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The effects of stress-induced cortisol responses on approach-avoidance behavior

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Summary High glucocorticoid stress-responses are associated with prolonged freezing reactions and decreased active approach and avoidance behavior in animals. The present study was designed to investigate the effects of cortisol responses and trait avoidance on approach-avoidance behavior in humans. Twenty individuals were administered a computerized approach-avoidance (AA)-task before and after stress-induction (Trier Social Stress Test). The AA-task involved a reaction time (RT) task, in which participants made affect congruent and affect incongruent arm movements towards positive and threatening social stimuli. Affect congruent responses involved arm extension (avoidance) in response to angry faces and arm flexion (approach) in response to happy faces. Reversed responses were made in affect incongruent instruction conditions. As expected, participants with high cortisol responses showed significantly decreased RT congruency-effects in a context of social stress. Low trait avoidance was also associated with diminished congruency-effects during stress. However, the latter effect disappeared after controlling for the effects of cortisol. In sum, in agreement with animal research, these data suggest that high cortisol responses are associated with a decrease in active approach-avoidance behavior during stress. These findings may have important implications for the study of freezing and avoidance reactions in patients with anxiety disorders, such as social phobia and post-traumatic stress disorder.

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1. Introduction

Emotions and affective evaluations are assumed to play an important role in preparing the individual for

appropriate actions (Darwin, 1872/1998; Lang et al., 1990). These actions are proposed to be organized by at least two different motivational systems that enable approach or avoidance behavior (Bargh, 1997; Cacioppo et al., 1993; Chen and Bargh, 1999; Davidson et al., 1990; Gray, 1994; Lang et al., 1990). In general, people tend to approach positively evaluated stimuli and to avoid negatively

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evaluated ones (Chen and Bargh, 1999; Rotteveel and Phaf, 2004; Solarz, 1960). Extensive animal studies have shown that approach and avoidance behavior is influenced by stress and stress-induced cortisol responses. However, in humans, the effects of these factors on approach-avoidance tendencies remain largely unexplored.

A relatively direct method to study approach-avoidance (AA) tendencies in humans is offered by reaction time (RT) paradigms, in which individuals evaluate the emotional valence of affective stimuli by making arm movements that are either congruent or incongruent with their action tendencies. For affect congruent arm movements participants are, for example, instructed to evaluate a stimulus as negative by pushing a response lever away (arm extension) and to evaluate a stimulus as positive by pulling the lever towards them (arm flexion). For affect incongruent actions, participants receive the opposite instruction. Using such an AA-task, Chen and Bargh (1999) and Solarz (1960) compared RTs for affect congruent and affect incongruent movements to positive and negative word stimuli and found faster responses for the affect congruent arm movements. Rotteveel and Phaf (2004) replicated these basic congruency-effects using pictures of happy and angry faces as positive and threatening stimuli, respectively.

In daily life, fast avoidance of a threatening stimulus is of particular importance when the stimulus information is relevant to its present context. Following this line of reasoning, one would predict faster avoidance responses towards angry facial expressions within a context of social stress than without such context. However, action tendencies such as those measured by the above-described AA-task have not been studied in relation to a task-relevant context yet. With the present study, we aim to examine AA-related action tendencies to happy and angry faces in the context of a social stressor. In the first place we will study the direct influence of stress on AA-action tendencies. Second, we will focus on the influence of individual differences in glucocorticoid stress-responses and trait avoidance on AA action tendencies.

Several studies have shown that the prefrontal cortex (PFC) plays an important role in the generation of approach and avoidance behavior. In general, affect related approach and avoidance reactions are associated with increased activity in the left and right prefrontal cortex (PFC), respectively (Davidson, 1992, 1995 for reviews). Although most hemispheric lateralization studies have been focused on the differentiation between approach and avoidance related affect (positive and negative

affect, respectively) a few recent studies have more directly addressed the tendencies to generate approaching or avoiding actions towards external stimuli. Sutton and Davidson (1997), for example, found participants with greater resting activation of the right PFC to show higher scores on a self report scale measuring behavioral inhibition (avoidance) tendencies (BIS: Carver and White, 1994) and those with greater relative left PFC activation to score higher on measures of behavioral approach tendencies (BAS: Carver and White, 1994). Other support for the involvement of the PFC in the performance of approach and avoidance behavior in humans is offered by a study by D'Alfonso et al. (2000), showing low frequency repetitive transcranial magnetic stimulation (rTMS) over left PFC to result in increased avoidance of (i.e. selective attention away from) angry faces, whereas rTMS over right PFC resulted in increased approach of (i.e. selective attention towards) angry faces.

There is increasing evidence from animal studies that the relation between threat and PFC mediated approach and avoidance behavior may be influenced by activity of the Hypothalamic-Pituitary-Adrenal (HPA) axis, an important stress system resulting in the release of the stress-hormone cortisol. Primates with extreme asymmetric right-sided prefrontal activation have been found to show higher basal levels of cortisol (Kalin et al., 1998a) and higher cerebrospinal fluid levels of corticotrophin-releasing hormone (Kalin et al., 2000). In addition, high basal and reactive cortisol levels were found to be associated with increased freezing and diminished active approach and avoidance reactions to stress-stimuli in primates (Kalin et al., 1998b) and rats (Nunez et al., 1996). The PFC is indeed found to be a significant target for glucocorticoids involved in the stress response (e.g. Meaney and Aitken, 1985; Radley et al., 2004; Sanchez et al., 2000). Lyons et al. (2000), for example, found impairments in prefrontal inhibitory control of behavior in primates after prolonged exposure to stress-levels of cortisol. Also studies among healthy young men showed pharmacologically administered cortisol to impair prefrontal functions, such as working memory (Lupien et al., 1999; Wolf et al., 2001; Young et al., 1999). However, to our knowledge, only one human study directly addressed the relation between cortisol and prefrontal mediated approach and avoidance behavior. Buss et al. (2003) found that 6-months old infants, who showed relatively increased basal and reactive cortisol levels, demonstrated more avoidance behavior when faced with approaching strangers. The elevated cortisol levels and avoidance behavior were, moreover, associated with

extreme right prefrontal EEG asymmetry. Avoidance behavior, however, was operationalized by 'observations of signs of fear and sadness' and no systematic measurements of affect congruent motor actions, such as arm-flexions or extensions were conducted.

