, 1979), the Social Behaviours Questionnaire SBQ (Clark et al., 1995), the Trait form of the State-Trait Anxiety Inventory STAI-T (Spielberger et al., 1983), and the Eysenck Personality Questionnaire (Eysenck and Eysenck, 1991) to be completed at home. On-site, we recorded demographic data and measured verbal IQ with the National Adult Reading Test NART (Nelson and O'Connell, 1978). Volunteers then completed the experimental tasks in fixed order: Facial Recognition task, Faces Dot Probe task, Emotional Stroop task, and Self Beliefs task. The administrators were not blind to participants' group allocation, but to their exact diagnoses and comorbid problems.

Following the computer tasks, participants completed the Brief Body Sensations Interpretations Questionnaire BBSIQ (Clark et al., 1997) and were interviewed with the SCID (First et al., 1997). These interviews were conducted by a clinical psychology doctorate trainee in their final year (AR) who was trained and supervised by a clinical psychologist (MC) and a psychiatrist (EF).

2.3. Experimental tasks

2.3.1. Facial Expression Recognition task

This task was the same as the one developed and used by Harmer et al. (Harmer et al., 2003a). Stimuli were pictures of faces (Ekman and Friesen, 1976), featuring anger, disgust, fear, sadness, happiness or surprise related emotional expressions. For each of these emotions, 10 intensity versions (10%–100%) were presented generated by morphing a 0% emotional intensity (neutral) with a 100% emotional intensity picture in 10% steps. For each emotion, each intensity was presented 4 times. In addition, a neutral expression was presented 10 times, yielding a total of 250 trials. In each trial, a face stimulus was presented for 500 ms. Participants were instructed to categorize the emotional expression of the face presented as quickly and accurately as possible by using labelled keys. Trials were presented in three blocks to allow for breaks. In total, the duration of this task was 15 min. SuperLab software (Cedrus Cooperation, 1998) was used for stimulus presentation.

2.3.2. Faces Dot Probe task

This task was the same as the one developed and used by Murphy et al. (2008). Stimuli were pairs of coloured photographs of 20 individual faces with either a neutral or an emotional facial expression (Matsumoto and Ekman, 1988). Three types of face pairs, neutral–neutral, neutral–happy, and neutral–fearful combinations, were used. Each pair consisted of two pictures of the same person. In each trial, one of the faces appeared above and the other below a central fixation position. As mask pictures, pictures of scrambled faces were used. The probe was a double dot oriented either horizontally (..) or vertically (:). Each of the three face pair conditions (neutral–neutral, neutral–fearful, neutral–happy) was presented 32 times in a masked-faces condition and 32 times in an unmasked-faces condition, yielding a total of 192 trials. Participants worked on 8 blocks of unmasked trials and 8 blocks of masked trials, presented in an alternating order. In the *unmasked* condition, a face pair was presented for 100 ms. In the *masked* condition, the face was presented for 16 ms and then replaced by a mask for 84 ms. Immediately after face-mask prime presentation, a dot probe replaced one of the faces. Participants were instructed to report the orientation of the probe as quickly and accurately as possible. Position of an emotional face, probe position and type were fully counterbalanced. Thus, this task design involved congruent trials (dot appears at the position of an emotional face) and incongruent trials (dot replaces a neutral face while an emotional face is present). Stimuli were presented using e-prime software (Psychology Software Tools, 2002).

2.3.3. Emotional Stroop task

Stimuli were 12 neutral (e.g. curtain, garage), 12 social-threat related (e.g. mistake, snub) and 12 panic-related (e.g. faint, stroke) words of the font size 24. The neutral and social words were identical to those used in an earlier study (Munafo et al., 2006), the panic words were additionally designed on the basis of panic disorder patients' main fears. Words were matched for length and frequency (Coltheart, 1981). Each of the experimental words existed once in blue, red, and green colours, respectively. Masks were symbol strings of the same font size, colour and length as the words preceding them. Stimuli were presented in six experimental blocks. In two blocks each, neutral, social vs. panic-related words were presented. In one block each, these were presented unmasked, staying on the screen until a response was made. In another block, target stimuli were replaced by a symbol string mask 17 ms after presentation onset. Block order was counterbalanced. Participants were instructed to name the colour of the word presented on the screen as quickly and accurately as possible into a microphone. At the beginning of the session, participants practised the response procedure in 4 trials. In addition, each block started with 2 practice trials. Words were presented using e-prime software (Psychology Software Tools, 2002).

