Losing control : anxiety and executive performance

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Chapter 7

Hydrocortisone affects cognitive interference from threatening and erotic stimuli under acute stress

ABSTRACT

Acute stress impairs cognitive performance by increasing bottom-up processing of salient stimuli while reducing top-down control. This effect depends on trait cognitive control and trait anxiety. Single administration of hydrocortisone increases top-down control and reduces emotional-interference. However, this has never been investigated under acute stress. The aim was to investigate the effects of cortisol on emotional-interference (negative and positive) under acute stress in highly anxious females, and the role of trait cognitive control and trait anxiety. Eighty female participants were randomly assigned to a 40 mg hydrocortisone group (n = 40) or placebo group after baseline EEG recording, in a double-blind design. After an hour, all participants went through a psychosocial stress-induction procedure followed by a pictorial emotional Stroop task (neutral, mild threat, high threat, and erotic scenes). Trait cognitive control and trait anxiety were assessed with self-report measures. Objective trait cognitive control was assessed with frontal EEG theta/beta ratio. TBR interacted with trait social anxiety (also general trait anxiety) moderating the effect of hydrocortisone on interference from high threat as compared to mild threat. Self-report trait cognitive control interacted with trait social anxiety moderating the effect of hydrocortisone on interference from erotic stimuli. Hydrocortisone increased state attentional control in participants with high self-report cognitive control. The current findings suggest that a single administration of hydrocortisone reduces interference from highly arousing emotional stimuli in highly anxious females with higher trait cognitive control (also depended on trait anxiety) under acute stress, possibly by increasing inhibitory control.

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Submitted for publication.

INTRODUCTION

Acute physiological and psychological stress rapidly increases catecholamine and glucocorticoid hormonal levels in brain (e.g., Hermans et al., 2014). Excessive levels of catecholamines disrupt the executive network, that includes prefrontal cortex (PFC; Hermans et al., 2011; Menon, 2011; Hermans et al., 2014) and accounts for goal-directed behavior and cognitive control over emotional information, and up-regulate the salience network, responsible for the automatic preferential processing of salient information (e.g., Bishop et al., 2007; Hermans et al., 2014). This effect results in altered automatic processing of emotional information, known as attentional bias (AB).

AB is considered to account for the negative effects of stress on cognitive performance by its strain on limited executive cognitive resources (e.g., Derakshan & Eysenck, 2009) and to contribute to the maintenance of anxiety disorders (e.g., Mogg & Bradley, 1998, 2016). Threat-level is important in the manifestation of AB. It is suggested to be adaptive avoiding mild threats (MT), allowing task-relevant behavior, and attending high threats (HT), in order to cope with environmental demands and/or sustain emotional integrity (Mogg & Bradley, 2016; 2018). This (threat-level dependent) effect on cognitive-affective processing is regulated by trait cognitive control and trait anxiety (e.g., Angelidis et al., 2018; Mogg & Bradley, 2016; 2018; van Son et al., 2018a). It is found that trait cognitive control and trait anxiety, as assessed with self-report (e.g., Bardeen & Daniel, 2017; Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Schoorl et al., 2014) and objective measures (e.g., Angelidis et al., 2018; van Son et al., 2018b), interact in their relation with AB. Specifically, higher trait cognitive control, as assessed with lower EEG frontal theta/beta ratio (TBR) and self-reported attentional control, has been related to more AB to HT than to MT (Angelidis et al., 2018; van Son et al., 2018a), also in interaction with anxiety: the most resilient individuals, with higher trait cognitive control and lower anxiety, show higher AB to HT than to MT (Angelidis et al., 2018).

The slow genomic effects of glucocorticoid hormone are theorized to adaptively restore executive control over emotional information, starting approximately an hour after stress-induced release of glucocorticoid hormone (Hermans et al., 2014). This slow genomic effect is found to activate PFC function (Yuen et al., 2009), which reverses the fast dysregulating effects of cortisol and catecholamines on amygdala and hippocampus (Maggio & Segal, 2009; Soravia et al., 2006). Moreover, Weckesser (2016) showed that a single hydrocortisone (HC) administration prevented these negative effects of stress on attentional dual-task performance. Accumulating evidence suggests the positive effects of HC on cognitive-affect regulation: single administrations of HC result in reduced automatic attentional processing of goal-irrelevant emotional (threatening, fearful, and erotic) salient information, also moderated by trait anxiety, supporting the notion that HC upregulates PFC-dependent cognitive control (Oei

et al., 2007; Putman et al., 2010a; Putman et al., 2007b; Putman & Berling, 2011; for a review see, Putman & Roelofs, 2011). This is important not only theoretically but also suggests potential future therapeutic use for corticosteroid manipulation in anxious pathology. However, there is no proof of principle yet demonstrating that HC administration modulates AB under acute stress. Since it is known that catecholamines and cortisol interact in subcortical (e.g., Roozendaal et al., 2002) but also cortical (e.g., Barsegyan et al., 2010) memory processing, it should not be assumed unquestionably that such evidence of HC increasing cognitive control over salient emotional information processing also translates to information processing during stress.

Finally, lower TBR, the ratio between power in the EEG theta and beta frequency bands, with high test-retest reliability (Angelidis et al., 2016), is thought to reflect greater frontal cortical executive control (e.g., Angelidis et al., 2016; Arns et al., 2013; Barry et al., 2003; Putman et al., 2010b; 2014), also specifically over emotional information (Angelidis et al., 2018; van Son et al., 2018a,b; Knyazev, 2007). As an electrophysiological marker of trait cognitive control, TBR is expected to moderate effects of HC-administration on the effects of acute stress on cognitive control over emotional information processing.

