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Highly neurotic never-depressed students have negative biases in information processing

STELLA W. Y. CHAN¹, GUY M. GOODWIN² AND CATHERINE J. HARMER^{1*}

¹ *Department of Experimental Psychology, University of Oxford, UK;* ² *Department of Psychiatry, University of Oxford, UK*

ABSTRACT

Background. Cognitive theories associate depression with negative biases in information processing. Although negatively biased cognitions are well documented in depressed patients and to some extent in recovered patients, it remains unclear whether these abnormalities are present before the first depressive episode.

Method. High neuroticism (N) is a well-recognized risk factor for depression. The current study therefore compared different aspects of emotional processing in 33 high-N never-depressed and 32 low-N matched volunteers. Awakening salivary cortisol, which is often elevated in severely depressed patients, was measured to explore the neurobiological substrate of neuroticism.

Results. High-N volunteers showed increased processing of negative and/or decreased processing of positive information in emotional categorization and memory, facial expression recognition and emotion-potentiated startle (EPS), in the absence of global memory or executive deficits. By contrast, there was no evidence for effects of neuroticism on attentional bias (as measured with the dot-probe task), over-general autobiographical memory, or awakening cortisol levels.

Conclusions. These results suggest that certain negative processing biases precede depression rather than arising as a result of depressive experience *per se* and as such could in part mediate the vulnerability of high-N subjects to depression. Longitudinal studies are required to confirm that such cognitive vulnerabilities predict subsequent depression in individual subjects.

INTRODUCTION

The aetiology of depression in community samples has been intensively investigated in twin studies that can broadly distinguish genetic from environmental factors. The existing literature suggests that the key vulnerability factors are neuroticism, family history of depression and early abuse/neglect or trauma, whereas the precipitating factor is often an adverse life event. Working with these variables, depressive episodes are moderately well predicted at the 12-month follow-up (Kendler *et al.* 1993, 2002, 2004, 2006).

While these findings are robust, the approach is essentially observational and thus insufficient to indicate the mechanisms whereby clinical depression emerges in high-risk individuals. The present study therefore set out to determine the cognitive and neurophysiological mechanisms of neuroticism, whereby adversity may lead to depression.

Cognitive theories of depression emphasize the role of negative biases in information processing in the aetiology and maintenance of the disorder (Beck *et al.* 1979). Biases on the interpretation and memory for emotional information have been reported. For example, in facial expression recognition tasks, depressed patients show reduced recognition of positive expressions and/or increased perception of negative expressions (Gur *et al.* 1992; Bouhuys

* Address for correspondence: Dr Catherine Harmer, Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, UK.

(Email: catherine.harmer@psy.ox.ac.uk)

et al. 1999; Surguladze *et al.* 2004), that is a bias away from positive towards negative. Negative perceptual and memory biases have also been found in healthy volunteers following negative mood induction (Teasdale & Russell, 1983; Bouhuys *et al.* 1995). Although attentional biases are less consistently found in depression, dot-probe tasks have revealed increased attention to negative stimuli in dysphoric patients and healthy volunteers undergoing a negative mood induction when longer stimulus durations are used (Bradley *et al.* 1997).

Although the state of severe depression is evidently associated with cognitive abnormalities, there are fewer comparable studies conducted in recovered patients. In general, global impairments of executive function resolve following recovery (Peselow *et al.* 1991; Austin *et al.* 2001), but certain residual emotional biases remain and may provide the mediating mechanisms in subsequent relapse. Thus, facial expression recognition was found to be negatively biased in recovered depressed patients (Bouhuys *et al.* 1999; Bhagwagar *et al.* 2004; Hayward *et al.* 2005) and this was associated with subsequent relapse (Bouhuys *et al.* 1999).

In parallel with the cognitive findings are reports of dysfunction of the hypothalamic–pituitary–adrenal (HPA) system in depression. HPA dysfunction can be indicated by an elevated cortisol response to awakening, as demonstrated in both acutely depressed (Pruessner *et al.* 1997) and recovered patients (Bhagwagar *et al.* 2003). Longitudinal studies have provided evidence that cortisol level predicts subsequent depression onset in adult women (Harris *et al.* 2000) and adolescents (Goodyer *et al.* 2000). Elevated cortisol levels may also contribute to the learning and memory impairments reported in depression (Young *et al.* 1999).

Thus, measurable cognitive and HPA abnormality may be present in recovery from depression, but we cannot rule out a scar effect, so called because the residual biases and elevated cortisol may be a consequence of depression, rather than implying occurrence before the onset of the first episode. The present study therefore recruited young euthymic college students with high *versus* low scores for neuroticism (N), and without a history of depression. We hypothesized that high-N volunteers would display affective processing biases favouring

negative *versus* positive information. These biases might also be accompanied by elevated morning cortisol levels, but global impairments of executive function were unlikely before a depressive episode.

METHOD

Volunteers and design

The study was approved by the local ethics committee. Seventy-two healthy college students with high or low N scores (see below) gave written informed consent to the study, and received payment for their participation. The Structured Clinical Interview for DSM-IV was used to screen for axis I disorders and seven volunteers were excluded from the study because of current or previous depression or anxiety disorders.

N scores for screening were derived from the 12-item neuroticism scale of the shortened Eysenck Personality Questionnaire (EPQ; Eysenck *et al.* 1985). Thirty-three (22 women) were in the high-N group (H: mean score = 9.58, range = 8–12) and 32 (18 women) in low-N group (L: mean score = 1.25, range = 0–3). The two groups were matched for age (18.82 ± 0.98 v. 19.06 ± 0.88), gender, verbal IQ (40.12 ± 2.80 v. 38.16 ± 5.54) and spatial IQ (26.19 ± 11.37 v. 22.43 ± 9.37) assessed with the National Adult Reading Test (NART; Nelson, 1982) and the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981).

