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Stress and Stress-induced Glucocorticoids Facilitate Empathic Accuracy in Men, with no Effects for Women

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Abstract:

Empathy, the ability to understand others' feelings, is critical for navigating our social world and maintaining social connections. Given that acute stress, and resulting increased glucocorticoids, triggers a shift in two large-scale brain networks, prioritizing salience over executive control, we predicted that acute psychosocial-stress would facilitate empathic accuracy (EA). We also investigated the moderating role of gender/sex, given that men typically show a more robust glucocorticoid response to acute stress than woman. As predicted, results from two independent studies (N= 267 college-aged participants; 2,256 observations) showed that acute psychosocial-stress facilitated EA for men, an effect related to their glucocorticoid response in the stress condition. Conversely, psychosocial-stress had no effect on EA for women, who also showed a smaller cortisol response to stress than men. Exploratory analyses further revealed that women taking oral-contraceptives performed worse on the EA task than regularly-cycling women. This research highlights the important, but complex, role of stress in cognitive empathy.

Keywords: Stress; Empathic Accuracy; Trier Social Stress Test; Gender/Sex; Cortisol; Oral Contraceptives

Statement of Relevance:

Research on the effects of acute psychosocial-stress suggests that stress undermines cognitive abilities, especially those involving executive functioning. Given this, one might expect acute psychosocial-stress to similarly impair cognitive empathy. However, research indicates that humans process social information differently from non-social information. Here, we examine the possibility that stress induced levels of glucocorticoids might have beneficial effects on cognitive empathy. Results from two studies showed that acute psychosocial-stress facilitated empathic accuracy for men, an effect that was related to their glucocorticoid response. Conversely, stress had no effects on empathic accuracy for women, who also showed a blunted cortisol response. Exploratory analyses revealed that women taking oral contraceptives, in general, performed more poorly on the empathic accuracy task than did regularly cycling women. This research highlights the important, but complex, role of stress in cognitive empathy and the importance of considering gender/sex specific effects.

1. Introduction

Cognitive empathy—the ability to understand the emotions of others—is critical to navigating daily life and plays an important role in the development and maintenance of social bonds (de Waal & Preston, 2017). To date, a great deal of research has been devoted to understanding the factors that can influence cognitive empathy. One factor that has received relatively little attention is acute stress, notwithstanding its ubiquity to the human experience.

Acute stress is a momentary response to an aversive or challenging situation that results in the activation of several biological and psychological processes, aimed at restoring homeostatic balance. While the human stress response is complex and multifaceted, involving the interplay between numerous biological and psychological processes, the two biological systems that are frequently investigated are: 1) the fast-acting autonomic nervous system (ANS), specifically its sympathetic branch, indicated by increased heart rate and release of catecholamines, and 2) the slower acting hypothalamic-pituitary-adrenal (HPA) axis, which results in an increase of its downstream marker cortisol. While an adaptive response, arguably, necessitates the co-activation of these systems (Ali, Nitschke, et al., 2020; Andrews et al., 2013); of particular relevance to the present investigation, is the stress-induced activation of the HPA axis, thought to have important consequences for cognition and information processing. Through a negative feedback loop, cortisol reaches the central nervous system and is thought to induce a shift in neural activation to deal with the stressor. As Hermans and colleagues (2014) argue, immediately following the stressor, resources are reallocated from the executive control network to the salience network; this reallocation of resources facilitates vigilance to contextual cues, especially cues to salient contextual information, presumably, to facilitate dealing with the challenge at hand. Once the immediate stressor has passed, resources are shifted back to the executive control network.

Meta-analytic data support the idea that these two neural systems are modulated in a reciprocal manner following stress: performance on attentional vigilance tasks is generally better when such tasks are administered immediately following a stressor (within ~1 hour) and decline afterwards, whereas performance on executive control tasks is typically poorer when such tasks are administered immediately following a stressor but improve as the time relative to stressor onset increases (Hermans et al., 2014). To the extent that cognitive empathy relies on the salience network, we might expect acute stress to have beneficial effects on this kind of information processing.