2.3.4. Self Beliefs task

The task was developed specifically for this study, based on a self schema paradigm investigating patients with eating disorders (Markus et al., 1987). Stimulus words were 15 positive (e.g. capable, independent), 15 negative (e.g. disliked, immature) and 15

panic-related (e.g. helpless, insecure) words matched for length and frequency (Coltheart, 1981). Word selection was based on Ball et al. (Ball et al., 1995). To assess explicit core beliefs, volunteers made a speeded response whether the single word presented on the screen does or does not describe them. The task was completed in 3 min. As dependent measures, the numbers of me vs. not-me responses and mean RT were recorded. Stimuli were presented using SuperLab presentation software (Cedrus Cooperation, 1998).

2.4. Statistical analysis

Data were analysed by performing repeated measures ANOVAs and additional *t*-tests as required using SPSS 15. An alpha-level of 0.05 was used for all statistical tests. Effect sizes are reported as Cohen's *d* (Cohen, 1988).

3. Results

3.1. Questionnaire measures

Mean questionnaire scores and significance values of independent sample *t*-tests are presented in Table 1. The PPD group had significantly higher scores on the trait form of the STAI, on the EPQ neuroticism scale, and on the FQ agoraphobia subscale than healthy controls (HC). The PPD group also expressed the use of more safety strategies in fearful situations, measured with the SBQ. They also reported more dysfunctional cognitions related to loss of control and physical concerns, measured with the ACQ subscales and total score. Compared to HC, they also reported higher belief in the validity of these catastrophic thoughts, especially when these are related to physical concerns. In the BBSIQ, PPD interpreted body sensations in a more panic-related manner, but also evaluated non-physical, external events in a more negative way than controls. In addition, PPD showed significantly higher scores on the anxiety and depression subscale of the HADS, though ratings of depression were still below clinically relevant cut-offs. This is in contrast to earlier studies on information processing in panic which usually report clinically relevant depression average scores (Ehlers and Breuer, 1995; Kroeze and van den Hout, 2000; Kessler et al., 2007).

3.2. Facial Expression Recognition task

3.2.1. Accuracy

Accuracy of facial expression recognition was examined across the different intensity levels using group × intensity analyses of variance for each emotion, see Table 2. For all emotions and both groups recognition rates were higher with higher emotional intensity, *intensity:* all $F(9,387) > 50.0$, all $P<0.001$, all $d>2.12$, *intensity × group:* all $F(9,387)<1.4$, all $P>.179$, all $d<0.41$. Participants with panic disorder showed enhanced recognition of sad facial expressions, *group:* $F_{sad}(1,43)=4.9$, $P<0.05$, $d=0.67$. There was no group difference in recognition of other facial expressions, all $F(1,43)>0.57$, all $P>0.456$, all $d<0.29$.

Table 2
Accuracy in the Facial Recognition task depending on the intensity of the facial expression, separated for all expression types and the two groups (panic: $N=23$, control: $N=22$). An * reflects group differences at the 0.05 level of significance.

Emotion	Group	10	20	30	40	50	60	70	80	90	100
Anger	Panic	0.9	1.2	1.0	1.5	2.0	2.7	2.4	2.2	2.5	2.7
	Control	1.0	1.0	0.9	1.5	2.1	2.4	2.5	2.3	2.5	2.7
Disgust	Panic	0.1	0.6	0.7	1.3	2.0	2.5	3.0	3.0	3.2	3.3
	Control	0.3	0.5	0.7	1.1	2.0	2.9	3.2	3.4	3.4	3.5
Fear	Panic	0.0	0.1	0.4	1.7	2.7	2.7	2.8	2.8	3.1	3.0
	Control	0.0	0.2	0.7	1.6	2.0	2.7	2.9	2.8	2.9	3.0
Happiness	Panic	0.1	0.4	0.9	2.6	2.7	3.0	3.7	3.9	3.8	3.8
	Control	0.3	0.5	1.4	2.5	2.7	3.3	3.6	3.9	3.8	3.9
Sadness*	Panic	0.3	0.9	1.0	1.3	2.4	2.9	3.0	3.0	3.0	3.2
	Control	0.5	0.6	0.9	1.1	2.1	2.3	2.6	2.6	2.3	2.4
Surprise	Panic	0.0	0.2	0.4	1.6	2.3	3.0	3.4	3.5	3.3	3.4
	Control	0.0	0.0	0.5	1.6	2.5	3.1	3.1	3.3	3.3	3.2

Note: The columns 10–100 label the intensity of the corresponding facial expression in percent.