The aim of this study was to investigate the effect of 40 mg HC-administration on interference from emotional stimuli under acute stress. In addition to interference from MT and HT, we will assess interference from erotic stimuli as there is no strong theoretical nor empirical precedence to expect valence specificity. We will also assess the moderating role of trait cognitive control and trait anxiety in these effects, as they are suggested to be pivotal (Angelidis et al., 2018; Mogg & Bradley, 1998, 2018; van Son et al., 2018a,b). Specifically, we first hypothesized that the effect of HC on threat-interference under stress would be dependent to distinct levels of threat (MT vs HT). Second, we expected that HC-administration would modulate the effect of acute stress on interference from erotic stimuli. Finally, we expected that both these effects would be moderated by trait cognitive control and/or trait anxiety. Trait cognitive control was assessed with the commonly used self-report attentional control scale (Derryberry & Reed, 2002) and, objectively, with frontal EEG TBR. These predictions were tested in healthy highly anxious young females.

METHODS

Participants

Eighty Dutch-speaking high test anxious female participants, between 18 and 25 years old, were recruited at Leiden University campus and were randomly allocated to the placebo (n = 40) or 40 mg HC group (n = 40). Only females were tested due to practical reasons and due to previous evidence suggesting that females have higher levels of test anxiety (e.g., Beidel, Turner, & Trager, 1994;

Putwain, 2007). Participants with high trait cognitive test anxiety were selected from a large pool of respondents who completed the Cognitive Test Anxiety Scale (CTAS; Cassady & Johnson, 2002), measuring cognitive performance anxiety (see below for details). Exclusion criteria were BMI < 18 or > 25, self-reported axis I disorder, frequent use of psychoactive substances, history of neurological disorder, any major medical condition, use of cardiac or antihistamine medication, injuries (including small injuries in the mouth), recent change of pharmaceutical birth control procedure, pregnancy or lactation, history of concussion. Also, students from the natural science faculties, who are in general more proficient at and confident about their mathematical problem solving skills, were excluded because of the nature of the stressor (see below). Participants were instructed not to drink anything but water, refrain from food, not to smoke, brush their teeth, and to minimize physical exercise during an hour prior to the experiment. They were also instructed not to drink more than two alcohol units on the evening prior to their participation. Oral contraceptive users were invited to the lab between the 10th and the 27th day of their menstrual cycle. Participants who did not use oral contraceptives were invited during the early follicular phase of their menstrual cycle (between the 2nd and the 9th day; Kirschbaum et al., 1999). Informed consent was provided before any assessment took place. Information regarding the stress manipulation was initially withheld but all participants were extensively debriefed at the end of the procedure. The study was approved by the certified medical ethics committee of Leiden University Medical Centre (LUMC; Leiden, The Netherlands)

Apparatus and Materials

Drug capsules

HC and placebo were administered double-blind (random group allocation), in identical capsules. Placebo capsules contained Primogel while HC capsules contained Primogel and 40 mg HC. A single dose of 40 mg, is found to result in very high salivary cortisol levels (e.g., Abercrombie et al., 2003; Putman & Berling, 2011) and is similar to previous relevant studies (Het and Wolf, 2007; Putman et al., 2007a,b; Oei et al., 2009; Putman et al., 2010a; Putman & Berling, 2011; van Peer et al., 2010).

EEG set up

An eight-minutes resting-state EEG recording (in alternating 1-minute blocks of closed and open eyes) was performed as in previous studies using Biosemi Active Two system (e.g., Putman et al., 2010b, 2014; Angelidis et al., 2016, 2018; van Son et al., 2018a,b). Frontal EEG activity was acquired with Ag/AgCl electrodes on the F3, Fz, F4 10/20 positions as previously reported (e.g., Angelidis et al., 2016, 2018; Putman et al., 2010b, 2014; van Son et al., 2018a,b) with a sampling rate of 256 Hz (Allen, Coan, & Nazarian, 2004).

Questionnaires

Trait attentional control The Attentional Control Scale (ACS; Derryberry & Reed, 2002; Verwoerd, de Jong, & Wessel, 2006) consists of 20 items, rated in a 4-point Likert scale (1 to 4), and had a good internal consistency in this study (Cronbach's α = .822).

Trait cognitive test anxiety The Cognitive Test Anxiety Scale (CTAS; Cassady & Johnson, 2002) consists of 27 items, rated in a 4-point Likert scale (1 to 4), and had a good internal consistency in the present study (Cronbach's α = .878)

Trait social anxiety The Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987) consists of 24 items. Each item refers to a social situation (e.g., "Taking a test" and "Being the center of attention") and participants have to rate on a scale from 0 to 3 how anxious or fearful they are, and how often they avoid the situation. Internal consistency of the total score was excellent in this study (Cronbach's α = .944).

Trait anxiety Spielberger's trait version of the State-Trait Anxiety Inventory (STAI-t; Spielberger, 1983; Van der Ploeg, Defares, & Spielberger, 1980) consists of 20 items, rated on a 4-point Likert scale (1 to 4), and had an excellent internal consistency in the present study (Cronbach's α = .920).

State anxiety and attentional control State anxiety and the state attentional control were assessed with visual analogue scales (VAS), as in Angelidis et al. (2019; similar to, Putman et al., 2014). VAS consisted of 7 items for state performance anxiety (4 items for emotionality and 3 items for cognition) and 6 items for state attentional control. Finally, 8 items were included as fillers. Participants had to respond on a visual analogue scale by crossing 100 mm lines, anchored "not at all" and "completely" to the left and right end. The internal consistency for state anxiety and state attentional control was good (for t_1 Cronbach's α = .849 and .744, respectively; for t_2 Cronbach's α = .906 and .812, respectively).