So, although these findings suggest that there may indeed be a relation between the stress-reactivity of the HPA-axis and prefrontal mediated AA-behavior, there are no studies available in which approach- and avoidance-related action tendencies are systematically evaluated in relation to HPA-axis functioning. We therefore designed a study in which subjects were administered the above described AA-task before and after stress-induction by means of the Trier Social Stress Task (TSST; [Kirschbaum et al., 1993](#)). The stress-inducing social evaluation during the TSST provides a meaningful context to the evaluation of angry and happy facial expressions and is known to elicit a significant glucocorticoid stress-response in the majority of the subjects ([Kirschbaum et al., 1993](#)). In the first place we expected affect congruent AA-reactions towards the happy and angry facial stimuli to increase (i.e. increased congruency-effects on the AA-task) in the context of the social stressor. However, based on the previously found negative effects of elevated cortisol levels on prefrontal executive functions in both humans and animals, we expected participants with a high cortisol response to show impaired approach-avoidance reactions during stress (i.e. decreased congruency-effects on the AA-task) when compared to participants who do not show such cortisol response.

Secondly, we investigated the relation between behavioral inhibition tendencies in daily life situations (trait avoidance) and approach-avoidance reactions towards threat stimuli on the AA-task. For this purpose we compared participants with relatively low and high scores on the Behavioral Inhibition Scale (BIS; [Carver and White, 1994](#)) with respect to their AA-strategies and expected participants with relatively low BIS scores (low trait avoidance) to show slowed avoidance reactions towards angry faces.

2. Methods

2.1. Participants

Twenty-two students (12 males and 10 females) recruited from the University of Leiden participated in the experiment for financial or course credit. Due to technical problems, task administration failed in two men, leaving 20 participants (10 males, 10

females) with a mean age of 21.40 years ($SD = 4.23$). Exclusion criteria were: any psychiatric disorder on AXIS-I, including substance abuse (DSM-IV, APA, 1994), any clinical significant medical disease, use of medication (including use of oral contraceptives), and age < 18 or > 37 . Because cortisol responses are influenced by the menstrual cycle, women were measured in their luteal phase (days 21-25 of their menstrual cycle), when cortisol increases in response to the TSST appear to be as high as in men ([Kirschbaum et al., 1999](#)). Participants were instructed to minimize physical exercise during the hour preceding the experiment and not to take large meals, coffee, drinks with low pH or cigarettes, because these variables can affect cortisol levels. All participants were right-handed and had normal or correct-to-normal vision. The study was approved by the local ethics committee and all participants provided written informed consent.

2.2. Materials

2.2.1. AA-task

In this affect-evaluation task, eighty pictures with facial expressions from [Ekman and Friesen \(1976\)](#), [Martinez and Benavente \(1998\)](#), [Matsumoto and Ekman \(1988\)](#) and [Lundqvist et al. \(1998\)](#) served as stimuli. Both the happy and angry expression were taken from the same model (total of 40 models). The set of stimuli was subdivided into four fixed series (A-B-C-D) with each 10 happy and 10 angry expressions of different models. Ten of these pictures were taken from female and 10 were taken from male models. Each series thus contained 5 happy expression of female models, 5 happy expressions of male models, 5 angry expression of female models and 5 angry expressions of male models. Each picture was presented on a 15" computer screen with a vertical visual angle of 14° and a horizontal visual angle of 10.7° and lasted 100 ms.

Participants were individually tested and received all four series of trials once in a semi randomized order. Two series were presented before and the two other after stress-induction (first and second task administration, respectively). Before stress-induction, half of the participants started with an affect congruent instruction block of trials (i.e. positive evaluations with pushing the upper button and negative evaluations with pushing the lower button). Subsequently an affect incongruent instruction block of trials (i.e. negative evaluations with pushing the upper button and positive evaluations with pushing the lower button) followed after an unrelated working memory task (digit span), that served to ease the transition from congruent to incongruent instruction or visa versa.

The other participants received the reversed order of instruction. Half of the participants who started with a congruent instruction before stress-induction started with a congruent instruction after stress-induction and the other half started with an incongruent instruction. The same counted for participants who started with an incongruent instruction before stress-induction.

Each series was preceded by six practice trials that contained pictures that were not included in the experimental series. Trials started with a 400 ms lasting black fixation point at the center of the screen with an inter-trial interval (ITI) of 1500 ms.

Responses were given by means of three one-button boxes that were fixed to a vertical stand (see Rotteveel and Phaf, 2004 for a photograph of this experimental set-up). Participants were seated to the left of the stand allowing them to respond with their right hand. For the resting position of the right hand participants were instructed to push the home-button (fixed in the middle) loosely with the back of the right hand as long as no response was given. The height of this home-button was set for each participant individually, so that the angle between the forearm and the upper-arm was 110° in the resting position. In this way both the biceps and the triceps were equally tensed when holding the home-button pressed. The response-buttons (both 16 cm²) were positioned above and below the home button (at a distance of 10.3 cm). This allowed participants to simply flex or extend their arm in responding without any need for precise aiming at the response-buttons.