In the present research, we investigated the effects of acute psychosocial stress on cognitive empathy, specifically “empathic accuracy”—i.e., the ability to dynamically track the emotional state of another individual over time. Furthermore, in line with prior theory and empirical work (Hermans et al., 2014; Putman & Roelofs, 2011), we investigated the role of stress-induced glucocorticoids. To this end, we conducted two studies in which we induced acute psychosocial stress with the Trier Social Stress Test (TSST; Kirschbaum et al., 1993), and then had participants watch videos of targets discussing negative autobiographical events and rate how they thought the targets were feeling. Critically, targets themselves also rated how they were feeling, which allowed us to calculate an index of empathic accuracy (cf. Zaki et al., 2008). Because empathic accuracy relies on the ability to update one’s representations based on (often) subtle changes in the target’s affect, it should be particularly sensitive to glucocorticoid-induced changes in attentional vigilance for social-emotional information (Hermans et al., 2014; Putman & Roelofs, 2011).

We also aimed to investigate whether the effects of acute stress on empathic accuracy depend on gender/sex. To date, women are under-represented in stress research, largely because of the (perceived) complexity in females’ biology, which makes them

methodologically difficult to study (Bale, 2019; Shansky, 2019). Importantly, as Kirschbaum et al. (1999) and Kudielka et al. (2004) report, compared to men, women typically show an attenuated salivary glucocorticoid response to the TSST (an effect that seems to be linked to ovarian hormones and, in particular, elevated levels of the corticosteroid-binding globulin, which reduces the availability of free unbound cortisol)(for a recent meta-analysis on the differences in cortisol secretion for men and women see: Liu et al., 2017). Evidence indicates that this attenuated cortisol response is not because women find the TSST less stressful than do men; indeed, they typically show as high, or higher, levels of psychological distress (Ali, Nitschke, et al., 2020; Childs et al., 2010). This difference in physiological stress reactivity could have important implications for the present study: If the aforementioned stress-induced shift in cognition is, at least partly, related to unbound cortisol, and women show a more blunted cortisol response to the TSST, women may be less likely than men to show facilitatory effects of stress on empathic accuracy. Indeed, preliminary evidence supports gender/sex moderated effects: Smeets and colleagues (2009) found that men who showed a high (vs. low; median split) glucocorticoid response to the TSST performed better on the Movie for the Assessment of Social Cognition (MASC), whereas women showed the opposite pattern. The MASC, however, assesses mentalizing more broadly, and does not target the kinds of negative social-emotional information that is typically conveyed in empathy-inducing situations (e.g., sadness, anger, etc.), leaving this an open question.

Finally, we also took this opportunity to explore the role of women's oral contraceptive use. Women taking oral contraceptives can show an even more blunted stress-induced cortisol response than regularly cycling women, due to the higher availability of corticosteroid-binding globulin caused by exogenous oestrogen administration (Kirschbaum et al., 1995). Very little is known about whether women taking oral

contraceptives show different effects of stress on empathic accuracy. This is an important knowledge gap given the number of women taking oral hormonal contraceptives (i.e., approximately 14% of women aged 15-49 in the US and 28% in Canada; United Nations, 2019).

2. Experiment-1 (between-subjects)

2.1 Overview

In Experiment-1 we randomly assigned participants to the TSST or control condition; participants then completed the empathic accuracy task and tasks assessing other research questions (Nitschke & Bartz, 2020). To account for diurnal cortisol fluctuations (Goodman et al., 2017), testing sessions took place between 9:00am and 2:00pm. See Figure-1 for timeline. Cortisol (and other stress markers, i.e., salivary alpha amylase and subjective distress) was assessed throughout the testing session (see below).

2.2 Sample

To determine sample size, we referred to Smeets et al. (2009); based on that study, we estimated that we would need a minimum of 26 participants per cell to detect a comparable effect ($f=0.25$; $1-\beta=80\%$)(see Supplementary Online Material, SOM, for detailed information). Thus, we recruited 158 participants from classifieds-ads and online advertisements; specifically, we recruited men, regularly cycling (“RC”) women, and women taking oral contraceptives (“OC”); to reduce variance associated with cyclical changes in oestrogen, RC women came during the luteal phase of their menstrual cycle (see SOM for details). Due to computer malfunction, there was no empathic accuracy data for two female participants (one TSST, one control), and a third (female) participant opted out of the study

following the TSST. Thus, the final sample consisted of 61 men (mean age= 22.4; SD = 3.43), and 97 women (mean age= 22.1; SD= 3.42; 48 RC and 49 OC). There were 78 participants in the TSST condition (30 men, 23 RC and 25 OC women) and 80 participants in the control condition (31 men, 25 RC and 24 OC women; see SOM for participant demographics). Each session lasted 2-hrs. Participants were instructed to refrain from consuming food, and sugared or caffeinated beverages for 2hours prior to their visit. The research was approved by the McGill University Research Ethics Board and conducted in accordance with the Declaration of Helsinki, as was Experiment-2. Participants were compensated for their time and effort.