Pictorial Emotional Stroop Task (PEST)

Emotional interference was assessed with the PEST based on van Son et al. (2018b). The task consisted of 36 practice trials, 120 trials for threat-interference, and 80 trials for interference from erotic stimuli. After the presentation of a fixation cross on the center of a grey screen for 500 ms, a picture was presented for 200 ms. Then a colored square, of 2 cm by 2 cm, was superimposed on the picture for 1800 ms. Participants had to indicate the color of the square (red, yellow, or blue) as fast as possible, without sacrificing accuracy, with their index, middle or ring finger of their dominant hand using colored buttons on a keyboard. Interference from MT and HT was assessed using 10 neutral (e.g., a spoon), 10 midly threatening pictures (e.g., animal or human

attack), and 10 highly threatening pictures[1] (e.g., mutilated bodies), selected from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention). After the threat-block, interference from erotic pictures was separately assessed using 10 new neutral (e.g., neutral human scenes) and 10 erotic pictures (e.g., men and/or women in erotic scenes) from IAPS[2]. The pictures were subjectively matched on color and composition. Each picture was randomly presented four times with the target square superimposed in all of four different locations of the picture (7.5 cm from the vertical side/4.7 cm from the horizontal side of the left upper corner, right upper corner, bottom left corner, or bottom right corner of the picture), and the color of the square was not the same on more than two consecutive trials. Pictures were presented with a width of 23.5 cm and height of 14.8 cm. The task was programmed in E-Prime 2 (Psychology Software Tools, PST) and presented on a 22" monitor (resolution 1680 × 1050). Participants were seated in a chair with a viewing distance of approximately 60 cm from the screen.

Procedure

All participants were tested individually between 12:00 and 18:30. On arrival, participants completed some questionnaires and performed a baseline EEG measurement. Immediately after the drug administration, participants practiced a WM task, which was used further in the procedure, followed by light reading. An hour after the drug administration, subjects went through the stress manipulation, followed by a WM task, the Pictorial Emotional Stroop Task (+104 min after drug administration and +44 min after onset of stress induction procedure), and an operating working memory task. Results for the two working memory tasks are reported elsewhere (Angelidis et al., in preparation). Self-report cognitive interference was assessed after the two WM tasks for different research purposes. Self-report state anxiety and state attentional control were assessed right before and after the stress manipulation. Further procedures, after the Pictorial Emotional Stroop task, are described in another paper.

Stress procedure

We performed an extensive protocol combining the validated Leiden Performance Anxiety Stress Procedure (L-PAST; Angelidis et al., 2019; Putman et al., 2014) and the Social Evaluation Cold Pressure test (SECPT; Schwabe et al., 2008). Both standardized procedures were followed. This protocol was used to induce (and maintain) state performance anxiety and sympathetic ANS arousal,

[1]**Neutral pictures**: Valence: *M* = 5.2, *SD* = 0.5; Arousal: *M* = 3, *SD* = 1; 5334, 5900, 7004, 7010, 7038, 7039, 7050, 7175, 7211, 7285; **mild threatening pictures**: Valence: *M* = 3.3, *SD* = 0.4; Arousal: *M* = 5.4, *SD* = 0.5; 2692, 2694, 2716, 6190, 6800, 6834, 9102, 9584, 9630, 9925; **highly threatening pictures**: Valence: *M* = 1.6, *SD* = 0.3; Arousal: *M* = 6.8, *SD* = 0.3; 3000, 3010, 3068, 3071, 3100, 3102, 3120, 3053, 3063, 3150. [2]**Neutral pictures**: Valence: *M* = 5.5, *SD* = 0.9; Arousal: *M* = 3.4, *SD* = 0.5; 2000, 2005, 2010, 2200, 2210, 2214, 2222, 2102, 2190, 2493; **Erotic pictures**: Valence: *M* = 6.5, *SD* = 0.4; Arousal: *M* = 6.4, *SD* = 0.3; 4611, 4647, 4651, 4652, 4658, 4659, 4666, 4669, 4670, 4690.

including (nor-)adrenergic activation (Angelidis et al., 2019; Schwabe et al., 2008). See supplementary materials for further details.

Data reduction

One case was excluded from analyses relevant to LSAS, STAI-t, and CTAS as a univariate outlier on these measures (e.g., 3.9 *SDs* above the mean score of LSAS). One case was excluded from analyses relevant to STAI-t and CTAS due to at random data loss.

EEG analyses The same procedure was used as previously (Putman et al., 2014; Angelidis et al., 2016, 2018; van son et al., 2018a). Area power density (μV^2/Hz) in the theta (4-7 Hz) and beta (13-30 Hz) frequency bands was estimated by using a fast Fourier transformation (10% hamming window, using a resolution of .25 Hz). Then, frontal EEG TBR was calculated by dividing the average frontal power densities (F3, Fz, F4) of theta band by beta band (cf. Putman et al., 2014; Angelidis et al., 2016, 2018). Due to typical skewed distribution of average frontal TBR, LN-normalization was applied. Lower frontal TBR reflects relatively greater frontal beta compared to theta power (higher trait cognitive control). In total, six cases were excluded from relevant analyses: two cases due to technical problems (more than 50% of the recording was excluded due to artifacts); four cases because of extreme theta or beta power (> + 2.5 *SDs* from the mean).

PEST First, incorrect responses were removed. Then, trials with reaction times (RTs) < 300 or > 1200 ms were removed as premature or extremely slow responses. A second filter was applied, < or > than 3 *SDs* below or above the average RTs, to identify individual outliers. Both filters resulted in the removal of 7% of the trials from the total trials for threat-interference and 8.8% for interference from erotic stimuli. Threat-interference was calculated separately for MT and HT stimuli by subtracting average RT for neutral trials from average RT for threat trials. Similarly, erotic-interference was calculated by subtracting average RT for neutral trials from average RT for erotic trials. Positive scores indicate longer RTs for emotional stimuli (or more cognitive processing/vigilance for emotional stimuli) while negative scores indicate shorter RTs for emotional stimuli (or less cognitive processing/avoidance of emotional stimuli). Two cases were excluded from relevant analyses to threat-interference, and one case for erotic-interference, as univariate outliers on RTs (individual mean RTs > 2.5 *SDs* from the average RTs). Finally, one case was excluded from analyses relevant to threat-interference due to extreme number of errors, 25% of the trials.

