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FULL-LENGTH ORIGINAL RESEARCH

Trauma, stress, and preconscious threat processing in patients with psychogenic nonepileptic seizures

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Summary

Purpose: Psychogenic nonepileptic seizures (PNES) have long been considered as paroxysmal dissociative symptoms characterized by an alteration of attentional functions caused by severe stress or trauma. Although interpersonal trauma is common in PNES, the proposed relation between trauma and attentional functions remains under explored. We examined the attentional processing of social threat in PNES in relation to interpersonal trauma and acute psychological stress.

Methods: A masked emotional Stroop test, comparing color-naming latencies for backwardly masked angry, neutral, and happy faces, was administered to 19 unmedicated patients with PNES and 20 matched healthy controls, at baseline and in a stress condition. Stress was induced by means of the Trier Social Stress Test and physiologic stress parameters, such as heart rate variability (HRV) and cortisol, were measured throughout the experiment.

Results: No group differences related to the acute stress induction were found. Compared to controls, however, patients displayed a positive attentional bias for masked angry faces at baseline, which was correlated to self-reported sexual trauma. Moreover, patients showed lower HRV at baseline and during recovery.

Discussion: These findings are suggestive of a state of hypervigilance in patients with PNES. The relation with self-reported trauma, moreover, offers the first evidence linking psychological risk factors to altered information processing in PNES.

KEY WORDS: Psychogenic nonepileptic seizures, Dissociative seizures, Masked emotional Stroop, Angry faces, Psychotrauma, Stress.

Psychogenic nonepileptic seizures (PNES) can be defined as paroxysmal involuntary behavioral patterns that mimic epileptic events but for which no organic cause can be identified. PNES lack ictal epileptiform activity in the brain and are thought to be mediated by psychological factors (World Health Organization, 1993; American Psychiatric Association, 1994). They are characterized by a sudden and time-limited alteration of consciousness and are associated with a disturbance in controlling motor, sensory, autonomic, cognitive, emotional, and/or behavioral functions (e.g., Kuyk et al., 1999).

It is estimated that up to 30% of patients referred to specialized epilepsy centers experience PNES (e.g., Gumnit, 1993; Martin et al., 2002; Benbadis, 2005) and several authors emphasize the high load that patients with PNES impose on health service resources (Martin et al., 1998; LaFrance & Benbadis, 2006).

PNES form one of the major manifestations of conversion disorder as described in the DSM-IV (American Psychiatric Association, 1994). In ICD-10 (World Health Organization, 1993) PNES are categorized under dissociative disorders, more specifically under dissociative convulsions. Both classification systems specify that the etiology of PNES is related to psychological stress factors.

Previous research has shown that PNES are associated with a history of psychological trauma, such as sexual and physical abuse (e.g.. Betts & Boden, 1992; Bowman, 1993; Moore & Baker, 1997; Kuyk et al., 1999; Fiszman

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et al., 2004; Sharpe & Faye, 2006). However, how these increased interpersonal trauma rates may be related to PNES remains under explored.

Conversion/dissociative symptoms such as PNES have long been regarded as attention-related complaints caused by psychological stress factors (Janet, 1907; Ludwig, 1972; Brown, 2004). Pierre Janet (1907); for example, proposed that these symptoms result from an impairment of the attentional functions caused by severe stress or trauma. There is empirical evidence for altered attentional functioning in trauma-related disorders. For example, patients with posttraumatic stress disorder (PTSD) commonly allocate their attention toward trauma-related stimuli, as evidenced by studies using the emotional Stroop task (for reviews see McNally, 1996; Buckley et al., 2000). These studies demonstrated that patients with PTSD are slower in color-naming trauma-specific threat words, as compared to trauma-unrelated words indicating that attention is allocated automatically toward the threat-value of the word (Williams et al., 1996).

These findings may be relevant for our understanding of the theorized impairments of attentional functions in patients with PNES, although studies on stress and attentional functioning in patients with PNES are scarce. Compared to healthy control groups, patients with PNES show decreased attentional functioning in standard neuropsychologic test batteries (for a review see Cragar et al., 2002) There is, however, only one study in which the effects of stress on cognitive functions in PNES were examined. Bendefeldt et al. (1976) investigated attentional processing in 17 patients with conversion symptoms (10 had PNES) and found some evidence for worsened attentional processing (compared to a nonpsychotic patient control group) in both baseline and stress conditions, using a face-recognition task and a mental switch-task. Only the processing of neutral stimuli was, however, assessed. The processing of stimuli relevant to interpersonal trauma, such as trauma-related words or threatening faces, has not been examined. In addition, no studies have addressed the relationship between interpersonal trauma and attentional deficits in PNES.