2.3 Measures

Empathic Accuracy Task (EA) (Zaki et al., 2008). In this task, participants watch short (~2-mins) videos of individuals (“targets”) discussing autobiographical events. For the present study, we used videos in which targets expressed negative emotions such as grief, sadness, apathy, and helplessness (topics included, e.g., losing one’s job, death of parents, rejection). Each participant watched six videos (to ensure that any effects we observed were not due to the idiosyncratic nature of particular videos, we randomly assigned participants to watch one of two video sets, with an equal number of male and female targets). Participants are asked to rate, throughout the video, how they think the target is feeling using a 9-point Likert-scale, ranging from ‘very negative’ to ‘very positive’. Following Zaki et al. (2008), ratings were unprompted, meaning that we left it up to participants to change their ratings when they perceived changes in the target’s affect (note: to ensure enough responses for data analyses, we asked participants to update their ratings every few seconds, even if they did not want to change their actual rating). Importantly, the targets also provided similar ratings of

how they felt while discussing the events, on the same 9-point Likert scale. Empathic accuracy is operationalized as the correlation between the ratings made by perceivers and targets; specifically, following Zaki et al., we z-scaled ratings within participants (to account for individual differences). Ratings were binned for every two seconds, and subsequently correlated with the target's ratings to index empathic accuracy (r-scores).

Trier Social Stress Test (TSST) (Kirschbaum et al., 1993). In the TSST, participants deliver a mock-job interview in which they present their qualifications to two “behavioural experts” (research confederates who, critically, are instructed to give no verbal or non-verbal feedback) and then perform an oral arithmetic task in front of the judges. The TSST has been shown to reliably induce a stress response as indicated by cortisol (Goodman et al., 2017), sympathetic nervous system activation (Rohleder et al., 2004), and subjective stress measures (Ali et al., 2017). For participants in the control condition we used the “placebo TSST” (Het et al., 2009; from here on, “control condition”), in which participants talk about a recent life event for 5-minutes and then count upwards in 15-step increments in an empty room.

Stress-markers. Throughout the testing session (see Figure 1), we took saliva samples (i.e., “Salivette”; Sarstedt AG & Co, Nümbrecht, Germany) in 10-minute intervals (-prior to stress (-10 minutes), 0, +10, +20, +30, +40, and +50) to assess cortisol; at these time-points we also measured salivary alpha amylase (sAA; a marker of sympathetic activation) (Ali & Nater, 2020), and subjective-stress using a visual analogue scale (i.e., “how stressed do you feel?”). Cortisol levels (nmol/l) were assessed using a time-resolved fluorescence immunoassay (Dressendörfer et al., 1992) and sAA (U/ml) levels were determined using the enzyme kinetic method (Engert et al., 2011) in this Experiment and Experiment-2. As noted, our primary

analyses concerned the main effect of our stress manipulation and cortisol given the aforementioned theoretical and empirical work highlighting the role of stress-induced cortisol in cognition; however, we also conducted parallel exploratory analyses with sAA and subjective distress. We summarize any findings from these exploratory analyses in the main text, and provide a complete description in the SOM for interested readers.

Analytic Approach. We first sought to confirm successful stress manipulation. We conducted a repeated measures mixed-effects model (rMEM) (Gueorguieva & Krystal, 2004) to test for differences in stress responsivity (cortisol levels at each measurement time-point) between the stress and control condition. Condition (0= control, 1= stress), Gender/Sex (men, RC women, and OC women; see below), and sampling-time were included as predictors, as well as all 2-way interactions, and the 3-way Condition $\times$ Gender/Sex $\times$ sampling-time point interaction. Time was nested within Participant-ID as a random-factor (see SOM, Note 1).