Characterization of state and trait variables

To assess mood, personality, family background and life experience, participants were interviewed with the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1967) and filled in the following questionnaires: the State-Trait Anxiety Inventory (STAI; Spielberger *et al.* 1970), Beck Depression Inventory (BDI; Beck *et al.* 1961), Befindlichkeits Scale of Mood and Energy (Bf-S; von Zerssen *et al.* 1974), Fear of Negative Evaluation Scale (FNE; Watson & Friend, 1969), Buss–Durkee Hostility Inventory (Buss & Durkee, 1957), Social Adaptation Self-Evaluation Scale (SASS; Bosc *et al.* 1997), Dysfunctional Attitude Scale (DAS; Weissmann, 1979, factors taken from Cane *et al.* 1986), ruminative items of the Response Styles Questionnaire (modified by Treynor *et al.* 2003),

EPQ (Eysenck & Eysenck, 1975), Parental Bonding Inventory (PBI; Parker *et al.* 1979), stressful life events (adopted from Goodyer *et al.* 1997), and family history of psychiatric disorders. Two participants did not complete all the questionnaires.

Emotional categorization

Main task: personality characteristics categorization

Sixty personality characteristics chosen to be extremely desirable (e.g. honest) or undesirable (e.g. rude) (Anderson, 1968, matched on word length, frequency and meaningfulness) were presented on a computer screen for 500 ms. Participants were asked to categorize these traits as likeable or dislikeable by pressing the labelled key on the keyboard. To encourage self-referent judgement, participants were asked to imagine whether they would be pleased or displeased if they overheard someone describing them in this way.

Control task: animal attributes categorization

A similar task was carried out as a control, using 60 attribute words (30 per valence). This time participants were asked to classify each attribute as an 'advantage' (e.g. strong) or 'disadvantage' (e.g. weak) for a predatory animal. In both tasks classifications and reaction times for the correct identifications were recorded.

Emotional memory

A surprise memory task comprising recall and recognition (60 target words plus 60 distracters) was conducted 15 min after completing each of the categorization tasks. The number of correctly and incorrectly recalled words was counted. Recognition data were analysed using signal detection theory (Green & Swets, 1966; Grier, 1971) to derive a measure of accuracy corrected for subjects' response tendency. The proportion of correctly recognized words (y) and the proportion of falsely recognized words (x) were entered into the following equations to give the sensitivity measure d' and the response bias β : $d' = 0.5 + [(y - x)(1 + y - x)] / 4y(1 - x)$; $\beta = [y(1 - y) - x(1 - x)] / [y(1 - y) + x(1 - x)]$. This allowed an assessment of accuracy (hits) unconfounded by the response criterion used by the volunteer.

Facial expression recognition

Stimuli and procedure

Pictures of faces representing six basic emotions (happiness, surprise, sadness, fear, anger, and disgust) were taken from the Pictures of Affect Series (Ekman & Friesen, 1976). These were morphed between each full emotion (100%) and neutral (0%) in 10% steps (Young *et al.* 1997): four examples were given per intensity per emotion. Each face was also presented in a neutral expression, giving a total of 250 stimuli. Each stimulus flashed up on a computer screen for 500 ms followed by a blank screen. Participants were asked to recognize the emotion by pressing the appropriate key. Accuracy and reaction times for correct choices and misclassifications were recorded. Accuracy was defined by the threshold, that is the intensity level at which the participant gave three or more (i.e. $\geq 75\%$) correct responses across three consecutive intensity levels.

Dot-probe task

Stimuli and procedure

The emotional stimuli included 60 social threatening negative words and 60 positive words, each of which was paired with a matched neutral word. Another 60 neutral-neutral word pairs were given as fillers. Preceded by a fixation cross (500 ms), a word pair was presented on the screen with one word above another. In the unmasked condition the word pair was presented for 500 ms, whereas in the masked condition the word pair appeared for 14 ms followed by the display (186 ms) of a mask. After that, a probe (one or two stars) appeared in the position of either preceding word, and participants were asked to indicate the number of stars. These 360 trials were presented in three blocks in random order. Reaction time and accuracy were recorded. Attentional vigilance scores were calculated for each participant by subtracting the mean score of 'congruent trials' (where the probe and emotional words appeared in the same position) from that of the 'incongruent trials' (where they appeared in opposite positions).

Emotion-potentiated startle (EPS)

Stimuli

Sixty-three pictures of three categories (pleasant, unpleasant, neutral) were taken from the

International Affective Picture System (gender-specified, Larson *et al.* 2000). Each picture was presented for 13 s (mean inter-trial interval = 13 s) on a computer screen. The pictures were presented in three blocks in a fixed order so that no two of the same category would appear successively.

Procedure and recording

The eye-blink component of the startle response was recorded from the orbicularis oculi using electromyography (EMG startle response system, San Diego Instruments, Inc., San Diego, CA, USA). Acoustic probes were 50-ms, 95-dB bursts of white noise with a nearly instantaneous rise time (generated through the noise generator and amplifier of the EMG startle response system) and were delivered binaurally through headphones at 1.5, 4.5 or 7.5 s following picture onset. To minimize expectation, startle probes were skipped from two trials per valence per block, and three probes were given within the inter-trial interval. A practice session presenting nine neutral pictures and startle probes was used in the beginning to habituate participants to the startle probes.

EMG signals were filtered (low cut-off: 0.5 Hz; high cut-off: 100 Hz) and rectified. Eye-blink reflex magnitudes in μV were calculated by subtracting the amount of integrated EMG at reflex onset from the first peak amplitude of integrated EMG between 20 and 120 ms following probe onset. Trials with no traceable eye-blink reflex were assigned a magnitude of zero and included in the analysis. Eye-blink reflexes with an excessively noisy baseline (within 20 ms after the probe) were rejected. Four participants (two from each group) were excluded from the analysis because they displayed fewer than 25% blink responses. Magnitude and latency of the eye-blink reflex were recorded.

Subjective rating

After the recording, participants were asked to review the pictures and rate the valence and arousal levels of each picture on a 1–10 scale (from negative to positive, low arousal to high arousal).

Global executive functions

As global cognitive impairments (e.g. Austin *et al.* 2001; Elliot *et al.* 1996) and over-general

autobiographical memory (for a recent review, see Williams *et al.* 2004) were widely demonstrated in depression, we included the following tasks to examine whether neuroticism has an effect on memory, learning and problem solving.

Auditory Verbal Learning Test (AVLT)

The AVLT (Rey, 1964) was used to assess learning and memory. In the immediate recall phase, participants were read aloud a 15-item word list and asked to recall as many words as possible. This procedure was repeated five times. A distracter list was then presented to create a short delay, after which free recall of the first list was measured. Fifteen minutes later, participants were tested again with a free recall and recognition test (15 target words plus 35 distracters).