3.2.2. Median reaction time

A group × expression ANOVA revealed no group differences in expression categorisation speed, *group × expression*: $F(6,258)=0.74$, $P=0.619$, $d=0.26$, *group*: $F(1,43)=0.17$, $P=0.682$, $d=0.13$. An additional independent samples *t*-test for sad faces confirmed that increased accuracy in PPD as previously described is not due to a speed-accuracy trade-off, $t(44)=1.11$, $P=0.272$, $d=0.33$, see Table 3.

3.2.3. Misclassifications

Analyses revealed no group differences in misinterpreting emotional expressions, *group × expression*: $F(6,258)=0.70$, $P=0.654$, $d=0.26$, *group*: $F(1,43)=0.58$, $P=0.449$, $d=0.23$. An additional independent sample *t*-test for sad faces confirmed that PPD's increased accuracy in detecting sad faces is not due to a generally lower response threshold for sad faces, $t(44)=0.54$, $P=0.596$, $d=0.16$, see Table 3.

3.3. Faces Dot Probe task

Attentional vigilance scores were calculated by subtracting the median RT in congruent trials (dot at the position of the emotional face) from the median RT in incongruent trials (dot at the position of the neutral face), see Fig. 1. A negative score indicates avoidance of allocation of attention to the emotional face, a positive score reflects vigilance.

3.3.1. Unmasked condition

When a face pair was presented for 100 ms, participants in both groups showed no vigilance or avoidance of attention to fearful and happy faces, *emotion:* $F(1,43)=0.37$, $P=0.548$, $d=0.18$, *emotion × group:* $F(1,43)=0.32$, $P=.576$, $d=0.17$, *group:* $F(1,43)=0.10$, $P=0.749$, $d=0.09$.

3.3.2. Masked condition

When a face pair was presented for only 16 ms, PPD showed a quick orientation of attention towards a fearful face, leading to a quicker categorization of the dot when presented at the same position. Analyses revealed this significant vigilance effect for fearful faces in the PPD, but not in the control group, *emotion × group:* $F(1,43)=6.30$, $P<0.05$, $d=0.77$, *emotion:* $F(1,43)=3.86$, $P=0.056$, $d=0.60$, *group:* $F(1,43)=1.13$, $P=0.293$, $d=0.33$; independent t-test fear: $t(43)=2.26$, $P<0.05$, $d=0.79$, HC: $t_{0\ fear}(21)=0.74$, $P=0.467$, $d=0.22$, PPD: $t_{0\ fear}(22)=2.72$, $P<0.05$, $d=0.80$. This enhanced attention to an emotional face was not found for happy expressions, independent t-test happy: $t(43)=0.90$, $P=0.374$, $d=0.27$, HC: $t_{0\ happy}(21)=0.01$, $P=0.989$, $d=0.00$, $t_{fear-happy}(21)=0.43$, $P=0.675$, $d=0.15$; PPD: $t_{0\ happy}(22)=1.10$, $P=0.282$, $d=0.33$; $t_{fear-happy}(22)=2.94$, $P<0.01$, $d=0.78$.

3.4. Emotional Stroop task

For social- and panic-related words, Emotional Stroop scores were calculated by subtracting the individual median reaction time in

Table 3
Mean median RT for correct classifications and mean number of misclassifications (and standard deviations) for the panic ($N=23$) vs. control group ($N=22$) in the Facial Recognition task.