With the present study we aimed to test the proposed relationship between attentional processing of social threat stimuli and psychological stress factors in a sample of PNES patients. We were specifically interested in testing the hypothesis that patients with PNES automatically allocate their attentional resources toward social threat stimuli. To test this hypothesis, patients and matched healthy controls were administered a masked emotional Stroop task, in which pictures of angry, happy, and neutral facial expressions were presented backwardly masked and participants were asked to color-name the masks (Van Honk et al., 1998, 2000; Putman et al., 2004; Hermans et al., 2006, 2008; Roelofs et al., 2007). The major outcome of emotional Stroop tasks is the attentional bias score, which is calculated by subtracting the color-naming latencies for neutral faces from the latencies needed to color-name emotional faces. A positive attentional bias score (i.e., color-naming latencies for emotional faces are larger than those for neutral faces) is taken to indicate vigilance, whereas a negative attentional bias score (i.e., color-naming latencies for emotional faces are shorter than those for neutral faces) is thought to indicate avoidance (e.g., Mathews & MacLeod, 1994; Van Honk et al., 1998, 2000; Putman et al., 2004). We used a masked version of the emotional Stroop task, in which the stimulus processing remains preconscious owing the short stimulus presentation (14 ms), making it unlikely that subjects exerted strategic effort to control possible attentional bias effects (e.g., MacLeod & Hagan, 1992; Van den Hout et al., 1995; Williams et al., 1996; Putman et al., 2004). Masked Stroop tasks have yielded more consistent results (Putman et al., 2004) and are more predictive than unmasked Stroop tasks of actual coping with stressful life-events (MacLeod & Hagan, 1992). On the basis of the previous findings in trauma-related disorders we expected that patients with PNES would show a positive attentional bias for angry faces.

Secondly, we tested whether such positive attentional bias would be related to interpersonal trauma reports in patients with PNES. Finally, we tested whether acute psychological stress affects the attentional bias toward interpersonal threat cues in patients with PNES. Therefore, we administered the Stroop task in a baseline and a social stress condition. Physiologic and subjective stress markers (cortisol, heart rate, blood pressure, and subjective anxiety) were assessed throughout the experiment.

Methods

Participants

Patients with PNES who were admitted to SEIN, Epilepsy Institute in the Netherlands were recruited by their neurologists. Inclusion criteria were (1) diagnosis of PNES based on an ictal video-EEG (electroencephalography) recording of a typical seizure; (2) PNES is characterized by complete or partial loss of consciousness (specified as an ictal diminished or loss of adequate responsiveness or postictal memory impairments of the ictal event); (3) the occurrence of at least two seizures in the year prior to the experiment; (4) no history of epileptic seizure; (5) no comorbid neurologic disease diagnosis; (6) no current use of antidepressants, corticosteroids, lithium, beta-blockers, cimetidine, or ketoconazole; and (7) no significant endocrine disorder(s). Two of the 21 patients who participated in this study were excluded post hoc from the analysis as one was found to be using antidepressant medication, and the other experienced a PNES during testing. The remaining patients (four males, 15 females) had a mean age of 27.58 (SD = 7.30) years.

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Table 1. Patients' and controls' demographic characteristics, DSM-IV axis I comorbid psychopathology, and rates of reported interpersonal traumas and seizure characteristics

Variable	Patients (N = 19)	Controls (N = 20)	Statistics
Age (SD) in years	27.6 (7.3)	22.1 (4.2)	$t(28.51) = 2.85, p < 0.01$
Number of women	15	18	$\chi^2(1) = 0.91, p = 0.34$
Using contraceptives[a]	6	10	$\chi^2(1) = 0.51, p = 0.48$
Luteal menstruation cycle[b]	7	8	$\chi^2(1) = 0.14, p = 0.71$
Educational level			$\chi^2(1) = 2.51, p = 0.11$
Primary and secondary	15	11	
Higher	4	9	
Comorbid psychopathology			
None	4	20	
Mood disorder	4		
Anxiety disorders			
Panic disorder	2		
Agoraphobia	4		
Social phobia	3		
Generalized anxiety disorder	4		
Obsessive compulsive disorder	1		
Post traumatic stress disorder	1		
Somatoform disorders			
Pain disorder	4		
Somatization disorder	1		
Subjects reporting psychotrauma			
Any interpersonal trauma	17	2	$\chi^2(1) = 24.63, p < 0.001$
Sexual	14	1	$\chi^2(1) = 19.42, p < 0.001$
Emotional	14	2	$\chi^2(1) = 16.33, p < 0.001$
Physical	12	1	$\chi^2(1) = 14.83, p < 0.001$
Seizure characteristics			
Age (SD) at onset in years	21.1 (7.9)		
Disease duration (SD) in years	6.5 (7.4)		
Frequency per 4 weeks (SD)	27.8 (30.2)		

[a]Use of contraceptive was unknown in one patient.
[b]Menstruation cycle was indeterminable in two patients and one control.

Table 1 shows the subjects' demographics as well as use of contraceptives, menstrual cycle, comorbid DSM-IV axis I diagnoses (assessed using the MINI: Mini-International Neuropsychiatric Interview, Sheehan et al., 1998), self-reported interpersonal traumatic experiences and seizure characteristics.