Tower of London (TOL)

In this task two sets of three coloured balls were presented on a touch-sensitive computer screen, with each set being arranged like snooker balls hanging in three pockets. Participants were asked to rearrange the balls in one set to match the other set under certain rules. The minimum number of moves (2, 3, 4 or 5) required for each trial was indicated. Participants were instructed to work out the whole solution in mind before making the first move. In addition, two control blocks were used to measure the time for actual movement. In these, the balls were constantly moved by the computer in one set and participants were asked to copy this movement on the other set. Task performance was assessed by three variables: number of problems solved with minimum moves, average number of moves, and thinking time. Thinking time was computed by subtracting the reaction time of the control trials from that of the main trials.

Autobiographical Memory Test (AMT)

In the AMT (Williams & Broadbent, 1986), participants were presented with 18 cue words (nine positive and nine negative), each at a time, and asked to recall a memory of a specific event that the cue word reminded them of. Instructions defined a specific event as any event that took place on a particular day at a particular place and no more recent than a week ago, and that participants should not recall the same event for more than one cue word. Each word

was shown on a card and read aloud by the experimenter. If a participant did not respond after 30 s, the next word would be presented. A practice trial with a neutral word ('chicken') was used in the beginning to check that the participant understood the instructions. Latency (duration between the presentation of a cue word and the start of the recall) and number of specific responses were recorded.

Awakening salivary cortisol

At the end of the experiment, participants were given instructions to collect five salivary samples at home in the following morning: the first sample was taken immediately upon waking (Time 1), and subsequent samples were taken at 15-min intervals for the next hour (Times 2, 3, 4 and 5 respectively). Participants were not allowed to eat or drink during the test and not to consume alcohol the night before. Nine subjects (seven from H) failed to return their samples. Cortisol was measured with an in-house double-antibody radioimmunoassay. Cortisol levels of the five samples (M_1, M_2, M_3, M_4, M_5) were entered into the following formula to compute the area under the curve (Pruessner *et al.* 2003): $[(M_2 + M_1) + (M_3 + M_2) + (M_4 + M_3) + (M_5 + M_4)] \times 15/2$.

Statistics

Independent-samples *t* tests were used to reveal group differences in psychological characteristics, AVLT (delayed recognition), and TOL (number of trials solved in minimum moves) and salivary cortisol. Other data were analysed by using two-way (facial expression recognition, EPS, AMT, AVLT, TOL) or three-way (emotional categorization, emotional memory, dot probe) analyses of variance (ANOVAs), with between-Ss variable as group (H, L) and within-Ss variable(s) as emotion, trial and/or task conditions. Individual ANOVAs and *t* tests were run to clarify significant interactions.

RESULTS

Psychological characteristics

Using the full EPQ scale, the two groups were confirmed to have significant difference in neuroticism scores (17.91 ± 2.84 v. 5.72 ± 3.27 , $p < 0.01$). Although none of the volunteers had ever met criteria for DSM-IV depression, and

Table 1. Psychological characteristics of the two groups

Task	High-N	Low-N	<i>t</i>	<i>p</i>
HAMD	3.55 (3.33)	1.34 (2.36)	3.08	$\leq 0.00^{**}$
BDI	8.33 (5.97)	2.59 (2.67)	5.03	$\leq 0.00^{**}$
STAI State	37.82 (9.90)	27.56 (6.33)	4.99	$\leq 0.00^{**}$
STAI Trait	47.18 (11.84)	28.75 (5.19)	8.17	$\leq 0.00^{**}$
Bf-S	45.97 (28.43)	14.88 (13.96)	5.62	$\leq 0.00^{**}$
FNE	21.88 (6.13)	8.31 (4.73)	9.91	$\leq 0.00^{**}$
SASS	41.66 (5.47)	47.34 (4.09)	-4.71	$\leq 0.00^{**}$
Hostility	32.00 (9.03)	24.13 (8.94)	3.51	$\leq 0.00^{**}$
Rumination	51.75 (8.95)	39.31 (8.51)	5.70	$\leq 0.00^{**}$
DAS				
Overall	142.81 (20.93)	105.59 (21.12)	7.08	$\leq 0.00^{**}$
Perfectionism	46.91 (10.61)	33.22 (11.75)	4.89	$\leq 0.00^{**}$
Approval by others	44.81 (8.54)	32.47 (8.20)	5.90	$\leq 0.00^{**}$
Stressful life events	1.44 (1.24)	1.16 (1.55)	0.80	≤ 0.43

N, Neuroticism; HAMD, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; Bf-S, Befindlichkeits Scale of Mood and Energy; FNE, Fear of Negative Evaluation Scale; SASS, Social Adaptation Self-evaluation Scale; DAS, Dysfunctional Attitude Scale.

Values represent means (\pm standard deviations).

Asterisks represent significance of group comparisons: ** $p \leq 0.01$.

mean scores on clinical symptom scales did not exceed usual levels for remission, H participants showed a significantly higher level of depressive mood, anxiety and hostility than L. They also reported more rumination, dysfunctional attitudes, parental over-protectiveness, and lower social adaptation. By contrast, the two groups did not differ in family history of psychiatric disorder, parental care, and stressful life experience (all $p > 0.10$) (Table 1).

Emotional categorization

There was a significant group \times task \times emotion interaction [$F(1, 63) = 4.73$, $p = 0.03$] for reaction time in the self-referent *versus* animal categorization tasks. Sensitivity analyses showed a significant group \times emotion interaction in the emotional categorization [Fig. 1(a): $F(1, 63) = 3.88$, $p = 0.05$] but not in the control task [Fig. 1(b): $F(1, 63) = 0.51$, $p = 0.48$]. H volunteers were quicker at classifying negative *versus* positive personality characteristics than L. Furthermore, within the H group, the reaction time for positive items was significantly correlated with N scores [$r(33) = 0.37$, $p = 0.04$], so reaction time for positive items increased with neuroticism.