		Neutral	Anger	Disgust	Fear	Happy	Sadness	Surprise
Misclassif.	Panic	67.7 (18.3)	13.0 (8.3)	6.3 (4.9)	8.8 (6.3)	3.0 (5.3)	10.3 (5.4)	8.4 (5.4)
	Control	66.9 (16.1)	9.9 (6.6)	8.8 (8.3)	12.4 (10.1)	3.1 (2.7)	9.4 (6.3)	10.0 (5.3)
Median RT	Panic	960 (221)	1149 (255)	1230 (365)	1451 (359)	1205 (259)	1228 (300)	1250 (295)
	Control	1062 (471)	1129 (430)	1213 (331)	1485 (603)	1098 (255)	1161 (222)	1223 (374)

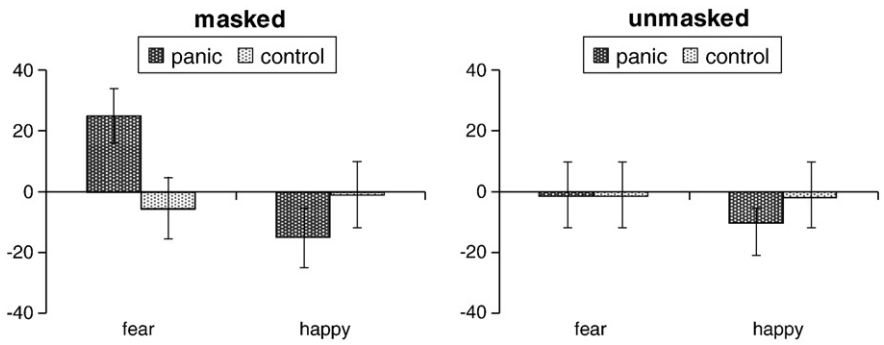

Fig. 1. Mean RT in the unmasked vs. masked Faces Dot Probe task, for panic participants ($N=23$) vs. controls ($N=22$). Error bars show the standard error of the mean.

colour-naming neutral words from a subject's median reaction time to the emotional words, separated for the masked vs. unmasked condition, see Fig. 2. Positive scores indicate an enhancement effect, negative scores imply a distraction effect in reaction to the emotional words. Repeated measures ANOVAs with the factors group and word type (social, panic) were calculated separately for the two masking conditions.

3.4.1. Unmasked condition

If emotional words were clearly visible on the screen, participants in the two groups showed no differences in colour-naming social vs. panic-related words, *word type:* $F(1,43)=0.01$, $P=0.966$, $d=0.00$, *word type×group:* $F(1,43)=0.35$, $P=0.557$, $d=0.18$, *group:* $F(1,43)=1.78$, $P=0.189$, $d=0.40$.

3.4.2. Masked condition

When emotional words were quickly followed by a symbol string mask, PPD showed significant delays in responding to both social and panic-related words, *group:* $F(1,43)=10.10$, $P<0.01$, $d=0.97$, *word type×group:* $F(1,43)=0.04$, $P=0.842$, $d=0.06$, *word type:* $F(1,43)=0.48$, $P=0.492$, $d=0.21$, indicating a similar degree of distraction by both emotional word types in these participants, PPD: $t_{pan\text{-}soc}(22)=0.35$, $P=0.730$, $d=0.08$, social words $t_0(22)=2.47$, $P<0.05$, $d=0.73$, panic words: $t_0(22)=1.89$, $P=0.073$, $d=0.56$. In contrast, HC showed no enhancement or distraction effect for social words, $t_0(21)=0.86$, $P=0.399$, $d=0.26$, and a tendency of even an enhancement effect for panic-related words, $t_0(21)=1.82$, $P=0.083$, $d=0.55$. Nevertheless, reaction to social vs. panic-related words was not significantly different in the HC, $t_{pan\text{-}soc}(21)=0.63$, $P=0.536$, $d=0.20$. Additional independent samples *t*-tests separated for the two word types confirmed the group differences in reacting to social and panic-related words, social: $t(43)=2.45$, $P<0.05$, $d=0.73$, panic: $t(43)=2.57$, $P<0.05$, $d=0.77$.

3.5. Self Beliefs task

Missing data (produced by 3 PPD and 6 HC never giving a me-response to the negative word category and 4 PPD and 13 HC never giving a not-me response to positive words) was imputed using the closest match method (Elliott and Hawthorne, 2005). Two separated repeated measure ANOVAs were calculated for the number of words accepted as self-descriptive and for RT differences in accepting vs. rejecting.