The task provides two outcome measures: the initiation time (RT) is the time between stimulus onset and the release of the home-button and the movement time (MT) is the time between the release of the home-button and the response. RT constitutes an index of central processes reflecting stimulus evaluation, response selection and programming the execution of movements, and is relatively independent of MT which reflects the magnitude of the neuro-muscular response (Fitts, 1954). RT increases, for example, as a function of the amount of stimulus information (Sternberg, 1966), or with the number of target alternatives (Brainard et al., 1962). Although, MT can be influenced by such parameters as well (Fitts, 1954; Sternberg et al., 1978, 1980), it is primarily influenced by the distance towards the target and the size of target-location (Fitts and Peterson, 1964). The influence of affect on the latency times is therefore primarily expected in RT, rather than MT (see Solarz, 1960; Rotteveel and Phaf, 2004).

RTs that deviated more than 2.5 SD from the individual RT averages per cell [cells defined by

Movement (flex, extend), Facial Expression (FE: happy, angry), and Stress (before, during stress)] were excluded from the analyses. For MT the same outlier procedure was applied. If RT data were excluded, corresponding MT data were also excluded and visa versa. Following this procedure, a total of 17 outliers (1.1%) from the affect congruent conditions and 20 (1.3%) from the affect incongruent conditions were excluded from analysis. Incorrect responses were also excluded from the analyses.

2.2.2. The Trier Social Stress Test

This psychological challenge test, which mainly consists of a free speech and mental arithmetic task of 15 min duration, has been found repeatedly to induce significant endocrine and cardiovascular responses in 70-80% of the participants (Kirschbaum et al., 1993). The exact description of the procedure of the test is reported under the subheading 'procedure'.

2.2.3. Physiological and subjective measures

All physiological and subjective stress-measures were obtained at 8 assessment points over a 95-min period, at respectively -45, -30, -15, -5, +10, +20, +35 and +50 min with reference to the start of the stressor. All assessments were performed between 9:30 and 12:00 a.m.

Cortisol: 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), as described elsewhere (Van Aken et al., 2003).

Norepinephrine activity was also assayed non-invasively utilizing salivary alpha-amylase levels, which have been shown to correlate with plasma norepinephrine levels and to be sensitive to psychological stress (Chatterton et al., 1996). Biochemical analysis of alpha-amylase was performed using the maltoheptaoside method on Hitachi 911 (Roche Diagnostics) (ref.range 12,000-3,00,000 U/L).

Heart rate (HR) was recorded continuously by an Ambulatory Monitoring System (AMS; Vrije Universiteit Amsterdam, version 3.6), a small battery powered device for ambulatory recording. It was measured via three Ag-AgCl disposable electrodes (ConMed), placed just above the sternum, at the left side of the chest, and at the bottom right side of the chest (cleaned with alcohol). For each participant, HR was post-hoc averaged for 2 min starting from a marker given at each of the 8 assessment points.

Systolic (SBP) and diastolic blood pressures (DBP) were measured from the non-dominant arm using an automatic blood pressure monitor (Omron R5-l) that could be initiated manually.

Finally, a subjective measure of tension rated on a visual analogue scale, ranging from 0 to 10, was administered at each assessment point.

2.2.4. Trait avoidance (TA)

The Behavioral Inhibition Scale (BIS; Carver and White, 1994) is a 7-item self-report scale designed to measure trait sensitivity to show behavioral inhibition to cues of threat. It is based on Gray's personality dimension of behavioral inhibition (Gray, 1982). Items are statements such as 'I worry about making mistakes' or 'I feel pretty worried or upset when I think or know somebody is angry at me'. Answers are coded on a likert type scale with four possibilities ranging from 'absolute agreement' to 'absolute disagreement'. The BIS was found to have good reliability and validity ratings (e.g. Carver and White, 1994; Casesas et al., 2003).

2.3. Procedure

Participant arrived at the laboratory at 9.00 a.m., after which the VU-AMS device was connected and checked by the experimenter. After the first series of the physiological assessment the AA-task was introduced. Participants were instructed to evaluate (i.e. positively or negatively) facial expressions. They received either an affect congruent or an affect incongruent instruction. An affect congruent instruction entailed the pressing of the lower button with negatively valenced faces and the upper button with positively valenced faces. With the affect incongruent instruction the reference to the response buttons was reversed. All possible references in the instructions to congruence versus incongruence, approach behavior or avoidance behavior, or for that matter flexion or extension were avoided. Task administration took place just before the third assessment (– 15 min with reference to the onset of the stressor), and was followed by a battery of additional cognitive tests, of which the results will be reported elsewhere (Elzinga and Roelofs, *in press*). Subsequently, the experimenter introduced the TSST by telling the participants that they would be taking on the role of a job applicant for a position at the University of Leiden (the type of position was a-priori defined, based on which position would be challenging and relevant to the current situation of the participant). Participants were given 3 min to prepare a 5-min free speech to an audience of 3 psychologists who were in another

room waiting to interview them. They were told that the speech would be videotaped, that the psychologists were specially trained to monitor nonverbal behavior, that a voice frequency analysis of nonverbal behavior would be performed, and that the speech would be criticized on content and presentation style. They were also told that following the interview, they would be asked to complete an oral arithmetic challenge that would be judged on speed and accuracy. After this introduction, the experimenter left the room. Following the preparation time, the audience (three persons) entered the room and prominently switched on the camera and microphone. Participants were instructed to stand in front of a table with the audience sitting at the other side and the chairman who was seated in the center asked the participant to describe his/her qualifications for the job. A stopwatch lying prominently on the table was set to keep time. Participants were expected to utilize the entire 5 min for the speech as described by Kirschbaum et al. (1993). For the mental arithmetic task (5 min duration) participants were instructed to serially subtract 13 from 1587. The audience responded to any mistakes by instructing participants to 'Start from the top; subtract 13 from 1587'. Immediately after the TSST, the audience called the experimenter back into the room and requested him to administer the AA-task again in their presence. In this way, the social stress context remained present during the second administration of the AA-task (+20 min with reference to onset TSST). Subsequently the audience left the room and returned for a short debriefing after the last physiological assessment had taken place.