The control group was recruited through advertisements in local newspapers. Inclusion criteria were (1) no psychiatric diagnoses assessed; (2) no clinically significant medical disease; (3) no neurologic disease diagnosis; and (4) not using medication. Twenty healthy controls (two males, 18 females) with a mean age of 22.10 (SD = 4.22) years were recruited. Table 1 shows that patients were slightly older than controls but did not differ with respect to educational level, gender, use of contraceptives, or menstrual cycle. PNES patients reported higher rates of all types of interpersonal trauma compared to the control group.

All participants were instructed to minimize physical exercise during the hour preceding the experiment and to avoid large meals, coffee, drinks with low pH, or cigarettes, because these variables can affect cortisol levels. All participants had normal or correct-to-normal vision. The study was approved by the local ethics committee and all participants provided written informed consent and received financial compensation for participation.

Measures

Emotional Stroop task

The preconscious attentional processing of happy and angry faces was assessed using a masked pictorial emotional Stroop task. Facial stimuli of 10 different individuals (five males, five females) were taken from Ekman and Friesen's Pictures of Facial Affect (Ekman & Friesen, 1976), each displaying a neutral, a happy, and an angry expression. The facial stimuli were presented for 14 ms. immediately after the stimulus presentation the pictures were replaced by a masking stimulus. This procedure was extensively piloted in the laboratory of Van Honk and colleagues (Van Honk et al., 1998, 2000), who established an objective threshold for the recognition of emotional expressions for the displays. These pilots indicated that a 30-ms masking interval effectively precluded recognition of the emotional valence of targets in every subject

(Van Honk et al., 1998, 2000; Putman et al., 2004; Hermans et al., 2006; Roelofs et al., 2007; Hermans et al., 2008). The masking stimuli consisted of randomly cut, reassembled, and rephotographed pictures of faces. At each trial, the stimulus and mask were presented in the same color (red, green, or blue), and participants were instructed to vocalize this color. Upon vocal response initiation, the presentation of the masking stimulus was terminated. After a random inter-trial interval (2–4 s), new trials started with a 750-ms lasting fixation point. A total of 30 happy, 30 angry, and 30 neutral faces were presented in a random order with the restriction that the same color was never repeated more than twice consecutively (Van Honk et al., 1998, 2000; Putman et al., 2004; Hermans et al., 2006, 2008; Roelofs et al., 2007). The main outcome variable in the emotional Stroop task is the attentional bias score for emotional facial expressions, which is based on correct responses only and calculated on basis of interference scores, by subtracting the mean individual color-naming latencies of neutral faces from the individual mean color-naming latencies of emotional faces. A positive attentional bias score, indicating slower color-naming to emotional faces as compared to neutral faces, is interpreted as a vigilant response, whereas a negative attentional bias score, indicating faster color-naming to emotional faces as compared to neutral faces, is interpreted as an avoidant response (e.g., Mathews & MacLeod, 1994; Van Honk et al., 1998, 2000; Putman et al., 2004). In addition, error rates were registered for each group, condition and facial expression separately.

To maximize the quality of the voice key registration, the subjects were instructed to speak loudly and clearly, to keep their mouths open during the task, to avoid smacking their lips or coughing before responding, and to avoid correcting their answers in case they had already started vocalizing an erroneous response. All instructions were rehearsed in a practice phase of nine stimulus presentations in which only masks were used (i.e., without facial stimuli).

Awareness check

To ascertain that subjects remained unaware of the facial expressions in the Stroop task, the efficacy of the masking procedure was checked by means of a separate awareness check administered at the end of the experiment. During this three-alternative, forced choice, happy-angry-neutral recognition procedure, a random set of 30 masked faces was shown to the subjects. In advance of the test, the subjects were told explicitly that the set contained 10 happy, 10 neutral, and 10 angry faces. Participants were instructed to indicate (or guess), whether the presented picture contained a neutral, happy, or angry expression by pushing the corresponding button (see also Van Honk et al., 1998, 2000; Putman et al., 2004; Hermans et al., 2006, 2008; Roelofs et al., 2007).

Stroop Color-Word task

Attentional processing of neutral stimuli was assessed using a computerized Stroop color-word task (Stroop, 1935). Our version consisted of two series. In the first "congruent" series, four bars in the colors green, blue, red, and yellow were each presented six times in random order and subjects were instructed to name the color of the bar as quickly as possible. The second "incongruent" series of stimuli consisted of a total of 48 color words presented in a color different from the meaning of the word (e.g., the word red presented in green print). Participants were instructed to name the color of the print as quickly as possible. Each trial was presented centrally, and presentation of the stimuli was terminated upon vocal response initiation. After a random inter-trial interval (2–4 s), new trials started with a 750-ms lasting fixation point. All instructions were practiced in a practice phase, and preceding the first series, each of the four colored bars was presented once. To give participants a chance to adjust to the instructions of the second "incongruent" series, 12 practice trials preceded these series.