3.5.1. Frequency

Participants in both groups significantly more often chose positive words as self-descriptive compared to negative and panic-related words, and they chose more panic-related than negative words as describing them, *word type:* $F(2,86)=261.32$, $P<0.001$, $d=4.90$, all $t(44)>6.04$, all $P<0.001$, $d>0.85$. While HC associated more positive words with themselves than PPD, *group×word type:* $F(2,86)=20.28$, $P<0.001$, $d=1.37$, *group:* $F(1,43)=4.64$, $P<0.05$, $d=0.66$, $t(43)=3.96$, $P<0.001$, $d=1.23$, PPD chose more negative and more panic-related words than HC, both $t(44)>3.20$, both $P<0.01$, both $d>0.95$ (Table 4).

3.5.2. Reaction time

More automatic Self Beliefs effects were calculated by subtracting the mean reaction time in rejecting a word from the mean RT in accepting a word as self-descriptive, separated for each category. A positive score indicates quicker reaction in rejecting a word as self-descriptive, a negative score reflects quicker reaction in accepting a characteristic as self-related. The groups were similar with respect to RT differences, *group×word type:* $F(2,86)=1.81$, $P=0.169$, $d=0.41$, *group:* $F(1,43)=0.88$, $P=0.354$, $d=0.29$. In general, participants were quicker in accepting

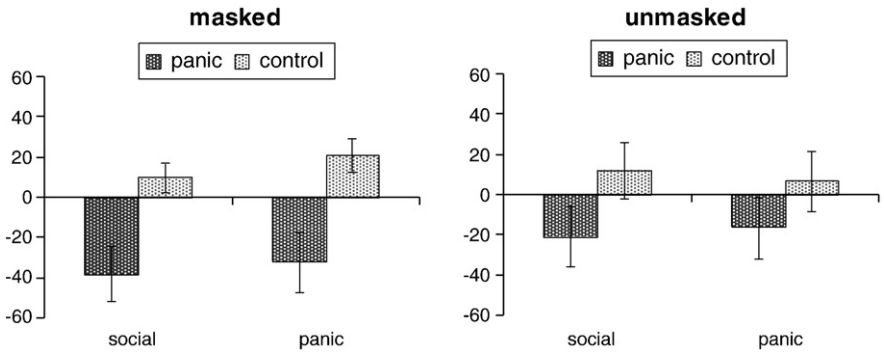

Fig. 2. Mean RT in the masked vs. unmasked Emotional Stroop task, for panic participants ($N=23$) vs. controls ($N=22$). Error bars show the standard error of the mean.

Table 4
Means and standard deviations separated for panic group and healthy controls in the Self Belief task.

Experimental parameter		Panic group ($N=23$)		Control group ($N=22$)	
		M	S.D.	*M*	S.D.
Frequency "me"	Negative	3.4	2.3	1.5	1.6
	Positive	11.3	2.8	14.1	1.6
	Panic	5.9	2.6	2.9	1.7
RT "me"–"not me"	Negative	333	−437	369	−216
	Positive	−403	−490	−471	−433
	Panic	−93	−333	154	−504

than rejecting a positive word, and they were slower in accepting than rejecting a negative word, *word:* $F(2,86)=44.36$, $P=0.000$, $d=2.03$, both $t_{0\ pos}(44)/t_{0\ neg}(44)>6.38$, both $P<0.001$, both $d>1.34$. For panic-related words, RT in accepting and rejecting were similar, $t_{0\ pan}(44)=0.43$, $P=0.672$, $d=0.09$, see Table 4.

3.6. The effect of comorbidity on attentional bias

To assess the effect of comorbid diagnoses on biases previously described, all analyses were re-run, excluding the nine PPD participants who presented with an additional anxiety or depressive disorder. In the Facial Expression Recognition task, we still found a trend for an increased recognition accuracy for sad faces in PPD, $F(1,34)=3.28$, $P=0.079$, $d=0.62$. The masked Faces Dot Probe task still revealed a trend-significant vigilance effect for fearful faces in PPD compared to HC, $F(1,34)=4.34$, $P<0.05$, $d=0.71$, $t_{fear}(34)=1.82$, $P=0.077$, $d=0.59$, $t_{happy}(34)=1.24$, $P=0.222$, $d=0.40$. In the masked Emotional Stroop task, PPD still showed significant delays in colour-naming panic words compared to HC, and a non-significant trend for increased reaction time to social words, $F(1,34)=8.11$, $P<0.01$, $d=0.98$, $t_{panic}(34)=2.04$, $P<0.05$, $d=0.73$, $t_{social}(34)=1.91$, $P=0.065$, $d=0.68$.