2.4. Statistical analyses

The influence of stress induction on physiological and subjective stress measures, as well as the influence of stress, cortisol responses and trait avoidance on the task performance (AA-task), were tested using repeated measures Analyses of Variance (ANOVA *rm*). All statistical analyses described employed a two-tailed alpha of 0.05.

3. Results

3.1. Physiological and subjective stress responses

3.1.1. Stress-induction

Separate one-way ANOVA's *rm* for the physiological and subjective stress measures (each measured at 8 time points) showed significant increases on all

stress measures over time: cortisol ($F(7,12)=5.95$, $p<0.005$); alpha-amylase ($F(7,12)=8.49$, $p<0.0001$); HR ($F(7,12)=12.64$, $p<0.0001$), SBP ($F(7,12)=11.29$, $p<0.0001$); DBP ($F(7,12)=10.21$, $p<0.0001$) and subjectively experienced tension ($F(7,12)=7.85$, $p<0.001$).

3.1.2. Cortisol responses

The stress-related cortisol-response (CR) of each individual was computed by calculating the percentage increase from baseline (during the first administration of AA-task, 15 min before onset of the stressor; see Fig. 1) to the maximum, at 20 min after onset of the stressor (during the second task-administration). The mean CR of the total group was 33.38% (standard error of mean (SEM)=5.83%). Because of the high variance in cortisol responses (ranging from -37.94 to 134.36%) participants were subdivided (median split) into a high and a low CR group (see Fig. 1). The high CR group consisted of 6 males and 4 females with a mean cortisol response of 74.97% (SEM=6.64%; range: 15.73% min, 134.36% max). The low CR group (4 males, 6 females) showed a mean cortisol response of 8.21% (SEM=2.24%; range: -37.94% min, 13.80% max). In the high CR group 100% ($N=10$) showed an increase and in the low CR group 70% ($N=7$) showed a decrease in cortisol level after stress-induction. A two-way ANOVA rm for the individual cortisol levels (8 assessments in time) with CR (high, low group) as between-subject confirmed that the high CR group displayed significantly higher cortisol levels right after the TSST until the end of the experiment (assessments 5-8) compared to the low CR group, whereas no differences were found between the two group prior to the TSST (assessments 1-4) ($F(7,12)=3.44$, $p<0.05$). High and low CR groups did not differ with respect to alpha-amylase ($F(7,12)=0.81$, $p=0.60$); HR ($F(7,12)=0.38$, $p=0.90$), SBP ($F(7,12)=0.05$, $p=1.000$), DBP ($F(7,12)=1.15$, $p=0.39$), and

subjectively experienced tension ($F(7,12)=1.12$, $p=0.40$).

3.2. Behavioral results

3.2.1. The influence of cortisol response (CR) on approach-avoidance behavior

Error rates: The error rates for affect congruent and affect incongruent trials were 4.6 and 6.0% for the low CR group and 6.6 and 3.9% for the high CR group, respectively. There were no significant group- or congruency-effects with respect to the error rates.

Initiation times (RT): To test our hypothesis that congruency-effects are diminished in the high CR group we conducted a four-way ANOVA rm for the RT, with Movement (flex, extension), Facial expression (FE: happy, angry face) and Stress (before, during stress) as within-subject factors and CR (high, low) as between-subject factor. As to be expected from the AA-task, a significant two-way interaction between Movement and FE ($F(1,76)=15.91$, $p<0.0001$), showed that participants were faster on affect congruent than on affect incongruent arm movements. Most importantly, there was a significant four-way interaction for 'Movement $\times$ FE $\times$ CR $\times$ Stress' ($F(1,76)=10.92$, $p=0.001$). The proportion of explained variance by this interaction (partial eta squared [η^2]) was 0.13. Post-hoc F -tests showed that in the low CR group the congruency-effects (Movement $\times$ FE) were only significant during ($F(1,38)=8.73$, $p<0.005$) and not before ($F(1,38)=0.87$, $p=0.87$) stress, whereas in the high CR group, the congruency-effects were only significant before ($F(1,38)=16.01$, $p<0.0001$) and not during ($F(1,38)=0.25$, $p=0.63$) stress (see Fig. 2). The effect of stress ('Movement $\times$ FE $\times$ Stress' interaction) was, however, only significantly in the high CR group ($F(1,38)=9.52$, $p<0.005$) and not in the low CR group ($F(1,38)=2.51$, $p=0.12$). Thus, in agreement with our hypothesis, participants with a relatively high glucocorticoid stress-response showed diminished congruency-effects during stress (see Fig. 2). Moreover, in line with our hypothesis that high cortisol responses interfere with both approach and avoidance reactions (both are thought to be prefrontal mediated), additional post-hoc F -tests showed the negative effects of stress on the congruency-effects in the high CR group to count both for the approach ($F(1,38)=4.51$, $p<0.05$), and for the avoidance ($F(1,38)=4.19$, $p<0.05$) reactions (see Fig. 2).

Movement times (MT): There were no differential effects for CR on MT (all p -values >0.1).