Naming the color of the print when the meaning of the word is an incongruent color, results in color-naming latencies compared to the color-naming latencies of the colored bars. This effect, known as Stroop interference, is calculated by subtracting the color-naming latencies of the first series from those of the second "incongruent" series. This classic Stroop interference is consistently found and is explained by the costs for subjects to suppress a concurrent (automatic) competing response (for a comprehensive review see MacLeod, 1991). Details concerning validity and reliability have been described elsewhere (e.g., Strauss et al., 2005a; Alvarez & Emory, 2006).

Emotional, physical, and sexual trauma

Emotional, physical, and sexual traumas were measured by means of the Traumatic Experiences Checklist (TEC), a 26-item self-reported questionnaire with good reliability and validity (Nijenhuis et al., 2002). The scores for the presence of both emotional trauma (emotional neglect and emotional abuse in various settings) and sexual trauma (sexual harassment and sexual abuse in various settings) are based on six items. The scores for the presence of physical abuse in various settings are based on three items. All items are preceded by the phrase: *Did this happen to you?* An example of a sexual abuse item is: *Sexual abuse* (*unwanted sexual acts involving physical contact*) *by your parents, brothers*, *or sisters*. For all three types of interpersonal trauma a dichotomous score (*yes/no*) was calculated.

Trier Social Stress Task

This psychological challenge test consists of an anticipation period, a video- and audio-taped job application speech, and a mental arithmetic task in front of a two-individual audience. The Trier Social Stress Task (TSST) takes 15 min, and has been found repeatedly to induce significant endocrine and cardiovascular responses in 70–80% of the participants (for a detailed description see Kirschbaum et al., 1993). In a review paper on acute laboratory stressors, the TSST was found to be the strongest elicitor of cortisol elevations (Dickerson & Kemeny, 2004). To ensure that stress levels remained high during the second administration of both Stroop tasks, the audience remained in the room after the TSST. After this, the audience left the room and subsequently returned for a short debriefing.

Physiologic and subjective measures

To test the effectiveness of the stress induction, several physiologic and subjective stress measures were conducted as a manipulation check. With the exception of heart rate, all physiologic and subjective stress-measures were obtained at 11 assessment points over a 200-min period, at respectively −60, −40, −20, 0, (rest) +20, +40, (stress) +60, +80, +100, +120, and +140 (recovery) min with reference to the start of the stressor. All assessments were performed between 1:15 and 5:00 p.m. (see also Fig. 1).

Cortisol

Salivary (free) cortisol is a good indicator of glucocorticoid activity with the advantage (over blood cortisol samples) of stress-free (non-invasive) sampling. This method is, therefore, recommended in stress research where reliable "baseline-to-stress" comparisons are essential (Kirschbaum et al., 1993; Kirschbaum & Hellhammer, 1994). Saliva samples were obtained using Salivette collection devices (Sarstedt, Rommelsdorf, Germany). Saliva samples were stored at −20°C before assaying. Biochemical analysis of free cortisol in saliva was performed using a competitive electrochemiluminescence immunoassay (ECLIA, Elecsys 2010; Roche Diagnostics, Basel, Switzerland), as described elsewhere (Van Aken et al., 2003).

Systolic (SBP) and diastolic blood pressure (DBP)

SBP and DBP were measured from the nondominant arm using an automatic electronic digital blood pressure monitor, the Omron R5-I (Omron, Hoofddorp, The Netherlands), which could be initiated manually. This device fulfilled the validation criteria of international guidelines for both systolic and diastolic blood pressure (for more information see Omboni et al., 2007). Because of technical problems, both SBP and DBP data are missing for one patient and one control subject.

Heart rate (HR) and heart rate variability (HRV)

After the first sequence of physiologic and subjective assessments, HR was continuously measured by the Ambulatory Monitoring System (AMS; version 4.6; TD-FPP, Vrije Universiteit, Amsterdam, The Netherlands). This device has been used extensively and details of its reliability, validity aspects, and recording methodology have been published previously (De Geus et al., 1995; Willemsen et al., 1996). In the present study the electrocardiography signal was recorded using disposable pre-gelled Ag–AgCl electrodes (ConMed, New York, U.S.A.) that were placed at the jugular notch of the sternum, 4 cm under the left nipple and at the lateral right side. Using this three-electrode configuration, only the inter-beat interval time series was available for analysis. The device detects the R-wave of the electrocardiogram and records the time in milliseconds (with 1-ms resolution). From the raw interbeat intervals the device derives and stores 30-s averages of HR (in beats per minute) and root mean-square of successive differences of interbeat intervals (in milliseconds: RMSSD), which was used as an index of HRV. The RMSSD has been shown to be a reliable index of cardiac parasympathetic influence, and is recommended as a measure of vagally mediated HRV for its simplicity (Task Force Guidelines, 1996; Thayer & Brosschot, 2005). Both HR and HRV were averaged per phase separately, resulting in an average for the baseline period, for the stress condition and for recovery. Because of technical problems, both HR and HRV data are missing for one patient and two control subjects.