When only considering the 15 participants with panic disorder without agoraphobia, there was still a non-significant trend for increased recognition of sad faces in PPD, $F(1,35)=3.78$, $P=0.060$, $d=0.66$. The masked Faces dot probe task still revealed higher vigilance for fearful faces in PPD compared to HC, $F(1,35)=5.95$, $P<0.05$, $d=0.82$, $t_{fear}(35)=2.60$, $P<0.05$, $d=0.84$, $t_{happy}(35)=0.99$, $P=0.329$, $d=0.31$. Also, analyses still showed stronger colour-naming interference for panic and social words in PPD compared to HC in the masked Emotional Stroop task, $F(1,35)=8.95$, $P<0.01$, $d=1.01$, $t_{panic}(35)=2.58$, $P<0.05$, $d=0.82$, $t_{social}(35)=2.13$, $P<0.05$, $d=0.68$.

3.7. Association between attentional bias and panic severity

For the PPD, the attentional bias parameters that have been shown to significantly differ from HC were correlated with PDSS and ACQ scores in one-tailed Pearson correlational analyses. A higher PDSS score was related to higher attentional avoidance of masked happy faces in the Faces Dot Probe Task, $r(23)=-0.363$, $P<0.05$. Slower colour-naming of panic words in the Emotional Stroop task was associated with higher ACQ scores (subscale 'belief loss of control'), $r(23)=-0.392$, $P<0.05$. The same relationship was found for social words, ACQ 'loss of control': $r(23)=-0.467$, $P<0.05$, ACQ 'belief loss of control': $r(23)=-0.538$, $P<0.01$. There was a non-significant trend for an association between increased recognition of sad faces and the ACQ 'loss of control': $r(23)=.331$, $P=0.061$.

4. Discussion

The results from this study suggest that cognitive biases are apparent in untreated, community-based participants with panic disorder. In particular, the participants with panic disorder showed increased attentional biases toward negative face and word stimuli in two different paradigms and increased recognition of sad facial expressions of emotion. The sample also showed more panic- and threat-related interpretations on the Body Sensations Interpretation Questionnaire and endorsed more negative self-descriptors in the Self Beliefs task. In contrast, we found no evidence for an enhanced processing of negative core beliefs in panic disorder.

Earlier results from studies using the emotional dot probe task to assess attentional bias in panic disorder have been inconsistent, with some of them reporting vigilance for panic-related words (Asmundson et al., 1992), visually presented ECG information (Kroeze and van den Hout, 2000) or pain (Ehlers and Breuer, 1995), and others failing to find effects (Asmundson and Stein, 1994). The results presented here for a medication-free PD sample suggest that the disorder is related to vigilance for fearful faces measured in this paradigm. Future studies exploring the effects with other emotional stimuli should avoid medicated subjects given the growing body of evidence that treatments typically used in anxiety disorders can have profound effects on emotional attention (Browning et al., 2007; Murphy et al., 2008).

Our finding of an attentional bias in the Emotional Stroop task mainly replicates earlier results based on the same paradigm. An attentional distraction by the word content has been reported for supraliminal (Ehlers et al., 1988; Carter et al., 1992; McNally et al., 1994; Maidenberg et al., 1996; Lundh et al., 1999) and subliminal word presentation (Lundh et al., 1999; Lim and Kim, 2005). A recent review of Stroop task data in PPD (Compton, 2003) indicates stronger interference effects for subliminal stimuli presentations, which is in line with our results. Evidence of attentional bias seen here particularly at short exposure durations is consistent with cognitive models which predict increased initial orienting to threat across anxiety disorders (Williams et al., 1997; Mogg and Bradley, 1998).

It is also of interest that the interference effect in the Stroop task was as strong for subliminally presented social-threat words as it was to the physical and specifically panic-related threat words. This matches results of earlier studies using different types of negative material (McNally et al., 1994; Maidenberg et al., 1996; Uren et al., 2004) and is also in line with recent theories on panic disorder considering the relationship between panic symptoms and social fears (Salkovskis and Hackmann, 1997). The results — along with our results of biased facial affect processing in PPD — suggest that attentional bias in untreated panic disorder might apply to a wider range of materials than just very disorder-specific contents. This stimulus generalization effect also seems to apply to interpretation bias in PD: our finding of untreated PPD's tendency to not only interpret ambiguous panic-specific information, but also general threat scenarios in a more negative way than HC is in line with earlier studies not controlling for medication status (Clark et al., 1997).