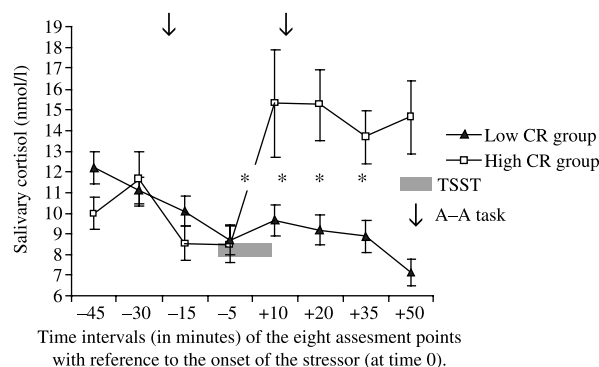
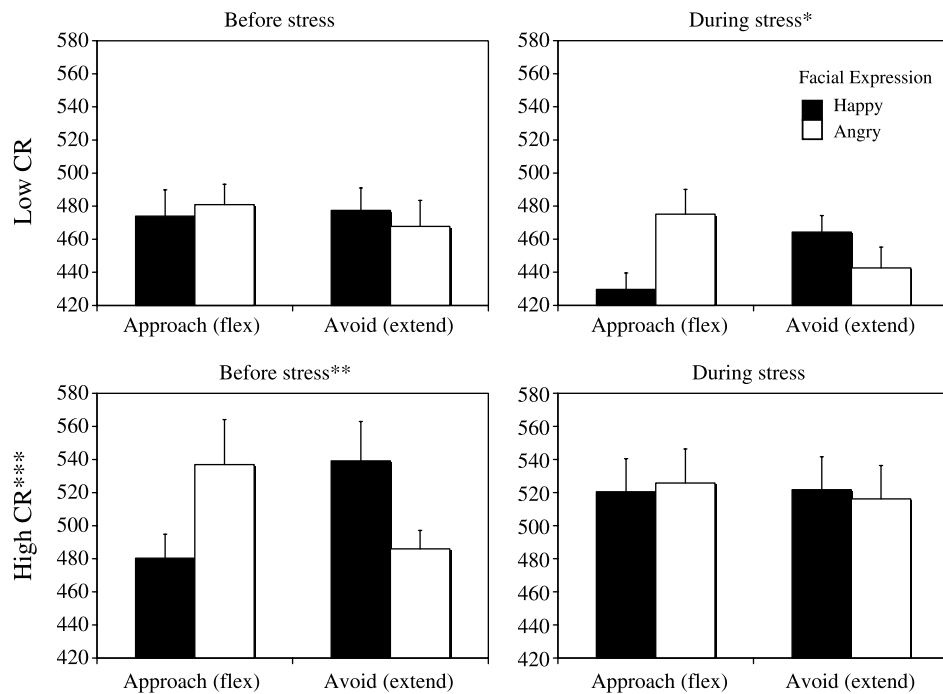


Figure 1 Free salivary cortisol in nmol/l (Mean $\pm$ SEM) for high and low cortisol response (CR) groups in TSST.



* 'Movement (approach, avoid) X Facial Expression (FE, happy angry)' effect after stress-induction ($p < 0.01$).

** 'Movement X FE' effect before stress-induction ($p < .0001$).

*** 'Movement X FE X Stress' interaction ($p < 0.005$) for High CR group only.

-Within the high CR group, the 'FE X Stress' interaction was significant for approach and avoidance (both $p < 0.05$).

-Note that the high and low CR groups already differed in their AA-reactions before stress induction ('Movement X FE XCR' ($F(1,76)=6.53$, $p < 0.05$)).

Figure 2 Mean (+SEM) reaction times (ms) on the AA-task for high and low cortisol response (CR) groups before and after stress-induction.

3.2.2. The influence of trait avoidance (TA) on approach-avoidance behavior

In order to study the effects of TA on the task performance, participants were post-hoc assigned (median-split) into a high (6 males, 4 females) and low TA group (4 males, 6 females) based on the BIS scores. The low TA group (mean=17.20, SEM=0.25) differed significantly from the high TA group (mean=20.40, SEM=0.18) in the mean BIS scores ($F(1,19)=25.6$, $p < 0.0001$) but not with respect to physiological or subjective stress measures (8 assessment points); cortisol response ($F(7,12)=0.91$, $p=0.53$), alpha-amylase ($F(7,12)=0.56$, $p=0.78$); HR ($F(7,12)=1.15$, $p=0.40$), DBP ($F(7,12)=1.88$, $p=0.18$), SBP ($F(7,12)=2.95$, $p=0.06$), and tension ($F(7,12)=1.09$, $p=0.43$).

Error rates: The error rates for congruent and incongruent trials were 5.5 and 4.3% for the low TA group and 5.7 and 5.5% for the high TA group, respectively. There were no significant group- or congruency-effects with respect to the error rates.

Initiation times (RT): To find out whether RT congruency-effects for angry faces are diminished

in participants with a low tendency to avoid threat in daily life situations (low TA group), we conducted a 4-way ANOVA rm for the RT with Movement (flex, extension), FE (happy, angry face) and Stress (before, during stress) as within-subject factors and TA (high, low) as between subject factor and found the four-way interaction to be significant ($F(1,76)=3.87$, $p=0.05$; partial $\eta^2=0.05$). Post-hoc F -tests showed that the expected Movement $\times$ FE $\times$ Stress effect was indeed only significant for the low TA group ($F(1,38)=4.80$, $p < 0.05$) and not for the high TA group ($F(1,38)=0.42$, $p=0.52$). Whereas in the high TA group the 'Movement $\times$ FE' interaction was significant both before ($F(1,38)=5.67$, $p < 0.05$) and during ($F(1,38)=19.91$, $p < 0.0001$) stress, in the low TA group this interaction was only significant before ($F(1,38)=5.41$, $p < 0.05$) and not during ($F(1,38)=0.30$, $p=0.59$) stress (see Fig. 3). These findings indicate that subjects with low TA indeed showed diminished AA-behavior towards social stimuli in a social stress-context. However, in contrast to our hypothesis, the low TA group showed this decrease in