Subjective anxiety

Participants rated their subjective anxiety on a visual analog scale, ranging from 0 (not anxious) to 10 (extremely anxious), at each assessment point.

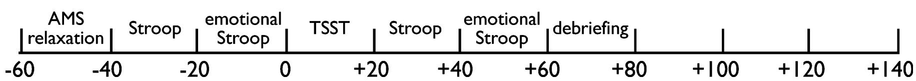

Figure 1.
Outline of the experiment. Assessment points (in min, with reference to the onset of the Trier Social Stress test: TSST) of the physiologic and subjective stress parameters. AMS, Ambulatory Monitoring System.
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Procedure

On the test day, participants arrived about 2 h before the first physiologic assessments and more than 2 h before the cognitive tasks were administered. Participants were submitted to a standard protocol to control for factors that may influence HPA-axis activity of the hypothalamus pituitary adrenal (HPA) axis and hence cortisol activity (e.g., exercise, lunch). Participants were first screened for DSM-IV axis-I psychopathology (American Psychiatric Association, 1994) using the MINI (Sheehan et al., 1998). No later than 30 min after arrival, subjects had a light lunch (sandwiches and soft drinks). Half an hour later the DSM-IV screening was continued (if necessary), the TEC questionnaire was completed, and subjects were interviewed briefly about their professional ambitions in preparation for the public speaking part of the TSST (although participants were unaware of the purpose of this interview). The participants were taken to the experimental room after an additional 45 min. The outline of the experiment is presented in Fig. 1.

Statistical analyses

For the emotional Stroop task, color-naming latencies outliers were filtered using a <150 and >1500 ms cutoff. For the correct responses, all color-naming latencies exceeding 2.5 SD from their cell mean were subsequently removed (cell defined by Condition, Group, and Emotional expression of the faces). The remaining latencies were averaged for each individual over Condition and Emotional expression, and attentional bias scores were calculated subsequently. For the color-word Stroop task the same procedure was followed, except that cells were defined by Condition, Group, and Series (congruent/incongruent).

For both the emotional and color-word Stroop tasks, percentages of incorrect responses were calculated per cell. For the awareness check, percentages of correct responses were calculated, and a nonparametric test was applied to determine whether the patients' and controls' percentage correct responses did not exceed chance level.

Physiologic and subjective stress measures were post hoc averaged per experimental phase (baseline: −20 to 0 min), stress (20 to 40 min), and recovery (60 to 140 min).

Performance on the emotional Stroop and the color-word Stroop, as well as the effects of stress induction on physiologic and subjective stress measures, was tested using repeated measures analyses of variance (ANOVA rm). The relationship between attentional bias scores and trauma ratings was calculated using Pearson correlations. All statistical analyses described employed a two-tailed alpha of 0.05.

Results

Manipulation checks

Stress induction

To check whether the stress induction was successful, separate two-way ANOVAs rm for the physiological and subjective stress measures were conducted with Group (Patients, Controls) as between-subject factor and Condition (baseline, stress, recovery) as within-subject factor. The results showed a significant main effect of Condition for cortisol [$F(2,36) = 19.01$, $p < 0.001$], SBP [$F(2,34) = 40.24$, $p < 0.001$]; DBP [$F(2,34) = 24.31$, $p < 0.001$]; HR [$F(2,33) = 35.44$, $p < 0.001$]; HRV [$F(2,33) = 6.07$, $p < 0.01$]; and self-reported anxiety [$F(2,36) = 34.61$, $p < 0.001$].With the exception of HRV, post hoc F tests for these measures demonstrated a relative increase during stress followed by a decrease during the recovery phase for all parameters (all p-values < 0.01), indicating that stress-induction was indeed successful. Group effects were present for only HRV [main effect of Group: $F(1,34) = 5.30$, $p < 0.05$] and not for other subjective or physiologic measures (all p-values > 0.10). This finding indicated that patients had lower HRV than controls throughout the experiment. Post hoc testing demonstrated that this effect was particularly significant at baseline [$F(1,34) = 5.64$, $p < 0.05$] and during recovery [$F(1,34) = 4.93$, $p < 0.05$] but not during stress [$F(1,34) = 2.54$, $p = 0.12$; see Fig. 2].