Statistical analyses

The effect of HC on threat-interference was tested with a rm ANOVA, with Threat-level (2; MT and HT) as a within-subjects factor, and Group (2; PLC and HC) as a between-subjects factor. The same rm ANOVAs with trait cognitive control and trait anxiety as covariates were performed to investigate the

moderating role of trait cognitive control and trait anxiety on threat-interference. In order to unravel significant Group × Threat level × cognitive control × trait anxiety interactions, simple slope analyses (Aiken & West, 1991) were performed for each group with trait cognitive control as a predictor (low = - 2 *SD*s below the mean; high = + 2 *SD*s above the mean), trait anxiety as a moderator (low = -1*SD* below the mean; high = +1 *SD* above the mean) and ΔThreat-level (Interference from MT minus interference from HT) as a dependent variable.

The effect of HC on erotic-interference was tested with an ANOVA, with erotic-interference as a dependent variable and the same factors and covariates as for threat-interference. Significant interactions with Group were again unraveled with the same simple slope analyses with erotic-interference as a dependent variable. For both threat-interference and erotic-interference, a factor 3 Bonferroni correction was used for statistical testing as we perform the same analysis separately for CTAS, LSAS, and STAI-t.

As TBR was expected to correlate negatively with both ACS and STAI-t, which are themselves typically negatively related, partial correlations for TBR and ACS controlling for STAI-t were performed in order to prevent obfuscating confounding (cf. Putman et al., 2010b, 2014; Angelidis et al., 2016, 2018; van Son et al., 2018a).

RESULTS

Flow of participation

In total, 1,350 individuals participated in an online study. Seven hundred forty six respondents were Dutch-speaking females, aged between 18 and 25 (CTAS scores: *M* = 60.2, *SD* = 12.9, *Mdn* = 59, range = 29 – 102; LSAS scores: *M* = 39.3, *SD* = 21.2, *Mdn* = 37, range = 0 – 130). See Figure 1 for a diagram of participation-flow. Three hundred forty eight of them were above the median on CTAS with a mean score of 70.5 (*SD* = 8.7) on CTAS. From the 133 people who were screened, 25 did not meet the exclusion criteria and two were excluded because they were familiar with the stress procedure of the study. Of the 110 who met the criteria, 21 declined to participate and 85 were randomly assigned to the placebo or hydrocortisone group. Five participants were excluded from the study: one participant dropped out because she did not tolerate the stress-manipulation (placebo group), one revealed by the end of the procedure that she was informed about the stress manipulation by another participant (HC group), and three cases did not adhere to the procedure (2 from placebo group and one from HC group). Finally, a total of 80 participants completed the entire procedure and was included in analysis. Their mean CTAS score was 68.1 (*SD* = 10.8; range = 60 – 86; LSAS scores: *M* = 43.2, *SD* = 20.9, *Mdn* = 41, range = 7 – 125) and they represented the 51st – 97th CTAS percentiles from the original respondent sample of 746.

Participants

No group differences were observed on background characteristics, trait measures, frontal TBR, state anxiety, and baseline salivary cortisol levels (see Table 1).

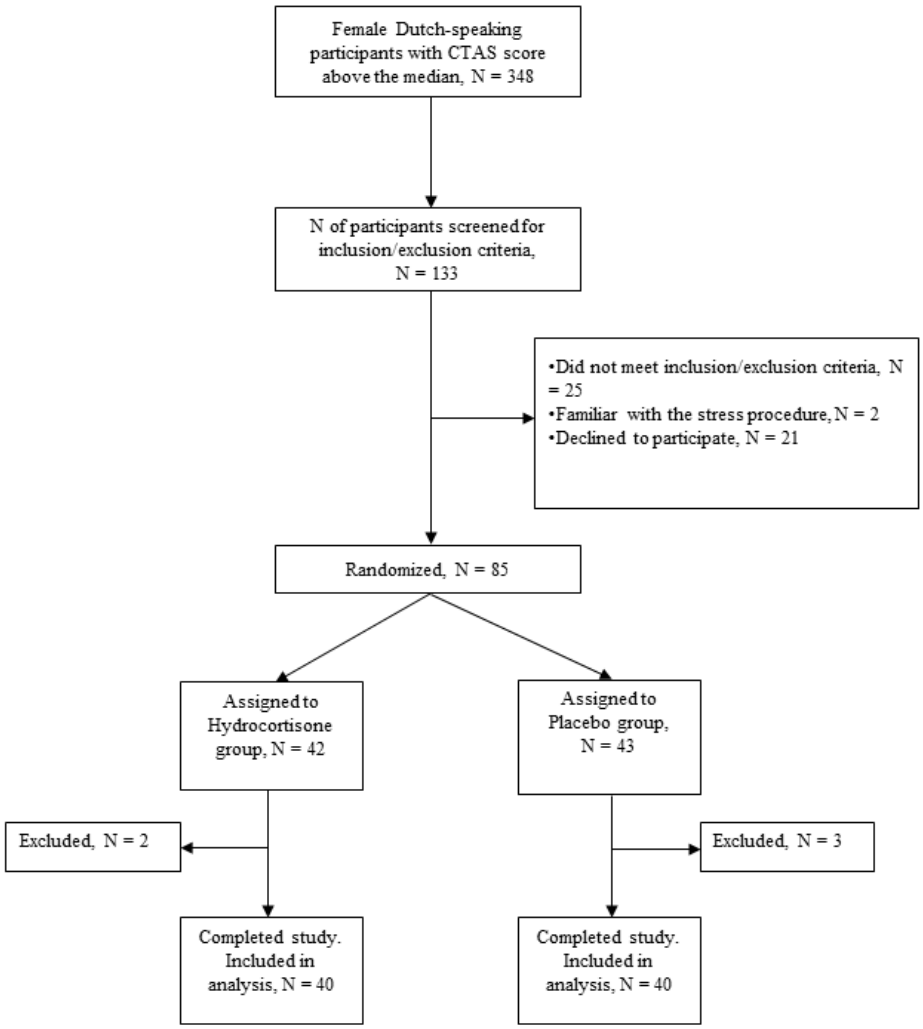

Figure 1. Participant flow

Table 1. Means (and standard deviations) and t-tests of background characteristics, trait measures, state anxiety, and salivary cortisol levels for the control (n = 40) and the stress group (n = 40).