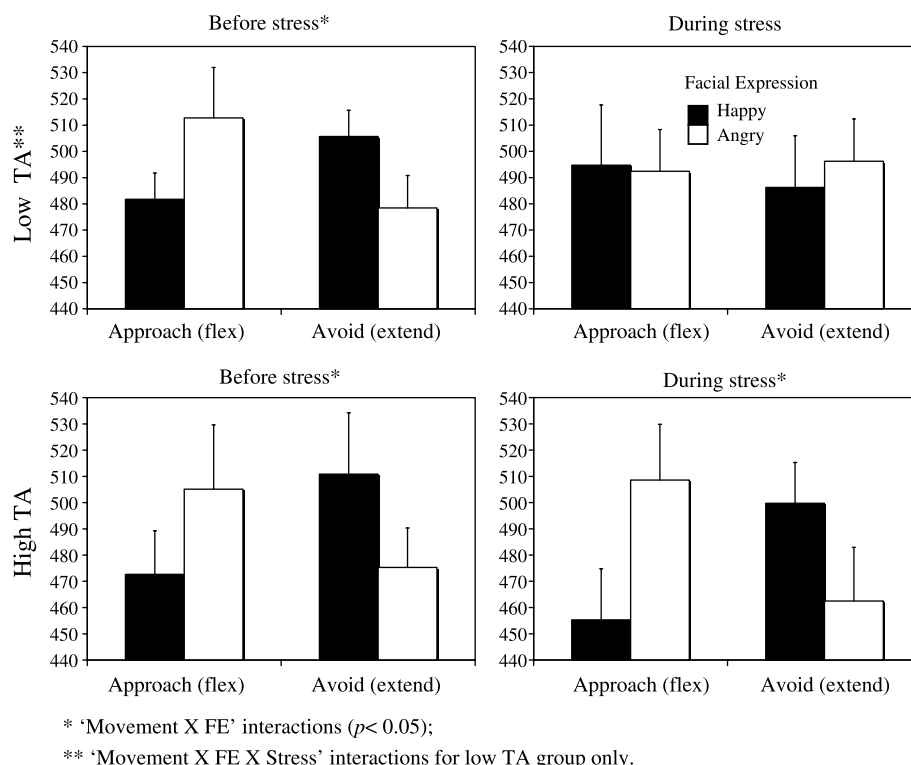


Figure 3 Mean (+SEM) reaction times (ms) on the AA-task for high and low trait avoidance (TA) groups before and after stress-induction.

congruency effects after stress induction not only for angry faces but also for happy faces. The decrease in congruency effects (drop in RT difference between flexion and extension) after stress induction was not larger for angry (38 ms) than for happy faces (32 ms) ($F(1,39)=0.03$, $p=0.86$), indicating that congruency effects were diminished for happy as well as angry faces (see Fig. 3).

Movement times (MT): The MT analyses showed a significant 3-way interaction for Movement $\times$ FE $\times$ TA ($F(1,76)=4.31$, $p<0.05$; partial $\eta^2=0.05$). Post-hoc analyses indicated that the 'Movement $\times$ FE' interaction was only significant for the high TA group ($F(1,38)=4.7$, $p<0.05$) and not for the low TA group ($F(1,38)=0.48$, $p=0.49$), again pointing at diminished congruency-effects in the low TA group (see Fig. 4). This effect was, however, not modulated by Stress, as indicated by a non-significant four-way-interaction between Stress, Movement, FE, and TA ($F(1,76)=2.27$, $p=0.11$). Interestingly, whereas the high TA group showed a significant RT advantage for an avoidance versus approach reaction towards angry faces (significant main-effect of Movement for angry faces ($F(1,19)=5.91$, $p<0.05$)), the low TA group did not show this advantage ($F(1,19)=0.32$, $p=0.581$). For happy faces we did not find such differential group-effects.

3.2.3. The relation between TA and CR

The fact that both high CR and low TA were associated with diminished RT congruency-effects after stress raises the question whether these variables are mutually related. We indeed found a negative correlation between the individual TA scores and the individual cortisol responses ($r(-0.46)$, $p<0.05$). In terms of overlap between the two groups, 6 of the 10 participants in the high CR group scored low on TA. To investigate whether the relation between CR and AA-behavior may be mediated by the effects of TA, we tested whether the previously found 4-way interaction between Movement, FE, Stress and CR ($F(1,76)=10.92$, $p=0.001$) remained significant after partializing out the effects of TA by adding TA as an additional between-subject factor in the ANOVA rm. The results showed that the original Movement $\times$ FE $\times$ Stress $\times$ CR interaction remained significant ($F(1,72)=8.55$, $p<0.01$, partial $\eta^2=0.11$), indicating that the RT effects of cortisol on the task performance were independent of TA.

Likewise, to test whether the relation between TA and AA-behavior may be mediated by the individual differences in CR, we tested whether the previously found 4-way interaction between Movement, FE, Stress and TA ($F(1,76)=3.87$, $p=0.05$) would remain significant after partializing out

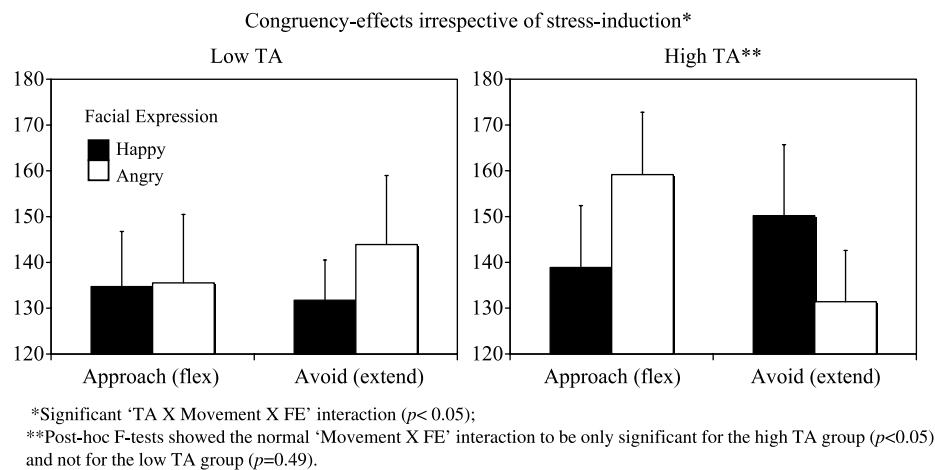


Figure 4 Movement times (Mean + SEM in ms) for high and low TA (trait avoidance) groups.