Emotional Stroop masking procedure

Chance performance in a three-alternative forced-choice recognition check using 30 stimuli is 10 (33.3%) correct identifications per subject. Because of technical problems, the data of one of the 19 patients were not

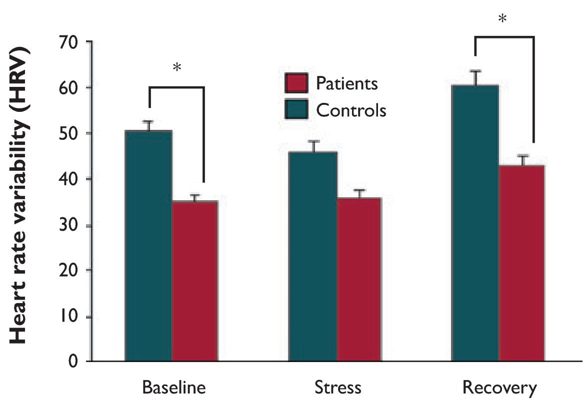

Figure 2.
Patients' and controls' mean heart rate variability (HRV) rates (±SEM) during baseline, stress, and recovery. *p < 0.05.
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available. Of the total numbers of 540 trials, 178 (33.3%) were correctly recognized by patients. All 20 controls completed the check (600 trials), of which a total of 199 (33.2%) was correctly recognized. Nonparametric tests showed that there was no significant deviation from chance detection for the patients ($p = 0.51$) or the control group ($p = 0.48$). It can be concluded that masking was successful.

Attentional bias (AB) scores

Emotional Stroop

To investigate the AB scores for angry and happy faces at baseline and in the social stress condition, we conducted a three-way ANOVA rm for the AB scores, with Facial Expression (FE: happy, angry) and Condition (baseline, stress) as within-subject factors and Group (patients, controls) as between-subject factors. There were no main-effects for FE [$F(1,37) = 0.96$, $p = 0.33$], Condition [$F(1,37) = 0.85$, $p = 0.36$] or Group [$F(1,37) = 0.07$, $p = 0.79$], but there was a significant FE × Condition × Group interaction [$F(1,37) = 5.91$, $p < 0.05$]. Post hoc F tests to investigate this three-way interaction indicated that the FE × Group interaction was significant at baseline [$F(1,37) = 9.18$, $p < 0.005$], but not during stress [$F(1,37) = 0.02$, $p = 0.88$]. Further investigation of the results at baseline showed that patients with PNES differed significantly from the controls in their response to angry faces [$F(1,37) = 4.18$, $p < 0.05$] but not to happy faces [$F(1,37) = 1.07$, $p = 0.31$]. As illustrated in Fig. 3, these results indicate that whereas patients showed a positive AB to angry faces, controls showed a negative AB for these stimuli at baseline. These group differences disappeared in the social stress condition.

Finally, we checked whether the FE × Group interaction at baseline remained significant after controlling for age by entering Age as a covariate in the analysis. We found that this effect remained statistically significant [$F(1,36) = 5.12$, $p < 0.05$].

Error rates

The FE × Condition × Group ANOVA rm for the error rates resulted in a main effect for Condition [($F(1,37) = 15.62$, $p < 0.001$: 2.7% (baseline) vs. 1.6% (stress)] and FE [($F(2,36) = 6.24$, $p < 0.01$): 2.9% (angry); 2.1% (neutral); 1.4% (happy)]. Moreover, there was a significant interaction effect for Condition × Group [$F(1,37) = 12.78$, $p<0.01$], indicating that whereas patients performed less accurately at baseline (3.6%) as compared to stress [(1.4%); ($F(1,18) = 22.07$, $p < 0.001$)], controls showed no such condition effect (baseline = 1.8%; stress = 1.7%; ($F(1,19) = .10$, $p = 0.76$)].

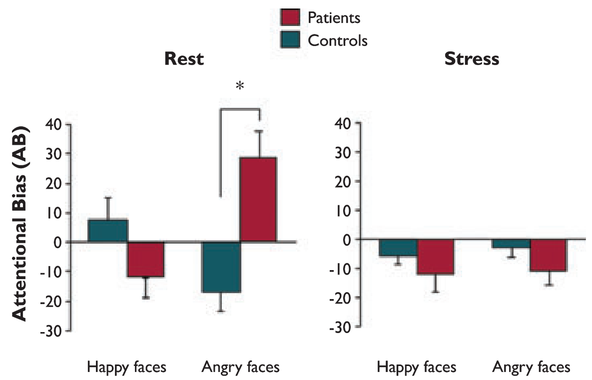

Figure 3.
Mean attentional bias (AB) scores (color-naming latencies of emotional faces minus color-naming latencies for neutral faces) in ms (±SEM) for happy and angry faces in baseline and social stress condition. A positive AB indicates vigilance; a negative AB reflects avoidance. *$p < 0.05$.
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Stroop Color-Word

To investigate the selective attention for neutral stimuli at baseline and during stress we conducted a two-way ANOVA rm for the Stroop interference scores, with Condition (baseline, stress) as within-subject factor and Group (patients, controls) as between-subject factors. There were no main effects for Condition [$F(1,37) = 1.04$, $p = 0.31$] and Group [$F(1,37) = 0.07$, $p = 0.80$], and no interaction effects for Condition × Group [$F(1,37) = 0.00$, $p = 0.98$], indicating that selective attention for neutral stimuli was unaffected in patients with PNES.