We also found increased recognition of sad facial expressions of emotion in the untreated PD participants. This directly contrasts with the results from a recent study which reported a generally reduced recognition performance in medicated PD volunteers, especially for the emotions sadness and anger (Kessler et al., 2007). However, SSRI treatment has also been found to reduce the recognition of negative facial expressions of emotion (Harmer et al., 2004) and neural responses to sad facial affect (Fu et al., 2004), suggesting an alternative explanation for these results. Considering of medication status may therefore help resolve the inconsistencies in this field regarding behavioural and neural responses to negative facial expressions in PD (Lundh et al., 1998; Pillay et al., 2006).

The results reported here are in line with the clinical presentation of panic disorder. Panic attacks are hypothesised to develop on the basis of a sensitive recognition of initial bodily symptoms and their misinterpretation as a sign of an imminent catastrophe such as a heart attack or a collapse (Clark, 1986). Our results of an automatic attentional bias for panic symptom words and fearful faces, as well as the preference for panic-related interpretations in the BSIQ, would be expected to fuel such clinical phenomena. The observation that the attentional biases mainly

occurred with short stimulus presentation times is not only in line with the clinical experience of patients that attacks seem to happen "out of the blue", implying how fast and automatic attention can be drawn to bodily symptoms, but also with theoretical research suggesting that anxiety is particularly associated with enhanced orienting rather than maintenance of attentional focus to threat cues (Mogg et al., 2004b).

While this study has the significant strength of recruiting participants not currently treated with medication or psychotherapy, this does limit the severity of symptoms which were captured in this sample. These volunteers showed characteristic negative biases both in the self-reported questionnaires and in the objective tasks, but it is unclear whether similar effects would be seen in a more disabled and affected group. It is also unknown how drug and psychological treatment affect these biases in PD and the extent to which these treatments can reverse these negative biases in information processing.

Also, our study design allows no conclusions about the specificity of these biases for PD, as no other clinical group was tested. Attentional bias is associated with other anxiety disorders as well, reflected in increased interference in the Emotional Stroop task (Martin et al., 1991; Foa et al., 1993; Mattia et al., 1993) or heightened vigilance in the dot probe task (MacLeod et al., 1986; Musa et al., 2003; Amir et al., 2009). However, it seems that stimulus material needs to be relevant to the investigated disorder in order to find attentional bias. Although patients with panic disorder seem to show an Emotional Stroop effect for all types of negative word material, they seem to be the only clinical group showing this bias for panic-related words. Delays in colour-naming panic-words have not been found in a social phobia (Maidenberg et al., 1996) or a major depression (Lim and Kim, 2005) comparison group. Therefore, it is likely that the Emotional Stroop effect found for panic words is specific for a panic sample.

Related to the fact that similar attentional biases occur across different anxiety disorders, the high comorbidity rate in our panic sample could potentially conflict with the interpretation of results. One could argue that the attentional biases found here were mainly driven by the comorbid diagnoses in our panic sample. However, the additional analyses excluding patients with comorbid anxiety or depression revealed similar results as the main analysis, indicating that the effects found here are reliably linked to panic. Nevertheless, no conclusions can be made regarding the role of these biases as causal factors in the development of anxiety. Study paradigms assessing the effect of cognitive bias training on anxiety symptoms (Mathews and Mackintosh, 2000; MacLeod et al., 2002) would be a worthwhile continuation of this research to explore whether these biases also act as a vulnerability factor in the onset of a panic disorder.

In summary, the results from this study support the existence of attentional and interpretational biases in untreated participants with panic disorder. The observation that these biases are apparent even in a community-based sample with only mild to moderate severity of panic disorder supports the role of these biases in the underlying aetiology and maintenance of the disorder. The challenge remains to assess whether these biases are an important target for drug or psychotherapy treatment strategies and whether these processes are involved in the initial vulnerability to the disorder. The tasks that were able to show group differences appear recommendable as outcome measures in treatment studies, as their results are based on a very pure, untreated sample.

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