For accuracy data there was neither a group difference [$F(1, 63) = 0.45$, $p = 0.51$] nor a group

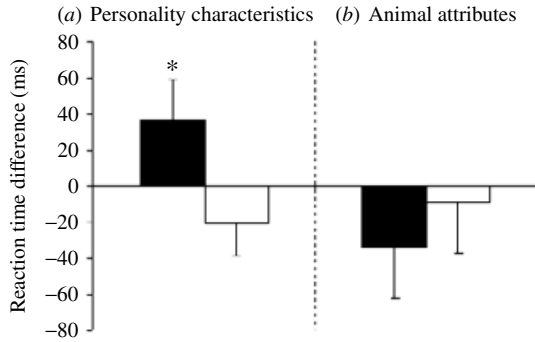


FIG. 1. Emotional categorization of self-referent personality characteristics (a) and animal attributes (b). Values represent mean difference scores of reaction time to identify positive minus negative words \pm standard error of the mean. Asterisks represent statistical significance of group comparisons (* $p < 0.05$). ■, High-N; □, Low-N.

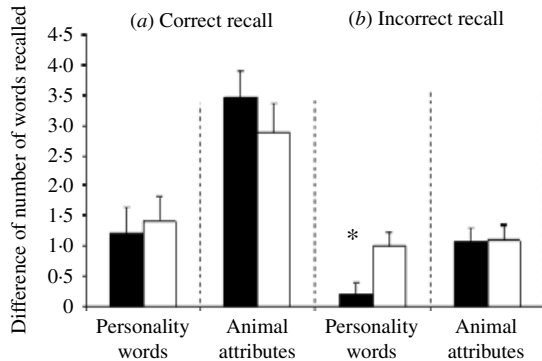


FIG. 2. Emotional memory: (a) correct recall; (b) incorrect recall, of personality characteristics and animal attribute words. Values represent mean difference scores of number of words recalled for positive minus negative words \pm standard error of the mean. Asterisks represent statistical significance of group comparisons (* $p < 0.05$). ■, High-N; □, Low-N.

\times emotion \times task interaction [$F(1, 63) = 0.51$, $p = 0.48$] but both groups achieved more than 90% accuracy in both categorization tasks, implying a potential ceiling effect.

Emotional memory

Recall

The two groups performed similarly in terms of correct recall [Fig. 2(a): group: $F(1, 63) = 0.47$, $p = 0.50$; task \times emotion \times group: $F(1, 63) = 0.87$, $p = 0.35$]. However, H volunteers produced fewer positive memory intrusions than L [Fig. 2(b): group \times emotion: $F(1, 63) = 7.54$, $p = 0.01$] for self-referent information, but not in the

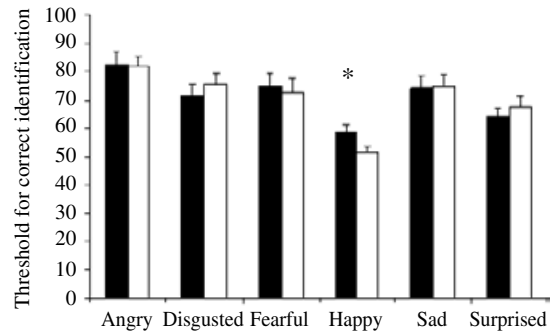


FIG. 3. Threshold of facial expression recognition in high-N (■) and low-N (□) volunteers. Values represent mean threshold levels (\pm standard error of the mean) required to correctly identify each emotion at a level of $> 75\%$. Asterisks represent statistical significance of group difference (* $p < 0.05$).

control task [group \times emotion: $F(1, 63) = 0.01$, $p = 0.92$].

Recognition

The two groups had similar accuracy (d') [group: $F(1, 63) = 0.07$, $p = 0.79$; task \times emotion \times group: $F(1, 63) = 3.09$, $p = 0.09$] and response bias (β) [group $F(1, 63) = 0.03$, $p = 0.87$; task \times emotion \times group $F(1, 63) = 0.50$, $p = 0.48$].

Facial expression recognition

There were no main effects on accuracy, reaction time or misclassifications in this task (all p values > 0.10). However, differences in recognition of each emotion were further explored using independent t tests, given a strong *a priori* hypothesis for individual emotions. This revealed a significant group difference for accuracy of happy faces [Fig. 3: $t(63) = 2.05$, $p = 0.04$] but not in any other emotions (all p values > 0.40). Specifically, H had a higher threshold in identifying happy faces than did L; that is, they needed higher intensity levels to be able to correctly identify happy facial expressions.

Dot-probe task

There were no significant effects on the vigilance scores of reaction time [group: $F(1, 63) = 0.22$, $p = 0.64$; group \times emotion \times mask: $F(1, 63) = 0.03$, $p = 0.87$] or accuracy [group: $F(1, 63) = 1.92$, $p = 0.17$; group \times emotion \times mask: $F(1, 63) = 0.01$, $p = 0.95$]. This was also true when only the unmasked trials were considered: for reaction time [group: $F(1, 63) = 0.10$, $p = 0.76$, emotion \times group:

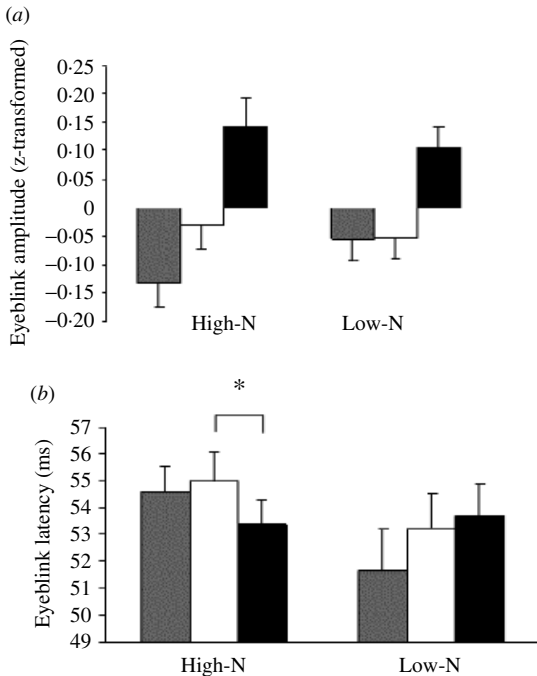


Fig. 4. (a) Amplitude of startle response (Z scores) and (b) average latency of startle response while viewing the three types of pictures. Values represent means \pm standard error of the mean. Asterisks represent statistical significance of comparisons between startle responses during pleasant and unpleasant pictures within each group (* $p < 0.05$). ■, Neutral; □, pleasant; ■, unpleasant.