Error rates

The Condition × Group ANOVA rm for the error rates revealed no significant main effects, but there was a significant Condition × Group interaction [$F(1,37) = 6.19$, $p < 0.05$], indicating that whereas patients were less accurate at baseline (7.8%) compared to stress [(4.3%); ($F(1,18) = 9.56$, $p < 0.01$)], controls showed no such condition effect [$F(1,19) = 1.27$, $p = 0.27$; baseline = 3.7%; stress = 5.9%].

AB and trauma reports

Because there were effects for only the emotional and not for the neutral Stroop task, correlations with trauma reports were only calculated with respect to the emotional Stroop task. The patients' positive AB for angry faces at baseline was positively correlated to the presence of sexual trauma reports (Pearson's point correlation: $r = 0.46$, $p < 0.05$), indicating that increased sexual trauma reports were associated with a positive AB for angry face stimuli on the masked emotional Stroop task. The correlation between the patients' positive AB angry faces at baseline and physical abuse was in the same direction but did not reach significance ($r = 0.39$, $p = 0.10$). There were no such effects for emotional trauma ($r = 0.18$, $p = 0.45$) and no such effects for the control subjects (all p-values > 0.30).

Discussion

In this study, patients with PNES and matched controls did not differ in their performance on a *neutral* (and unmasked) Stroop task, but they showed significant differences in the processing of *emotional* stimuli on a masked pictorial Stroop task. Whereas the healthy controls displayed a negative attentional bias (AB) for angry faces, patients showed a positive AB for these social threatening stimuli, indicating that on a preconscious level of processing, patients were vigilant for social threat stimuli. In addition, this increased threat vigilance was related to self-reported trauma in patients with PNES. We describe these results in detail and discuss their implications.

The finding that patients with PNES reported more traumatic events than controls fits with the generally found high trauma rates in patients with PNES (e.g., Betts & Boden, 1992; Bowman, 1993; Moore & Baker, 1997; Kuyk et al., 1999; Fiszman et al., 2004; Sharpe & Faye, 2006) and conversion disorder in general (Roelofs et al., 2002). Most importantly, self-reported sexual trauma was related to the positive AB for angry faces in the patient group but not in controls. This relationship between threat vigilance and trauma reports shows an interesting parallel with findings in patients with PTSD to trauma-specific threat stimuli (for a review see McNally, 1998; Buckley et al., 2000). In patients with PTSD, such vigilance for trauma-related stimuli is considered as a tendency constantly to scan the environment for any signs of potential threat (Buckley et al., 2000), or it could reflect an impaired suppression of trauma information once it is activated (McNally, 1998). A similar positive AB for preconsciously presented angry faces, using the same masked pictorial Stroop task, was found in traumatized subjects with Dissociative Identity Disorder (Hermans et al., 2006), which was interpreted as indicating a state of hypervigilance. The finding of increased allocation of attentional resources to social threat in the current study may similarly reflect a state of hypervigilance, an interpretation that is supported by the finding that patients with PNES showed decreased HRV throughout the experiment. Decreased HRV is associated with increased arousal and anxiety and was previously found in patients with anxiety disorders, such as panic disorder (Friedman & Thayer, 1998), generalized anxiety disorder (Thayer et al., 1996), and PTSD (Cohen et al., 1999), and has been suggested as being associated with poor emotion regulation (Ruiz-Padial et al., 2003) and a negativity bias (Thayer & Brosschot, 2005). It is interesting to relate these findings to previous findings of repressive coping styles in PNES (e.g. Frances et al., 1999; Goldstein et al., 2000). Cognitive vigilance and avoidance are considered as ways of coping in the face of threat (e.g., Calvo & Eysenck, 2000; Hock & Krohne, 2004), and so-called repressors are characterized by an initial disproportionate engaging in threat processing, followed by an avoidance of threat processing and high physiologic arousal (Calvo & Eysenck, 2000). Future studies should investigate whether the threat-vigilance identified in the present study may be associated by subsequent avoidance, for example by using a modified dot-probe paradigm (see Mogg et al., 1997; Bögels & Mansell, 2004). Such investigation is particularly relevant because seizure reduction or cessation is generally associated with more active coping strategies in patients with PNES (Bodde et al., 2007; Kuyk et al., 2008), and it may contribute to fine tuning of psychological treatment of PNES. In contrast, the (early) avoidant coping style exhibited by our healthy controls in the face of threat, is considered as an adequate manner to avoid injury and unnecessary energy loss (Sapolsky, 1990; Van Honk et al., 2000).