the effects of CR. When adding CR to the model the Movement $\times$ FE $\times$ Stress $\times$ TA interaction was no longer significant ($F(1,72) = 1.98$, $p = 0.163$, partial $\eta^2 = 0.03$), indicating that the RT effects of TA on the task performance were at least partly dependent on the effects of CR.

4. Discussion

The purpose of the present study was to investigate the influence of a social stress context on approach and avoidance (AA) behavior towards positive and negative social stimuli. In general, people tend to approach positive and to avoid negative stimuli, as reflected in faster initiation times (RT) for affect congruent actions on an AA-task (Chen and Bargh, 1999; Rotteveel and Phaf, 2004; Solarz, 1960). The present study replicated these findings by showing similar congruency effects on baseline task administration. Moreover, although we did not find a direct influence of stress-induction on the AA congruency-effects, we found that individual differences in cortisol responses (CR) during stress greatly influenced the AA congruency-effects. Only in participants with relatively high CR did the normal RT advantage for affect congruent trials disappear in the presence of the social stress context. These results indicate that it is not the social stress context itself but its interaction with CR that results in the diminished congruency-effects. This finding is in agreement with the results from animal studies (De Kloet et al., 1999) showing that cognitive impairments during stress depend on an interplay between glucocorticoid responses and the context in which they are elicited. Importantly, the high and low CR groups in our study differed exclusively in their cortisol responses and not on other stress measures, such as alpha-amylase, heart

rate, blood pressure and subjective stress-responses. The differential effects for CR can therefore be attributed to the individual differences in HPA-axis stress reactivity and not to catecholaminergic stress responses.

An interesting observation with respect to the influence of cortisol responses on AA-behavior was that the diminished congruency-effects in the high CR group applied to approach as well as avoidance reactions. These findings are in agreement with results from animal research showing that primates with high basal cortisol levels showed prolonged freezing responses and hence less active approach or avoidance reactions during exposure to a stressor (e.g. Kalin et al., 1998b). That not only active avoidance, but also active approach behavior can be disturbed under the influence of increased glucocorticoid stress responses was, moreover, demonstrated by a study of Nunez et al. (1996) showing that rats with a higher HPA-axis stress reactivity showed increased freezing and decreased approach responses in a punished drinking test.

Since approach-avoidance reactions are typically functions of the PFC (e.g. Davidson, 1992, 1995; D'Alfonso et al., 2000) our findings may be understood in a broader context of the influence of glucocorticoids on prefrontal executive functions. The PFC is a target for the stress-hormone cortisol and several studies have shown that cortisol administration can impair prefrontal functions, such as working memory (Lupien et al., 1999; Wolf et al., 2001; Young et al., 1999). Lupien et al. (1999), for example, reported a U-shaped curve between performance on a working memory task and changes in cortisol levels after hydrocortisone infusion. Also animal research showed that chronic corticosterone administration and chronic behavioral stress can lead to dendritic reorganizations in

the medial PFC (Wellman, 1993; Radley et al., 2004) and that exposure to stress-levels of cortisol results in impaired prefrontal behavioral control (Lyons et al., 2000). In our sample of high cortisol responders, such stress induced impairments in prefrontal executive functioning may have affected the task-performance in at least three ways. In the first place the increased cortisol levels may have resulted in an impaired prefrontal mediated capacity to inhibit the threatening stimuli that made part of the social stress context, resulting in an attentional bias towards the stress context and away from the AA task. However, such general drop in selective attention for the task performance would likely have been accompanied by a general slowing or a drop in accuracy in task performance and both were not the case. Another possible explanation for the diminished congruency-effects is that the high responders were less able to differentiate the emotional valence of the facial expressions in a context of social stress. It is well known that the medial PFC, especially the anterior part of the ACC, plays an important role in the processing of emotional stimuli (e.g. Bush et al., 2000) and is activated by tasks related to the emotional content of stimuli, such as emotional stroop tasks (e.g. Whalen et al., 1998). Unfortunately we collected no data on stimulus processing and we cannot rule out the possibility that problems with differentiating the emotional valence of the stimuli by the ACC are responsible for the fact that both approaching and avoidant affect congruent actions were slowed during stress. However, such problems in affective evaluation of faces would likely have resulted in diminished performance accuracy and we did not find higher error rates for the high responders during stress. In the third place, there is increasing evidence that the ACC is crucially involved in the detection of whether conflicting action tendencies are elicited by the stimuli (Carter et al., 1999; Botvinick et al., 1999). In the incongruent instruction condition of the AA task, such conflicting action tendencies are, for example, activated when participants are instructed to make an approaching movement towards an angry face (that initially elicits the tendency to avoid). According to conflict monitoring theory, upon detection of conflicting action tendencies, the ACC signals the need for extra cognitive control to the lateral prefrontal cortices. The latter provide control operations, including activation or inhibition of neural circuits, to eliminate the conflict between the action tendencies (e.g. Carter et al., 1999). Subsequent activation in left PFC is thought to facilitate approach, and in right PFC it is thought to facilitate