	Placebo	HC	p
Age	20.6 (2)	20.3 (1.8)	.524
Education	7.9 (0.6)	7.8 (0.7)	.565
CTAS	67.6 (9.4)	68 (11.1)	.869
LSAS	43.9 (19.9)	40.3 (17.9)	.839
STAI-t	42.5 (9.8)	43.2 (8.8)	.744
ACS	51.6 (7.2)	51.5 (7.4)	.964
Frontal TBR	1.236 (0.630)	1.214 (0.544)	.853
SA_1	20.5 (15.3)	22.1 (12.6)	.606
SA_2	50 (20)	46.9 (19.2)	.484

Note: Reported descriptives of cortisol levels and frontal TBR are not Ln-normalized for more intuitive appreciation and comparability with other studies. Education = a score of 8 reflects a university bachelor level in the Dutch academic system, STAI-t = Spielberger's state trait anxiety inventory - trait subscale, STAI-s = Spielberger's state trait anxiety inventory - state subscale SA = state anxiety, SA1 = before manipulation, SA2 = before the test-procedure of the EST.

Manipulation check

A rm ANOVA with Time as within-subject factor and Group as between-subject factor revealed a significant main effect of Time on self-report state anxiety, $F(1, 78) = 81.804$, $p < .001$, $\eta_p^2 = .703$, indicating that the total sample reported higher levels of state anxiety after the manipulation, at t_2 (M = 48.43, SD = 19.52), as compared to t_1 (M = 21.31, SD = 13.95). No other main effects or interactions were significant. Thus, state anxiety increased after the stress-manipulation, irrespective of drug condition.

Threat-interference

After running a rm ANOVA with centered **TBR** and **LSAS** as covariates, we found significant Threat level × TBR, $F(1,63) = 14.211$, $p < .001$, $\eta_p^2 = .184$, and Group × Threat level × TBR interactions, $F(1,63) = 11.684$, $p = .003$, $\eta_p^2 = .156$ (a 3-factor Bonferroni correction was applied). Simple slopes analysis for the PLC group (see Figure 2a), $\Delta R^2 = 8\%$, $p = .076$, illustrate a general negative relationship between TBR and ΔThreat-level (Interference from MT minus interference from HT), that is stronger and significant for low LSAS, $\beta = -0.650$, $t = -3.166$, $p = .003$, for average LSAS; $\beta = -0.400$, $t = -2{,}485$, $p = .018$, and not significant for high LSAS, $\beta = -0.150$, $t = -0.695$, $p = .492$. For the HC group,

simple slopes, ΔR^2 = 15.7%, p = .011, illustrate again a general negative relationship between TBR and ΔThreat-level. However, in the HC group (see Figure 2b), this relationship is stronger and significant for high LSAS, β = -0.734, t = -3.399, p = .002, for average LSAS scores; β = -0.347, t = -2.317, p = .027, and positive and not significant, for low LSAS, β = 0.039, t = 0.200, p = .843. In general, while in the PLC group, participants with low TBR and low LSAS showed lower interference (avoidance) from HT compared to MT, in the HC group, this pattern was observed for participants with low TBR and high LSAS.

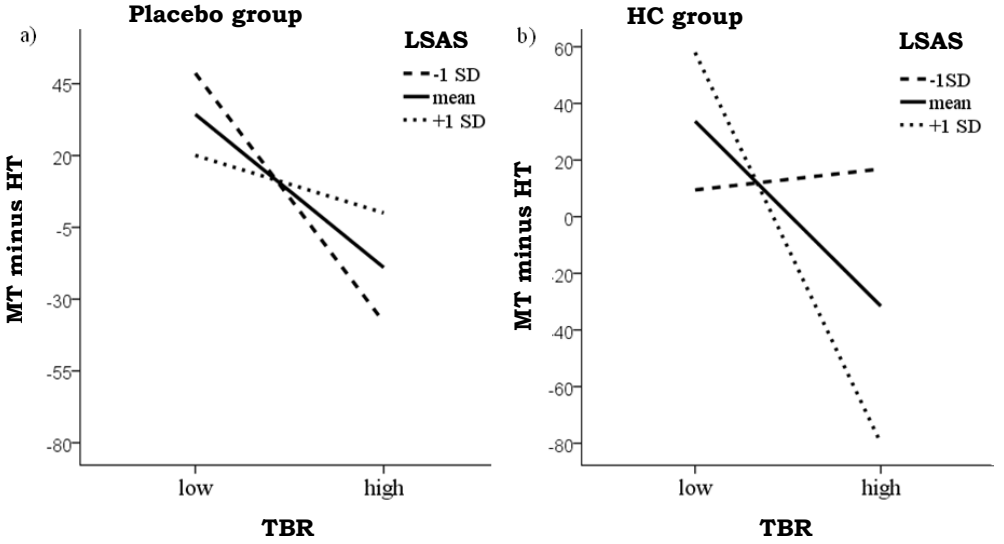

Figure 2. Simple slopes for the moderation of LSAS (low: - 1 SD; high: + 1 SD) on the relationship between Ln-normalized frontal EEG TBR (low = - 2 SDs below the mean; high = + 2 SDs above the mean) on ΔThreat-level (interference from MT minus interference from HT: higher scores indicate more lower interference (avoidance) to HT compared to MT) as assessed with the pictorial emotional Stroop task separately for a) the placebo and b) the HC group. Frontal TBR (Ln) = Ln-normalized frontal theta/beta ratio, LSAS = trait social anxiety.