To test our main hypothesis—the effect of acute psychosocial stress on empathic accuracy—we ran a mixed-effects model (MEM) (Holmes Finch et al., 2014) with empathic accuracy scores as the dependent variable, and the fixed-factors Condition (0= control, 1= stress) and Gender/Sex (men, RC, and OC women; see below); we also included the Condition $\times$ Gender/Sex interaction term to test for differential effects of stress on empathic accuracy for men, RC and OC women. AICs were used to test whether the inclusion of the interaction term resulted in a more parsimonious model fit (i.e., variance explained versus model complexity; see SOM) (Cohen et al., 2003). Finally, we included two random factors, Participant-ID and Video-ID, in our model. For this and all subsequent analyses, the planned contrasts (Helmert-coding) for the Gender/Sex variable were defined as follows: contrast-1, testing men vs. all women (men= 1, RC= -0.5, OC= -0.5), and contrast-2, testing RC vs. OC

women (Men= 0 (excluded), RC= 1, OC= -1). Finally, we included a covariate to account for video sets in this and subsequent models.

As noted, in addition to the overall effect of our stress manipulation, we theorize that the effect of stress on empathic accuracy is, at least partly, related to stress-induced glucocorticoids. To test this, we first calculated Areas Under the Curves for cortisol (AUCs; i.e., changes from pre-stress levels until immediately after the empathic accuracy task) using the formula described by Pruessner et al. (2003). We then conducted MEMs, as described above, but in addition included cortisol AUC (z-transformed) as a fixed-effect, as well as the Condition $\times$ cortisol interaction (i.e., to test the combined effect of acute stress and cortisol reactivity). [footnote 1] Of note, it has previously been reported (Nitschke et al., 2019; Smeets et al., 2009) that cortisol may have a nonlinear association with (social) cognitive abilities; thus, in an exploratory step, we included a second-degree polynomial effect of cortisol.

All confidence intervals were bootstrapped. All statistical analyses were conducted in R (Version: 3.6.3; R Core Team, 2020), and the lme4 (Bates et al., 2015) and lmerTest (Kuznetsova et al., 2017) packages for mixed-effects models. Significant interaction effects from the MEMs were decomposed using the emmeans package (Lenth et al., 2018). [footnote 2]

3. Results

Manipulation Check for Stress Induction: Cortisol

The rMEM testing the effect of stress on cortisol revealed a significant Condition $\times$ Gender/Sex $\times$ sampling-time interaction, $F(12, 584.6) = 4.499, p < 0.001$. Results showed significantly higher cortisol levels in the stress versus control conditions and, thus, successful

stress induction; moreover, consistent with prior work (Kudielka et al., 2004), results showed that men had a higher cortisol response than women (contrast-1) at time-points, 3, 4, 5, 6, and 7 (all p s < 0.05; see SOM for details and depiction of the cortisol response). Finally, there were no cortisol differences between RC and OC women (contrast-2) at any time-point. Finally, results also showed a significant effect of stress on sAA, but no gender/sex specific effects, further supporting successful stress induction (see SOM). Of note, parallel analyses investigating subjective distress showed significant effects for both men and women, which confirms that women were, indeed, stressed by the TSST even though they showed a more blunted cortisol response; see SOM.

Effect of Stress Induction on Empathic Accuracy

The MEM predicting empathic accuracy with Condition and Gender/Sex and their interaction as fixed-factors, and Participant-ID and Video-ID as random effects, revealed a significant Condition $\times$ Gender/Sex interaction effect for contrast-1 (men versus women), $b = 0.052$, 95%CI[0.003, 0.097], $t(156.12) = 2.184$, $p = 0.030$. Specifically, men in the stress condition had significantly higher empathic accuracy scores than men in the control condition, $b = 0.063$, 95%CI [0.006, 0.119], $z = 2.195$, $p = 0.028$. By contrast, there was no difference in empathic accuracy performance between women in the stress condition and women in the control condition, $b = 0.015$, 95%CI[-0.029, 0.059], $z = -0.661$, $p = 0.51$. Results also showed that, in the stress condition, men had significantly higher empathic accuracy scores than women, $b = -0.073$, 95%CI [-0.023, -0.124], $z = 2.867$, $p = 0.004$. Finally, there was no difference in empathic accuracy performance between women and men in the control condition, $b = 0.004$, 95%CI[-0.046, 0.054], $z = -0.153$, $p = 0.878$; See Figure 2, and Table S1 (SOM) for a summary of the model.

Regarding contrast-2 (comparing RC and OC women), results showed no significant interaction, $b = -0.032$, 95%CI[-0.07, 0.009], $t(156.12) = -1.456$, $p = 0.147$; however, there was a significant conditional effect for contrast-2, $b = 0.033$, 95%CI[0.005, 0.065], $t(156.12) = 2.153$, $p = 0.033$, indicating that women taking oral contraceptives performed worse on the empathic accuracy task than regularly cycling women across the control and stress conditions. See Table 1.