In the present study, an increase of subjective and physiologic stress parameters during stress in both patients and controls suggested that the stress induction by means of the Trier Social Stress Test was successful. The group difference in attentional processing of social threat stimuli reported for the baseline condition was no longer present when subjects were tested in the context of social stress. Although this finding was in contrast to our predictions derived from Bendefeldt et al. (1976), this result is in agreement with earlier studies in patients with PTSD (Constans et al., 2004) and social phobia (Amir et al., 1996) in which patients exhibited a positive AB for threat words in a emotional Stroop task at baseline, which was suppressed in anticipation of a stressor. Because a positive AB for angry faces is often taken as indicating hypervigilance for signs of social threat, the fact that this effect disappeared during stress may be related to the unambiguousness of the social stress context, which makes an AB toward social threat stimuli in the emotional Stroop task simply redundant. Such interpretation is supported by Pessoa et al. (2002), who found that processing of emotional stimuli in a highly demanding environment did not lead to an activation of the amygdala. It was previously argued that in a highly demanding environment, all available attentional resources are focused on the environment, not on the cognitive task, resulting in reaction patterns that are independent of the emotional valence of the emotional stimuli (Lavie, 1995). In our study, the disappearance of the patients' positive AB to angry faces in the social stress condition may reflect an allocation of all attentional resources towards the socioevaluative threat of the audience in this condition. Alternatively, it is possible that patients put more effort into complying with the task demand, in the context of social stress, resulting in a suppression of the AB for angry faces. The fact that patients made fewer errors in both Stroop tasks during stress, as compared to baseline, supports this notion, although this latter finding could also reflect a possible learning effect.

Patients and controls did not differ with respect to their basal and stress-induced cortisol levels. Although these findings are suggestive of a normal stress-reactivity of the HPA-axis in PNES, it should be noted that the currently used stressor was not specific for this disorder. In the context of trauma-related disorders, the use of personalized trauma scripts may constitute a more relevant or specific stressor, yielding different results (e.g., Elzinga et al., 2003).

When evaluating these results some strengths and limitations of the present study should be considered. A strong point is that all participating patients were diagnosed using the golden standard: an ictal video-EEG registration of a typical seizure in order to confirm the absence of epileptiform activity during a seizure (Reuber & Elger, 2003), making the diagnosis of PNES maximally reliable. Secondly, the fact that all participating patients were unmedicated rules out the possibility that the altered cognitive processing in our patients was the result of medication effects. As a consequence, however, we cannot automatically generalize these results to patients with PNES patient who are on medication. Thirdly, previous studies on neuropsychological functioning in patients with PNES were focused solely on the cognitive processing of non-emotional information (see Cragar et al., 2002 for a review). This is the first study investigating the cognitive processing of emotional stimuli in PNES. Facial expressions constitute important signals of threat or appeasement in the social environment (Öhman, 1986). Several neuroimaging studies have shown that viewing angry faces activates limbic structures, the amygdala in particular (for an overview see Adolphs et al., 2002; McClure et al., 2004; Strauss et al., 2005b), supporting the relevance of these stimuli in the study of stress-related disorders and the role of interpersonal trauma, in particular. Finally, the use of a masked Stroop task has the advantage that the subjects do not consciously perceive the stimuli, which was confirmed by the results from our awareness-check. This makes it unlikely that subjects exerted strategic effort to control AB effects (e.g., MacLeod & Hagan, 1992; Van den Hout et al., 1995; Williams et al., 1996; Putman et al., 2004) and makes the findings less vulnerable to uncontrollable subject factors.

A limitation of the present study is the lack of a clinical control group, making it difficult to state the specificity of the effects for the group with PNES and to exclude the possibility that the altered AB was mediated by comorbid psychopathology. However, in this respect it is relevant to mention that application of exactly the same masked emotional Stroop task in patients with social phobia resulted in opposite results; these patients allocated their attention away from the social threatening stimuli (E. Hermans, unpublished data). Despite this limitation, our data provide the first evidence linking interpersonal trauma with altered emotional processing in patients with PNES and give rise to several interesting questions for future research exploring the possible psychiatric mechanisms associated with PNES. For example, although we found clear results on the processing of masked emotional Stroop stimuli in our patient group, it remains to be tested whether the same findings hold for unmasked threat stimuli. Secondly, as stated earlier, it would be very interesting to replicate the present study by inducing stress using a more relevant/specific stressor, namely personalized trauma scripts or a physiologic stressor. Thirdly, considering that PNES is a rather heterogeneous group with respect to PNES characteristics, it would be interesting to investigate the effects of, besides psychotrauma, different PNES presentations (see e.g. Selwa et al., 2000) and comorbid psychopathology on the attentional processing of threatening stimuli. This is particularly relevant to gain insight into the possible different underlying mechanisms in the diverse semiology of PNES. Lastly, neuroimaging studies in PNES are needed to investigate which brain structures are involved in the processing of altered emotional information in neutral and stress conditions.

In conclusion, the present study showed impaired emotional information processing in patients with PNES. Compared to healthy controls, patients showed increased vigilance for masked angry faces. This preconscious AB for angry faces was significantly correlated to self-reported sexual trauma rates and probably reflects a state of hypervigilance. This interpretation is further supported by the finding of decreased HRV in patients with PNES, which was previously related to increased arousal/anxiety and poor emotion regulation. Given these results, further experimental research, investigating the relationship between attention, trauma, stress, and coping in patients with PNES seems promising to gain additional insight in possible neuropsychiatric mechanisms underlying this disorder with the ultimate purpose of improving (psychological) care for and treatment of this invalidating disorder.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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