After conducting the same ANOVA with centered **ACS** and **STAI-t** as covariates, significant Threat level × STAI-t × ACS, $F(1,68)$ = 4.713, p = .033, η_p^2 = .065, and Group × Threat level × ACS × STAI-t interactions, $F(1,68)$ = 6.873, p = .032, η_p^2 = .092 (a 3-factor Bonferroni correction was applied), were revealed. Simple slopes analysis for PLC group, ΔR^2 = 0.7%, p = .578, illustrate a general negative relationship between ACS and ΔThreat-level. For the HC group, simple slopes, ΔR^2 = 14.3%, p = .024, illustrate a general positive relationship between

ACS and ΔThreat-level. However, in the HC group, this relationship is stronger and significant for high STAI-t, β = 3.954, t = 2.167, p = .038, less for average STAI-t scores; β = 0.689, t = 0.694, p = .493, and negative for high STAI-t, β = -2.575, t = -1.648, p = .109.

Analyses did not confirm any other hypotheses, including CTAS. To sum up, HC had an effect on interference from different levels of threat, dependent on TBR and LSAS, and ACS and STAI-t; in the HC group, but not in the PLC group, individuals with lower TBR and higher LSAS/or higher ACS and lower STAI-t showed more avoidance of HT relative to MT, compared to the rest of the group.

Erotic-interference

After excluding a multivariate outlier (Cook's distance > 1), the same ANOVA with centered **ACS** and **LSAS** as covariates revealed significant Group × ACS interactions, $F(1,68) = 5.692$, p = .020, η_p^2 = .077, Group × ACS × LSAS interactions, $F(1,68) = 11.287$, p = .004, η_p^2 = .142 (a 3-factor Bonferroni correction was applied), interactions. Simple slopes analysis for the PLC group (see Figure 3a), ΔR^2 = 4.9%, p = .170, revealed a general positive relationship between ACS and erotic-interference. For the HC group (see Figure 3b), simple slopes, ΔR^2 = 21%, p = .004, illustrate a general negative relationship between ACS and erotic-interference. This relationship is negative and significant for low LSAS, β = -5.204, t = -3.444, p = .002, and for average LSAS scores; β = -1.973, t = -2.238, p = .032, and positive for high LSAS, β = 1.258, t = 1.056, p = .299.

The same ANOVA with centered **ACS** and **STAI-t** as covariates, showed a significant Group × ACS × STAI-t interaction, $F(1,68) = 7.641$, p = .022, η_p^2 = .101 (a 3-factor Bonferroni correction was applied). Simple slopes analysis for the PLC group, ΔR^2 = 2.6%, p = .339, revealed a general positive relationship between ACS and erotic-interference. For the HC group, simple slopes, ΔR^2 = 15.8%, p = .011, illustrate a general negative relationship between ACS and erotic-interference, that is negative and significant for low LSAS, β = -4.257, t = -2.834, p = .008, for average LSAS scores; β = -1.226, t = -1.487, p = .146, and positive for high LSAS, β = 1.805, t = 1.424, p = .164.

Analyses did not confirm any other hypotheses, including CTAS or TBR. To sum up, HC affected interference from erotic stimuli, dependent on ACS and trait anxiety (LSAS and STAI-t); in the HC group, but not in the PLC group, individuals with higher ACS and lower LSAS/or STAI-t showed lower interference compared to the rest of the group.

Secondary analyses

State attentional control A rm ANOVA with Time as within-subject factor and Group as between-subject factor revealed a significant main effect of Time on self-report state attentional control, $F(1, 78) = 125.104$, $p < .001$, η_p^2 = .616, indicating that the total sample reported lower levels of state attentional control after the manipulation, at t_2 (M = 39.56, SD = 15.03), as compared to t_1 (M =

58.59, *SD* = 11.78). No other main effects or interactions were significant. When adding ACS in the model, analyses revealed significant main effects of Group, $F(1, 76) = 5.105$, $p = .027$, $\eta_p^2 = .063$, and ACS, $F(1, 76) = 16.579$, $p < .001$, $\eta_p^2 = .179$, and a significant Group × ACS interaction, $F(1, 76) = 4.583$, $p = .036$, $\eta_p^2 = .057$. Post-hoc correlations showed that the relation between ACS and overall state attentional control was not significant in the placebo group, $r = .19$, $p = .235$, while it was positive and significant in the HC group, $r = .68$, $p < .001$, indicating that participants with higher ACS scores in the HC group reported overall higher state attentional control.

Self-reported attentional control and TBR A partial correlation, controlling for STAI-t (cf. Putman et al., 2010b, 2014; Angelidis et al., 2016; van Son et al., 2018a), revealed that TBR was not associated with ACS, $r = .000$, $p = .997$.

Blinding

Of the 80 participants, 36 (45%) guessed correctly if they were in the PLC or HC group. A binomial test showed that this percentage did not deviate from random performance ($p = .843$).