$F(1, 63) = 0.01$, $p = 0.94$] and for accuracy [group: $F(1, 63) = 0.49$, $p = 0.49$; emotion \times group: $F(1, 63) = 0.49$, $p = 0.49$] (see Table 2, available online).

EPS

Eye-blink magnitude

The z -transformed data revealed the expected potentiation effect in both groups [Fig. 4(a): overall effect of emotion: $F(2, 118) = 10.17$, $p = 0.001$], with volunteers showing a greater response to unpleasant than neutral or pleasant pictures. However, this was not affected by neuroticism [group: $F(1, 59) = 0.86$, $p = 0.40$; emotion \times group: $F(2, 118) = 0.85$, $p = 0.43$]. Examination of raw startle amplitudes showed a similar pattern [emotion: $F(2, 118) = 7.19$, $p = 0.001$; group: $F(1, 59) = 1.33$, $p = 0.25$; emotion \times group: $F(2, 118) = 0.36$, $p = 0.70$]. The average amplitudes were similar between H and L [mean = 1416.20 v. 1674.83; $t(59) = -1.15$, $p = 0.25$].

Eye-blink latency

There was a significant group \times emotion interaction [Fig. 4(b): $F(2, 116) = 3.08$, $p = 0.05$], but *post-hoc* comparisons failed to reveal group difference within each emotional category (all $p > 0.10$). As shown by paired-samples t tests, the interaction was mostly driven by H responding more slowly to pleasant than unpleasant pictures [$t(29) = 2.04$, $p = 0.05$].

Subjective ratings

There was no group difference in terms of rating for valence [group: $F(1, 58) = 0.12$, $p = 0.73$; emotion \times group: $F(2, 116) = 1.10$, $p = 0.34$] or arousal [group: $F(1, 58) = 0.43$, $p = 0.52$; emotion \times group: $F(2, 116) = 1.14$, $p = 0.32$].

Non-emotional cognitive functions

In these tests, high-N subjects showed modest trends to improved performance compared with low-N (see Table 3, available online). In the AVLT immediate recall there was a significant group \times trial interaction [$F(4, 253) = 3.27$, $p = 0.01$], with subsequent t tests suggesting that H outperformed L only in the first trial [$t(63) = 2.21$, $p = 0.03$]. For the short- versus long-delayed recalls there was no group difference [$F(1, 63) = 0.02$, $p = 0.89$] or interaction [$F(1, 63) = 1.77$, $p = 0.19$], nor was there any group difference on long-delayed recognition [hits: $t(63) = -1.14$, $p = 0.26$; false alarms: $t(63) = 1.26$, $p = 0.21$]. In the TOL there was a significant group effect [$F(1, 63) = 5.75$, $p = 0.02$] and a group \times trial interaction [$F(3, 189) = 3.32$, $p = 0.02$] in the number of moves required to solve the problem. Subsequent t tests found that H was better than L in the four-move problems [$t(63) = -2.29$, $p = 0.03$]. H also solved more problems in a minimum number of moves than did L [$t(63) = 2.16$, $p = 0.03$]. However, among H volunteers, this measure was negatively correlated with N score [$r(33) = -0.35$, $p = 0.05$], suggesting that the higher a participant scored in neuroticism the fewer problems s/he managed to solve in a minimum number of moves. There were no effects in terms of thinking times [group: $F(1, 63) = 0.55$, $p = 0.46$; interaction: $F(3, 189) = 0.48$, $p = 0.70$]. When the perfectionism score from the DAS was included as a covariate in these analyses, the differences were lost [AVLT Immediate Recall group \times trial: $F(4, 244) = 1.33$, $p = 0.26$; TOL Number of

Moves group effect: $F(1, 61) = 3.08$, $p = 0.08$; group \times trial $F(3, 183) = 2.21$, $p = 0.09$].

In the AMT, there were no effects on latency [group: $F(1, 63) = 0.01$, $p = 0.95$; group \times emotion: $F(1, 63) = 0.65$, $p = 0.42$] or number of specific memories produced [group: $F(1, 63) = 2.20$, $p = 0.14$; interaction: $F(1, 63) = 0.65$, $p = 0.42$] (see Table 3, available online).

Awakening salivary cortisol

The mean time of awakening did not differ between H and L participants (0838 *v.* 0813 h). The area under the curve of cortisol responses revealed no group difference (1375.80 ± 552.23 *v.* 1568.22 ± 593.85 , $p = 0.23$) (see Fig. 5, available online).

DISCUSSION

Our results show that biases in information processing are present in high-N students who are at risk of depression but have not been depressed. Decreased positive or increased negative processing was seen across a number of tasks including emotional categorization and memory, facial expression recognition and EPS, in the absence of global memory or executive deficits. However, there was no evidence for effects of neuroticism on attentional bias (measured with the dot-probe task), over-general autobiographical memory, or elevated morning cortisol levels.

As noted in the introduction, it has often been suggested that negative biases may be a trait vulnerability marker for depression. However, by eliminating subjects with previous depression, our results establish a direct association between cognitive abnormality and vulnerability to depression without the contamination of a scar effect.

Although the relationship between neuroticism and cognitive processing has been researched for decades (e.g. Lishman, 1974; Lloyd & Lishman, 1975; Martin *et al.* 1983), these studies were mostly performed on non-selective samples with which correlations were examined between N and response (e.g. speed of memory recall). In contrast to this approach, our study selected participants from the extreme range of N (high *versus* low) and thus directly illustrated the influence of high neuroticism on emotional processing.

In the emotional categorization and memory tasks, H volunteers were faster to classify dislikeable self-referent personality characteristics and produced fewer positive memory intrusions. This bias away from the positive was similarly revealed in the perception of social information, as measured by the facial expression recognition task. H volunteers had a higher threshold for identifying happy faces than the control volunteers. A reduction in positive facial perception echoes previous experimental findings in depressed patients (Murphy *et al.* 1999; Suslow *et al.* 2001) and healthy volunteers undergoing a negative mood induction (Bouhuys *et al.* 1995). By contrast, recovered patients also tend to show an *increased* perception of *negative* expression such as fear, disgust and sadness (Bouhuys *et al.* 1999; Bhagwagar *et al.* 2004; Hayward *et al.* 2005). This suggests the hypothesis that risk for depression is largely manifest as reduced positive processing of emotional information, which is accompanied by increased negative processing only after the actual experience of depression.