avoidance reactions (e.g. Davidson, 1992; 1995; D'Alfonso et al., 2000). Previous research indicated the ACC conflict detection system to be sensitive to cortisol administration (Hsu et al., 2003) and to be overactive in anxiety disorders such as OCD (Gehring et al., 2000; Hajcak and Simons, 2002; Ursu et al., 2003). Applying these insights to our findings, the fact that both affect congruent approach and affect congruent avoidance reactions were slowed in individuals with high CR may have been caused by an hyperactive ACC conflict detection system that signaled the need for extra cognitive control in response to all potentially threatening stimuli (e.g. happy as well as angry faces), irrespective of the response condition. Consequently, the longer RTs for affect congruent trials might reflect the extra cost associated with this increase in cognitive control by the lateral prefrontal cortices. Of course this conflict monitoring hypothesis is still speculative and further research, using Event Related Potentials (ERP) measures associated with the affect congruent and affect incongruent reactions on the AA-task, is needed to test it.

An unexpected finding from the present study was that the high and low CR groups already differed at baseline administration of the AA-task. Whereas the high CR group showed significant congruency effects before stress-induction, the low CR group did not show these effects and only displayed significant congruency-effects during stress. These findings indicate that the high and low cortisol responders did not only differ in stress-reactivity of the HPA-axis but also with respect to other variables that were not related to the stress-context. One explanation may be that high responders were more stressed at baseline. Data on physiological and subjective stress measures, however, did not point into this direction. The group difference also appeared to be independent of individual differences in BIS scores. Further research is needed to determine whether individuals with relatively low and high glucocorticoid stress responses may, for example, differ in the way they generally tend to perceive and respond to affective stimuli.

The second purpose of the present study was to investigate the influence of trait avoidance (BIS scores) on the tendencies to approach or avoid positive and threatening social stimuli in a context of social stress. Because the BIS measures a trait to show behavioral inhibition towards threat in daily life, we expected the low trait avoidance (TA) group to display slowed avoidance reactions towards angry faces in particular. We indeed found that only participants with relatively low TA displayed diminished RT congruency-effects after

stress. Also on the movement times (MTs) we found diminished congruency-effects for the low TA group, this time, however, irrespective of stress-induction. Interestingly, only for the MTs the decrease in congruency-effects emerged exclusively for the angry faces. For RTs, however, the alterations in congruency-effects did not differentiate for happy and angry faces. The low avoiders demonstrated slowed affect congruent reactions to happy, as well as angry faces. Thus, like high cortisol responders, individuals with low TA showed diminished RT congruency-effects during stress. Consequently, one could wonder whether these variables are mutually related. In terms of overlap between the groups, only a non-significant majority (6) of the 10 participants in the high CR group scored low on TA. There was, however, a significant (negative) correlation between the participants' individual BIS scores (TA) and cortisol responses. Also the effects of TA on the task performance disappeared after partializing out the effects of the cortisol responses on the task, suggesting that the relation between TA and AA-behavior was at least partly mediated by the cortisol responses.

To our knowledge the present study is the first to directly test the influence of stress-induced changes in cortisol levels on affect congruent and affect incongruent approach-avoidance action tendencies. Some limitations should be considered when evaluating these findings. Although the groups were large enough to show differential effects in HPA-axis reactivity, trait avoidance and AA-behavior, the findings should be replicated using larger group sizes, also allowing the study of gender differences. Furthermore, we did not study the way the emotional valence of the stimuli was processed by the participants in different conditions, preventing definite conclusions about the exact mechanisms that may have caused the diminished congruency-effects in the social stress context. A final remark concerns the operationalization of 'approach' and 'avoidance' by the AA task. Although we found the expected congruency effects (e.g. faster arm-flexion in response to happy faces and faster arm-extension in response to angry faces) the exact mechanisms that may underlie these effects remain uncertain. Cacioppo et al. (1993) suggest that the link between affective information processing and arm flexion/extension entails a form of higher order Pavlovian conditioning. Arm flexion is usually temporally related to the consumption of desired goods, whereas arm extension is mostly temporally coupled with the onset of unconditioned aversive stimuli. Further research is needed to investigate whether these mechanisms may indeed explain the congruency effects found using the AA

task. Despite these limitations, the data provide important directions for future research. Application of brain-imaging techniques may, for example, determine whether the influence of cortisol on the initiation and execution of approach and avoidance reactions is indeed attributable to the direct effects of the glucocorticoids on the medial PFC and to find out to what extent other brain structures, such as the lateral prefrontal cortices and amygdala, may also be differentially involved. Furthermore, the fact that high and low CR groups, in contrast to the high and low TA groups, already differed at baseline performance on the AA-task, suggests that different mechanisms may underlie the diminished congruency effects in the high CR group and the low TA group during stress. To more precisely study the unique influence of CR and TA on AA-behavior during stress these factors should be studied in a 2×2 group design with a priori selected groups. Finally, to assess the relative influence of cortisol and the social stress-context on AA-tendencies, future studies should examine the influence of high cortisol levels on AA-behavior in the absence of a social stressor, for example by administering hydrocortisone.

In summary, individuals with relatively high cortisol responses showed diminished affect congruent approach and avoidance action tendencies towards positive and threatening social stimuli in a context of social stress. These results indicate that the relation between high cortisol levels and diminished active approach-avoidance behavior previously found for animals, also holds for humans. In the second place, similar reductions in approach-avoidance behavior, associated with low trait avoidance, were at least partly mediated by the effects of cortisol. These findings not only provide insight into fundamental processes mediating human approach-avoidance behavior. They, moreover, offer a fruitful experimental model for the study of freezing and avoidance reactions in patients with anxiety disorders, such as social phobia and post-traumatic stress disorder, and in patients with somatoform disorders, such as psychogenic paralysis.

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