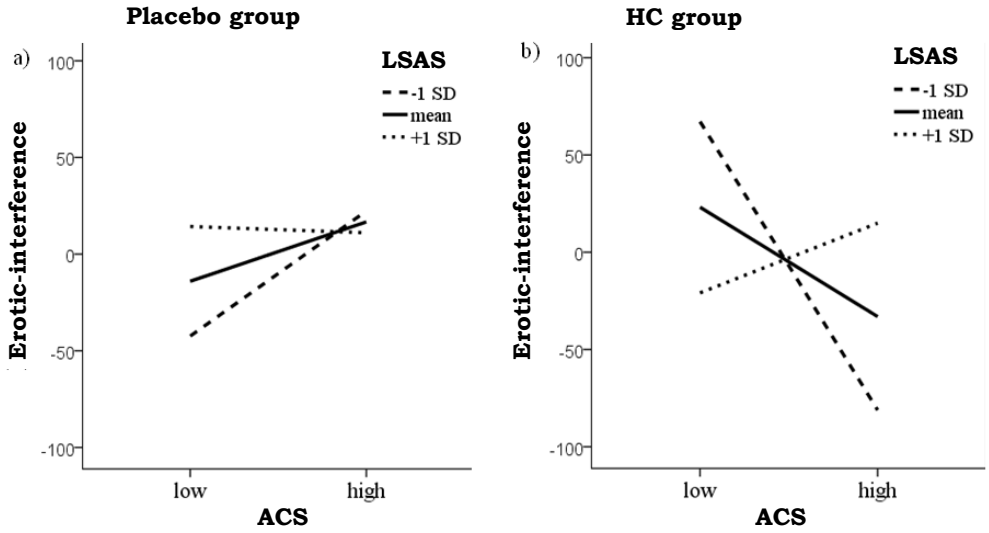

Figure 3. Simple slopes for the moderation of LSAS (low: - 1 SD; high: + 1 SD) on the relationship between ACS (low = - 2 SDs below the mean; high = + 2 SDs above the mean) on erotic-interference as assessed with the pictorial emotional Stroop task separately for a) the placebo and b) the HC group. ACS = trait attentional control, LSAS = trait social anxiety.

DISCUSSION

Single administration of 40 mg HC affected cognitive interference by emotional stimuli under acute stress in highly anxious females, but only in interaction with individual differences in trait cognitive control and trait anxiety. Specifically, objective trait cognitive control, assessed with TBR, in interaction with trait social anxiety moderated the effect of HC on threat-interference. Moreover, subjective trait cognitive control, assessed with ACS, in interaction with trait social anxiety or general trait anxiety, moderated the effect of HC on interference from erotic stimuli. Finally, HC increased self-report state attentional control in individuals with higher trait attentional control.

The aim of the present study was to investigate, for the first time, the effects of 40 mg HC on emotional interference under acute stress. Previous literature has shown repeatedly that HC-administration reduces such interference (for a review see, Putman & Roelofs, 2011), however, it had not been investigated under acute stress. This study importantly extends such studies as effects on (working) memory from GR activation are known to interact with other stress hormones (e.g., Roozendaal et al., 2002; Barsegyan et al., 2010) and thus the question remained if those previous effects on cognitive interference (Putman et al., 2007a,b; Putman et al., 2010a; Oei et al., 2007; Taylor et al., 2011; van Peer et al., 2010) would also occur under stress.

HC-effects were dependent on individual differences in trait cognitive control and trait anxiety. Specifically, in the HC group, the relation between objective trait cognitive control (TBR) and threat-level dependent interference was positive for individuals with higher trait social anxiety scores, indicating that participants with higher trait cognitive control (lower TBR) and lower social anxiety scores, showed less interference (more avoidance) from HT as compared to MT. This is in line with the cognitive-motivational framework (Mogg & Bradley, 1998, 2016) which describes the efficiency of cognitively controlled differential responding to MT and HT and specifically the adaptive attention to HT in order to cope with it (confirmed by Angelidis et al., 2018; van Son et al., 2018a,b). Specifically, Angelidis et al. (2018) reported that the most resilient individuals, with lower TBR and lower trait anxiety, demonstrated vigilance to HT as compared to MT. In the present study, participants with higher trait cognitive control (lower TBR) and higher trait social anxiety in the HC group showed avoidance of HT as compared to MT under acute stress. As it was observed for threat-interference, we found that subjective trait cognitive control (ACS scores) interacted with trait social anxiety, moderating the effects of HC administration on erotic-interference under acute stress; participants in the HC group, with high trait cognitive control and low trait social anxiety, are the participants who showed lower erotic-interference under acute stress. Similarly, Putman and Berling (2011) found that HC-administration reduced interference from erotic words in males. The comparable present findings for threat- and erotic-

interference indicate that the participants, who were brought into a state of performance anxiety, adaptively inhibited distraction from their performance from these highly arousing irrelevant threat and erotic cues which they would otherwise attend, as observed in studies without stress induction. In line with the present evidence, the attentional control theory (Derakshan et al., 2009) suggests the need to inhibit salient information in order to pursue goal-directed behaviour under acute stress. Importantly, the effects of HC on both threat- and erotic-interference were present for individuals with high trait cognitive control. This is also in line with the present evidence that HC was related to increased state attentional control in individuals with higher trait cognitive control, suggesting that any effects of HC are due to enhanced cognitive control (as previously suggested; for a review see, Hermans et al., 2014). All our effects of HC on cognitive control over emotional interference are observed for individuals with higher trait cognitive control. This might be due to the vulnerability of the sample, as only highly anxious females were included. High anxiety is typically related to lower trait cognitive control (e.g., Angelidis et al., 2016, 2018; Bishop et al. 2007; Putman et al., 2014). Moreover, participants were under acute stress which compromises executive resources (e.g., Hermans et al., 2014; Putman et al., 2014). Thus, it may be that the executive resources of participants with lower trait cognitive control were so depleted by acute stress that they did not benefit from the HC-administration. Future research should further investigate these effects by comparing pre-selected groups with high and low trait cognitive control. It is also noteworthy that these effects are not specific to threatening information but occurred for non-threatening arousing (erotic) stimuli, as it has been previously suggested for men under a non-stress condition (Putman & Berling, 2011). However, it still remains unclear whether the inhibitory effects of glucocorticoids are specific to emotional information or also non-emotional task-irrelevant stimuli. Previous studies showed that glucocorticoids did not enhance non-affective cognitive inhibition or attention (e.g., Wolf et al., 2001), while recent evidence (Weckesser, 2016) suggests that single HC-administration prevents the negative effects of stress on non-affective dual-task performance by enhancing the maintenance of task-relevant information. The absence of main effects of the HC manipulation might be due to several reasons. This is the first study investigating the effects of HC on emotional interference under acute stress, also in a highly anxious sample. It may be that the slow effects of cortisol do not restore top-down control when catecholamine levels are high for all the participants, especially when they are highly anxious as our sample (not further taking into account individual differences in trait anxiety and attentional control within in the sample).