EPS was used to give a physiological measure of reactivity to emotional information. Our sample, regardless of group membership, exhibited the expected EPS pattern with enhanced eye-blink during the presentation of aversive pictures relative to neutral or pleasant pictures, which is widely demonstrated in laboratory work (e.g. Bradley *et al.* 1990; Cook *et al.* 1991). The two groups gave similar pleasantness ratings for the pictures. Unexpectedly, while amplitude was unaffected, there was an effect of neuroticism on blink latency. H volunteers showed a significant delay in their reflexive response to pleasant pictures. A reduced physiological reactivity to positive stimuli in the absence of differential subjective rating implies that neuroticism involves biases in mechanisms that are highly automatic and thus not influenced by self-report. The current result is compatible with the theory that low activity in appetitive emotional systems is the core deficit in depression (Fowles, 1988; Depue & Iacono, 1989; Clark & Watson, 1991), although latency variables are infrequently reported for the EPS task.

The negative findings in this study may indicate domains in which deficits are simply not associated with depression vulnerability or,

instead, may arise solely from the experience of depression. Thus, the dot-probe task provides evidence that attentional biases play no role in neuroticism and, as noted in the introduction, attentional biases have never been reliably shown in depression either. By contrast, the negative results in autobiographical memory are notable because an over-general memory deficit has been robustly found across clinical samples. Among the few that examined over-general memory before depression (e.g. Mackinger *et al.* 2000*a, b*; von Minnen *et al.* 2005), the results were confounded to some extent by prior trauma experiences and/or unclear history of depression. A recent study (Gibbs & Rude, 2004) found that over-general memory interacts with stressful life events in predicting subsequent depression symptoms in randomly selected students, but the experience of depression was not defined. We propose that over-general memory does not contribute to the vulnerability to depression shown by high-N subjects.

Our negative findings for awakening cortisol in high-N students contrast with the hyperactivity of the HPA axis reported previously in a substantially older sample (Portella *et al.* 2005) and in an older subgroup of high-N subjects (Zobel *et al.* 2004). Our data are comparable with those obtained in the high-N subjects of a similar age range (Zobel *et al.* 2004). Therefore, it is possible that dysfunction of the HPA axis occurs with increasing age in vulnerable individuals, possibly as an interaction between risk and exposure to toxic life events. Alternatively, it cannot be ruled out from our data set that elevated cortisol responses may only be seen in a subpopulation of high neurotic subjects who will eventually develop depression. Longitudinal studies are required to test this hypothesis.

As anticipated, results from AVLT and TOL revealed no global cognitive impairment by neuroticism. These are consistent with the hypothesis that cognitive deficits are largely confined to periods of illness in depression rather than as a more general trait (Peselow *et al.* 1991; Austin *et al.* 2001). There was a tendency for H volunteers to perform better in these tasks, which appeared to be related to their enhanced drive or perfectionism. This enhanced cognitive function makes the specific reduction in positive

processing also found in this group more noteworthy.

The current study has a number of limitations. Although high neuroticism is a robust risk factor for depression, the relatively low prevalence rates of depression imply that only a small proportion of the high-N population will go on to develop depression, thereby potentially diluting any effects that we may have seen. While this could account for the lack of effect in terms of cortisol responses and autobiographical memory performance, it could not account for the negative biases that were seen in the group as a whole. Longitudinal studies are required to assess the predictive power of negative biases for subsequent depression in a sample adequately powered for the detection of infrequent events. Finally, in the current study the experimenters were not blind to group membership. Although this is unlikely to have an influence on the results because responses were collected automatically by computer and task instructions were standardized across participants, future studies may want to assess negative bias using a blinded design to confirm these findings.

Conclusion

There has been an ongoing controversy whether biased cognition is a state or trait marker for depression. Negative cognitive biases in healthy volunteers after a depressive mood induction give partial support for the 'state hypothesis' (Mathews & Bradley, 1983; Sutton *et al.* 1988). However, neuroticism in individuals without a history of depression was associated with reduced positive processing in our study, thus strongly suggesting that cognitive biases represent a trait vulnerability marker for depression. Furthermore, the processes that were found to be affected by neuroticism overlap with the processes that are affected by antidepressant drug treatment in healthy volunteers (Harmer *et al.* 2003, 2004). This overlap validates the earlier suggestion that antidepressants act on the key cognitive components of emotional processing related to the acquisition and maintenance of mood disorders. In the future, longitudinal studies are required to investigate whether, and to what extent, such cognitive vulnerability predicts subsequent depression. If so, this could pave the way for further studies evaluating the efficacy of early interventions targeting the

dysfunctional cognitive styles of the high-risk population.

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NOTE

Supplementary information accompanies this paper on the Journal's website (<http://journals.cambridge.org>).