Effect of Cortisol on Empathic Accuracy

We next investigated the effects of cortisol (AUC, z-transformed) on empathic accuracy. As the previous analyses indicated a differential effect of stress on empathic accuracy for men and women, and a significant difference in cortisol response to the TSST for men and women, we ran separate models for men and women (we combined the RC and OC women given that our main analyses showed no differential effects of stress for these two groups). (Note: if we run the model combining men and women, the Condition $\times$ Gender/Sex $\times$ cortisol interaction is also significant, see SOM). The MEM for men showed a significant interaction between Condition and cortisol on empathic accuracy, $b = 0.068$, 95%CI[0.012, 0.126], $t(56.00) = 2.270$, $p = 0.027$; as predicted, for men in the stress condition, cortisol was positively associated with empathic accuracy, $b = 0.034$, 95%CI[0.004, 0.065], $z = 2.267$, $p = 0.023$, whereas for men in the control condition, there was no association between cortisol and empathic accuracy, $b = -0.033$, 95%CI[-0.085, 0.018], $z = -1.298$, $p = 0.194$. The MEM for women did not result in a significant slope, $b = -0.015$, 95%CI[-0.061, 0.033], $t(92.99) = -0.647$, $p = 0.519$, indicating no association between cortisol and empathic accuracy. Finally, the inclusion of a polynomial cortisol effect did not show any significant result, suggesting that the association between cortisol and empathic accuracy is linear. Regarding our

exploratory analyses, there was no significant interaction or conditional marginal effect of sAA on empathic accuracy for either men or women, nor was there a significant interaction or conditional marginal effect of subjective distress on empathic accuracy for men or women (see SOM).

In sum, we show that acute psychosocial stress improves empathic accuracy performance for men, but has no effect on empathic accuracy for women. This finding does not appear to be due to ceiling effects on the empathic accuracy task for women—our results show no gender/sex difference in the control condition; rather, men’s performance improves in the stress condition. Additional analyses reveal that the effects of stress on empathic accuracy for men is, at least partly, dependent on their enhanced cortisol response. That is, men who showed a more robust cortisol response to the TSST also showed greater improvements on the empathic accuracy task. These findings are consistent with the notion that acute stress-induced glucocorticoids facilitate attentional vigilance (Hermans et al., 2014; Putman & Roelofs, 2011). Finally, intriguingly, we found that women taking oral contraceptives performed significantly worse than regularly cycling women on the empathic accuracy task, regardless of stress condition, suggesting a potential link between exogenous oestrogen administration and cognitive empathy.

4. Experiment-2 (within-subject)

4.1 Overview

In Experiment-2, we aimed to replicate the findings from Experiment-1. Although some prior work led us to expect that gender/sex might moderate the effect of stress on empathic accuracy, these findings warrant replication. Moreover, in Experiment-1, we used a between-subjects design; however, this design is vulnerable to the influence of individual

differences (e.g., in stress reactivity, endogenous hormones, and/or empathic accuracy performance). Thus, in Experiment-2, we used a within-subjects design to control for these sources of influence. During the first visit ('Visit-1'), participants completed the empathic accuracy task in the absence of stress as well as other tasks and questionnaires reported elsewhere (Nitschke et al., 2020; Nitschke & Bartz, 2020). Participants returned to the lab approximately 3-4 weeks later (or according to the menstrual cycle; see Supplemental Materials) for 'Visit-2'; they first underwent the TSST and, immediately after (same duration as in Experiment-1), completed the empathic accuracy task. See Figure-1 for timeline. Again, cortisol, sAA and subjective distress were assessed throughout the testing session (see below). As in Experiment-1, all sessions were conducted between 9:00am and 2:00pm.

4.2 Sample

We recruited men, RC women and OC women (see SOM), and applied the same inclusion and exclusion criteria as for Experiment-1. Sample size determinations were based on those used for Experiment-1 (~26 participants per cell). We recruited 119 participants, however, 10 female participants did not return for Visit-2, so the final sample consisted of 109 participants (men= 30; women= 79, 54 RCW, 25 OC). Participants were compensated \$10 an hour for their time (\$10 + \$20).