It was also found that subjective trait cognitive control (ACS) interacted with general trait anxiety (STAI-t) moderating the effect of HC on threat-level dependent interference. However, this finding is different than the moderation of TBR and LSAS, as avoidance was observed in females with higher trait cognitive

control but lower general trait anxiety. The same effect was present for females with high trait social anxiety. A possible explanation is that the participants were preselected for high scores for trait cognitive test anxiety. LSAS assesses social anxiety, also in the context of performance that is closely related to trait cognitive test anxiety, while STAI-t measures general trait anxiety. Thus, the difference in the two relevant findings for STAI-t and LSAS may be due to the fact that the sample was preselected for high CTAS scores and, as a result, represent a highly performance anxious/socially anxious population, but not a highly generally anxious population, rendering the scale of individual differences in the sample incomparable for these different constructs. Moreover, we used a psychosocial stress-procedure to induce performance-related stress, as previous evidence (in an unselected sample, see, Angelidis et al., 2019) showed that the effects of this stress procedure were related to CTAS but not STAI-t. Thus, results in relation to STAI-t should be interpreted with caution. Finally, contrary to expectations, there were no cortisol-effects in relation to CTAS even though this was expected. A possible explanation may be the limited variance in CTAS scores in our pre-selected, high-CTAS sample.

We also observed that the HC-manipulation did not affect self-report stress-reactivity, consistent with previous studies reporting that single HC-administrations have no effects on non-challenged affect (Abercrombie et al., 2003; Putman et al., 2007a; for a review see, Putman & Roelofs, 2011) or under induced stress (e.g., Weckesser et al., 2016; but see e.g., Het & Wolf, 2007). Besides the lack of cortisol-effects on stress, a positive effect was found on state attentional control for females with higher attentional control. Thus, the present findings are in line with previous evidence (for a review see, Putman & Roelofs, 2011) suggesting that HC-administration acutely affects cognitive control over processing of emotional information without effects on mood.

There are several limitations to the present study. Firstly, the sample consisted of only healthy young highly anxious females in order to control for variations in cortisol levels (e.g., Kirschbaum et al., 1999). Specifically, the naturally cycling females were tested in the follicular phase of their menstrual cycle in order to control for confounding influence of menstrual endocrine fluctuations. The present findings may not generalize to females during other menstrual phases or to males. Secondly, testing occurred only in the afternoon to control for diurnal effects of cortisol. The present results may not apply for a different time of the day since there is evidence (e.g., Het et al., 2005) that effects of cortisol may differ across the diurnal cycle. Finally, only a dose of 40 mg was investigated in this study. As it is previously suggested that effects of cortisol are dose-dependent for inhibition of negative information (Taylor et al., 2011) but also working memory (Lupien et al., 1999), future studies should also investigate dose-response effects on emotional information under acute stress.

To conclude, the present results show that a single administration of 40 mg HC reduces cognitive interference from highly arousing emotional stimuli under

acute stress, an effect that is dependent on individual differences in trait cognitive control and trait anxiety. Specifically, the effects are present for individuals with higher trait cognitive control, also depending on trait anxiety. These effects possibly reflect enhanced inhibition of emotional information that is not valence-specific. The present study further supports the notion that cortisol affects cognitive processing of emotional information, and for the first time this is shown under acute stress. Future research should investigate these effects of cortisol under acute stress in clinical populations with disturbed processing of emotional information.

SUPPLEMENTAL MATERIALS

Detailed description of the stress manipulation.

First, participants were instructed to immerse their dominant hand, including their wrist, in cold water (0-2˚C) for as long as possible, with a maximum of three minutes. On average, participants kept their hand in the water for 2 min and 47 sec. Participants were told that the whole procedure would be video-recorded and the footage would be used by specialized psychologists and students for further evaluation of their performance and facial expressions. They were also asked to sign an additional informed consent specifically for the use of the video-recording, in order to make the procedure more convincing. This entire procedure was in the presence of two committee members; a male who was introduced as a specialized psychologist and a female who was introduced as a trained psychology student. Participants were told that the committee would evaluate their performance as well as other aspects of their behavior.

Then, subjects received stressful instructions, as in Angelidis et al. (2019) and similar to Coy et al. (2011). They were specifically told that they would be evaluated in a series of cognitive test which are found to be related to academic performance and future career. First, participants were asked to introduce themselves in front of the camera (e.g. name, age, studies, average grade etc.). Then, they went through a mental arithmetic task, verbally administered by the stern male committee member, with bogus negative feedback, making them believe that they could not reach an average level of performance and finally telling them that because of their suboptimal performance, they would get a second chance after the computerized task to try again to do better. Committee members were trained to act coldly aloof and stern, to not engage in any informal social interaction, and to not reciprocate any informal social interaction initiated by the participants. Both committee members pretended to make notes of the participants' behavior on a clipboard. In short: the committee members created a

tense and judgmental atmosphere (for detailed description of the L-PAST see, Angelidis et al., 2019). Before the third computerized cognitive task, participants went again through a short version of the arithmetic test, the so-called stress booster, in order keep the stress levels high. Finally, the committee remained in the room during the computerized tasks, supposedly to evaluate their performance and behavior, in order to keep the element of social evaluation present. The complete stress procedure lasted 20 min.