DECLARATION OF INTEREST

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REFERENCES

- Anderson, N. H. (1968). Likeableness rating of 555 personality trait words. *Journal of Personality and Social Psychology* **9**, 272–279.
- Austin, M. P., Mitchell, P. & Goodwin, G. M. (2001). Cognitive deficits in depression: possible implications for functional neuropathology. *British Journal of Psychiatry* **178**, 200–206.
- Beck, A. T., Rush, A. J., Shaw, B. F. & Emery, G. (1979). *Cognitive Therapy of Depression*. Guilford: New York.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J. & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry* **4**, 561–571.
- Bhagwagar, Z., Cowen, P. J., Goodwin, G. M. & Harmer, C. J. (2004). Normalization of enhanced fear recognition by acute SSRI treatment in subjects with a previous history of depression. *American Journal of Psychiatry* **161**, 166–168.
- Bhagwagar, Z., Hafizi, S. & Cowen, P. J. (2003). Increase in concentration of waking salivary cortisol in recovered patients with depression. *American Journal of Psychiatry* **160**, 1890–1891.
- Bosc, M., Dubini, A. & Polin, V. (1997). Development and validation of a social functioning scale, the Social Adaptation Self-evaluation Scale. *European Neuropsychopharmacology* **7** (Suppl. 1), S57–S70.
- Bouhuys, A. L., Bloem, G. M. & Groothuis, T. G. G. (1995). Induction of depressed and elevated mood by music influences the perception of facial emotional expressions in healthy subjects. *Journal of Affective Disorders* **33**, 215–226.
- Bouhuys, A. L., Geerts, E. & Gordijn, M. C. (1999). Depressed patients' perceptions of facial emotions in depressed and remitted states are associated with relapse: a longitudinal study. *Journal of Nervous and Mental Disease* **187**, 595–602.
- Bradley, B. P., Mogg, K. & Lee, S. C. (1997). Attentional biases for negative information in induced and naturally occurring dysphoria. *Behaviour Research and Therapy* **35**, 911–927.
- Bradley, M. M., Cuthbert, B. N. & Lang, P. J. (1990). Startle reflex modification: attention or emotion? *Psychophysiology* **27**, 513–523.
- Buss, A. H. & Durkee, A. (1957). An inventory for assessing different kinds of hostility. *Journal of Consulting Psychology* **21**, 343–349.
- Cane, D. B., Olinger, L. J., Gotlib, I. H. & Kuiper, N. A. (1986). Factor structure of the Dysfunctional Attitude Scale in a student population. *Journal of Clinical Psychology* **42**, 307–309.
- Clark, L. A. & Watson, D. (1991). Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology* **100**, 316–336.
- Cook, E. W., Hawk, Jr., L. W., Davis, T. L. & Stevenson, V. E. (1991). Affective individual differences and startle reflex modulation. *Journal of Abnormal Psychology* **11**, 5–13.
- Depue, R. A. & Iacono, W. G. (1989). Neurobehavioral aspects of affective disorders. *Annual Review of Psychology* **40**, 457–492.
- Ekman, P. & Friesen, W. V. (1976). *Pictures of Facial Affect*. Consulting Psychologists Press: Palo Alto, CA.
- Elliott, R., Sahakian, B. J., McKay, A. P., Herrod, J. J., Robins, T. W. & Paykel, E. S. (1996). Neuropsychological impairments in unipolar depression: the influence of perceived failure on subsequent performance. *Psychological Medicine* **26**, 975–989.
- Eysenck, H. J. & Eysenck, S. B. J. (1975). *Manual of the Eysenck Personality Questionnaire*. Hodder and Stoughton: London.
- Eysenck, S. B. G., Eysenck, H. J. & Barrett, P. (1985). A revised version of the psychoticism scale. *Personality and Individual Differences* **6**, 21–29.
- Fowles, D. C. (1988). Psychophysiology and psychopathology: a motivational approach. *Psychophysiology* **25**, 373–391.
- Gibbs, B. R. & Rude, S. S. (2004). Over-general autobiographical memory as depression vulnerability. *Cognitive Therapy and Research* **28**, 511–526.
- Goodyer, I. M., Herbert, J., Tamplin, A. & Altham, P. M. (2000). Recent life events, cortisol, dehydroepiandrosterone and the onset of major depression in high-risk adolescents. *British Journal of Psychiatry* **177**, 499–504.
- Goodyer, I. M., Herbert, J., Tamplin, A., Secher, S. M. & Pearson, J. (1997). Short-term outcome of major depression: II. Life events, family dysfunction, and friendship difficulties as predictors of persistent disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* **36**, 474–480.
- Green, D. M. & Swets, J. A. (1966). *Signal Detection Theory and Psychophysics*. Wiley: London.
- Grier, J. B. (1971). Nonparametric indexes for sensitivity and bias: computing formulas. *Psychological Bulletin* **75**, 424–429.
- Gur, R. C., Erwin, R. J., Gur, R. E., Zwil, A. S., Heimberg, C. & Kraemer, H. C. (1992). Facial emotion discrimination: II. Behavioural findings in depression. *Psychiatry Research* **42**, 241–251.
- Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *British Journal of Social and Clinical Psychology* **6**, 278–296.
- Harmer, C. J., Hill, S. A., Taylor, M. J., Cowen, P. J. & Goodwin, G. M. (2003). Toward a neuropsychological theory of antidepressant drug action: increase in positive emotional bias after potentiation of norepinephrine activity. *American Journal of Psychiatry* **160**, 990–902.
- Harmer, C. J., Shelley, N. C., Cowen, P. J. & Goodwin, G. M. (2004). Increased positive versus negative affective perception and memory in healthy volunteers following selective serotonin and norepinephrine reuptake inhibition. *American Journal of Psychiatry* **161**, 1256–1263.
- Harris, T. O., Borsanyi, S., Messari, S., Stanford, K., Cleary, S. E., Shiers, H. M., Brown, G. W. & Herbert, J. (2000). Morning cortisol as a risk factor for subsequent major depressive disorder in adult women. *British Journal of Psychiatry* **177**, 505–550.
- Hayward, G., Goodwin, G. M., Cowen, P. J. & Harmer, C. J. (2005). Low-dose tryptophan depletion in recovered depressed patients induces changes in cognitive processing without depressive symptoms. *Biological Psychiatry* **57**, 517–554.

- Kendler, K. S., Gardner, C. O. & Prescott, C. A. (2002). Toward a comprehensive developmental model for major depression in women. *American Journal of Psychiatry* **159**, 1133–1145.
- Kendler, K. S., Gardner, C. O., Prescott, C. A. (2006). Toward a comprehensive developmental model for major depression in men. *American Journal of Psychiatry* **163**, 115–124.
- Kendler, K. S., Kessler, R. C., Neale, N. C., Heath, A. C. & Eaves, L. J. (1993). The prediction of major depression in women: toward an integrated etiologic model. *American Journal of Psychiatry* **150**, 1139–1141.
- Kendler, K. S., Kuhn, J. & Prescott, C. A. (2004). The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression. *American Journal of Psychiatry* **161**, 631–636.
- Larson, C. L., Ruffalo, D., Nietert, J. Y. & Davidson, R. J. (2000). Temporal stability of the emotion-modulated startle response. *Psychophysiology* **37**, 92–101.
- Lishman, W. A. (1974). The speed of recall of pleasant and unpleasant experiences. *Psychological Medicine* **4**, 212–218.
- Lloyd, G. G. & Lishman, W. A. (1975). Effect of depression on the speed of recall of pleasant and unpleasant experiences. *Psychological Medicine* **5**, 173–180.
- Mackinger, H. F., Loschin, G. G. & Leibetseder, M. M. (2000a). Prediction of postnatal affective changes by autobiographical memories. *European Psychologist* **5**, 52–61.
- Mackinger, H. F., Pachinger, M. M., Leibetseder, M. M. & Fartacek, R. R. (2000b). Autobiographical memories in women remitted from major depression. *Journal of Abnormal Psychology* **109**, 331–334.
- Martin, M., Ward, J. C. & Clark, D. M. (1983). Neuroticism and the recall of positive and negative personality information. *Behaviour Research and Therapy* **21**, 495–503.
- Mathews, A. & Bradley, B. (1983). Mood and the self-reference bias in recall. *Behaviour Research and Therapy* **21**, 233–239.
- Murphy, F. C., Sahakian, B. J., Rubinsztein, J. S., Michael, A., Rogers, R. D., Robbins, T. W. & Paykel, E. S. (1999). Emotional bias and inhibitory control processes in mania and depression. *Psychological Medicine* **29**, 1307–1321.
- Nelson, H. E. (1982). *National Adult Reading Test (NART): Test Manual*. NFER-Nelson: Windsor.
- Parker, G., Tupling, H. & Brown, L. B. (1979). A parental bonding instrument. *British Journal of Medical Psychology* **52**, 1–10.
- Peselow, E. D., Corwin, J., Fieve, R. R., Rotrosen, J. & Cooper, T. B. (1991). Disappearance of memory deficits in outpatient depressives responding to imipramine. *Journal of Affective Disorders* **21**, 173–183.
- Portella, M. J., Harmer, C. J., Flint, J., Cowen, P. & Goodwin, G. M. (2005). Enhanced early morning salivary cortisol in neuroticism. *American Journal of Psychiatry* **162**, 807–809.
- Pruessner, J. C., Kirschbaum, C., Meinlschmid, G. & Hellhammer, D. H. (2003). Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology* **28**, 916–931.
- Pruessner, J. C., Wolf, O. T., Hellhammer, D. H., Buske-Kirschbaum, A., von Auer, K., Jobst, S., Kaspers, F. & Kirschbaum, C. (1997). Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity. *Life Science* **61**, 2539–2549.
- Rey, A. (1964). *The Clinical Examination in Psychology*. Presses Universitaires de France: Paris.
- Spielberger, C. D., Gorsuch, R. L. & Lushene, R. D. (1970). *STAI Manual*. Consulting Psychologists Press: Palo Alto, CA.
- Surguladze, S. A., Young, A. W., Senior, C., Brebion, G., Travis, M. J. & Phillips, M. L. (2004). Recognition accuracy and response bias to happy and sad facial expressions in patients with major depression. *Neuropsychology* **18**, 212–218.
- Suslow, T., Junghanns, K. & Arolt, V. (2001). Detection of facial expressions of emotions in depression. *Perceptual and Motor Skills* **92**, 857–868.
- Sutton, L. J., Teasdale, J. D. & Broadbent, D. E. (1988). Negative self-schema: the effects of induced depressed mood. *British Journal of Clinical Psychology* **27**, 188–190.
- Teasdale, J. D. & Russell, M. L. (1983). Differential effects of induced mood on the recall of positive, negative and neutral words. *British Journal of Clinical Psychology* **22**, 163–171.
- Treynor, W., Gonzalez, R. & Nolen-Hoskema, S. (2003). Rumination reconsidered: a psychometric analysis. *Cognitive Therapy and Research* **27**, 247–259.
- von Minnen, A., Wessel, I., Verhaak, C. & Smeenk, J. (2005). The relationship between autobiographical memory specificity and depressed mood following a stressful life event: a prospective study. *British Journal of Clinical Psychology* **44**, 405–415.
- von Zerssen, D., Strian, F. & Schwarz, D. (1974). Evaluation of depressive states, especially in longitudinal studies. In *Psychological Measurements in Psychopharmacology* (ed. P. Pichot), pp. 189–202. Karger: Basel, Switzerland.
- Watson, D. & Friend, R. (1969). Measurement of social-evaluative anxiety. *Journal of Consulting and Clinical Psychology* **33**, 448–457.
- Wechsler, D. (1981). *Manual for the Wechsler Adult Intelligence Scale – Revised (WAIS-R)*. Psychological Corporation: New York.
- Weissmann, A. (1979). *The Dysfunctional Attitude Scale: A Validation Study*. Unpublished doctoral dissertation, University of Pennsylvania, Philadelphia.
- Williams, J. M. G. (2004). Experimental cognitive psychology and clinical practice: autobiographical memory as a paradigm case. In *Cognition, Emotion and Psychopathology* (ed. J. Yiend), pp. 251–269. Cambridge University Press: Cambridge.
- Williams, J. M. G. & Broadbent, K. (1986). Autobiographical memory in suicide attempters. *Journal of Abnormal Psychology* **95**, 144–149.
- Wust, S., Federenko, I., Hellhammer, D. H. & Kirschbaum, C. (2000). Genetic factors, perceived chronic stress, and the free cortisol response to awakening. *Psychoneuroendocrinology* **25**, 707–720.
- Young, A. H., Sahakian, B. J. & Robbins, T. W. (1999). The effects of chronic administration of hydrocortisone on cognitive function in normal male volunteers. *Psychopharmacology* **145**, 260–266.
- Young, A. W., Rowland, D., Calder, A. J., Etcoff, N. L., Seth, A. & Perrett, D. I. (1997). Facial expression megamix: tests of dimensional and category accounts of emotion recognition. *Cognition* **63**, 271–313.
- Zobel, A., Barkow, K., Schulze-Rauschenbach, S., von Widdern, O., Metten, M., Pfeiffer, U., Schnell, S., Wagner, M. & Maier, W. (2004). High neuroticism and depressive temperament are associated with dysfunctional regulation of the hypothalamic-pituitary-adrenocortical system in health volunteers. *Acta Psychiatrica Scandinavica* **109**, 393–399.