4.3 Measures

Empathic Accuracy Task. We used the same empathic accuracy task, with the same videos, described in Experiment-1. To avoid practice effects, participants watched, in randomized order, different videos on Visit-1 and Visit-2 (again, we included a variable to account for differences between video sets in our statistical analyses).

Trier Social Stress Test. We again used the TSST to elicit a stress response during Visit-2, and followed the same stress marker protocol; all measures (cortisol, sAA, and subjective stress) were taken at seven time-points throughout Visit-2, starting 20-minutes before the stress induction, prior to stress (-10), and following stress at: 0, +10, +25, +40, and +50. Again, we summarize the main findings from these exploratory analyses in the main text; interested readers are referred to the SOM for a detailed description.

Analytic Approach. We followed the same analytic plan as in Experiment-1, adjusting for the within-subjects design. We first ran a rMEM (Gueorguieva & Krystal, 2004) to test the effects of acute stress induction on cortisol levels for Visit-2 (stress day); we included Gender/Sex (same coding as Experiment-1), sampling-time, and the interaction between Gender/Sex and sampling-time as fixed-effects. Time was nested within Participant-ID as a random-factor.

Next we ran a MEM predicting empathic accuracy. Visit (0=Visit-1; 1=Visit-2) and Gender/Sex (men, RC women, and OC women) were entered as fixed-factors. We included an interaction between Visit and Gender/Sex to test for differential effects for men, RC women and OC women. Participant-ID and Video-ID were entered as random factors. Visit was nested within Participant-ID.

Finally, as in Experiment-1, we followed-up these analyses with MEM analyses that also included cortisol AUC (z-transformed) as an independent variable. Note that these analyses are restricted to Visit-2, as we did not measure cortisol on Visit-1; thus, whereas in Experiment-1, we predicted that condition would moderate the effect of cortisol on empathic accuracy (i.e., the magnitude of the glucocorticoid response, *in the stress condition*, would be

associated with better performance on the empathic accuracy task), in Experiment-2, we predicted a main effect of cortisol on empathic accuracy at Visit-2 (i.e., a stronger cortisol response to the TSST would be associated with better performance on the empathic accuracy task).

5. Results

Manipulation Check for Stress Induction: Cortisol (Visit-2 only)

The rMEM testing the effect of stress induction at Visit-2 on cortisol levels revealed a significant interaction between Gender/Sex and sampling-time, $F(12, 373.09) = 2.474$, $p = 0.004$, indicating that Gender/Sex moderated the effect of the stress induction on cortisol; specifically, consistent with prior work, and as observed in Experiment-1, men had a higher cortisol response compared to women (contrast-1) at time-points, 3, 4, 5, and 6 (all $ps < 0.05$; see SOM). We did not observe cortisol differences between RC and OC women (contrast-2) at any time-point. (For plotted cortisol-curves see SOM). Again, as in Experiment-1, additional analyses on subjective distress indicate that women were, indeed, stressed by the TSST even though they did not show a strong cortisol response (see SOM). Similar to Experiment-1 we found a significant stress-induced increase in sAA (see SOM).

Effect of Stress Induction On Empathic Accuracy

The MEM with empathic accuracy as dependent variable and Visit, Gender/Sex, and the Visit $\times$ Gender/Sex interaction entered as fixed-factors revealed a significant Visit $\times$ Gender/Sex interaction for contrast-1 (men vs. women), $b = 0.047$, 95% CI[0.007, 0.083], $t(108.13) = 2.467$, $p = 0.015$. As in Experiment-1, men showed a significant increase in empathic accuracy performance from Visit-1 to Visit-2 (stress induction visit): $b = 0.060$, 95%CI[0.013,

0.108], $z = 2.516$, $p = 0.012$. By contrast, for women, there was no difference in empathic accuracy performance from Visit-1 to Visit-2, $b = -0.01$, 95%CI[-0.039, 0.020], $z = -0.64$, $p = 0.523$. Results also showed that men had significantly higher empathic accuracy scores than women during Visit-2: $b = 0.064$, 95%CI[0.012, 0.116], $z = 2.418$, $p = 0.016$. Finally, there was no difference in empathic accuracy performance between men and women at Visit-1/baseline: $b = -0.01$, 95%CI[-0.041, 0.054], $z = -0.266$, $p = 0.791$. See Figure 3 and Table S2 (see SOM).

The interaction for contrast-2 (RC versus OC women) was not significant, $b = -0.015$, 95% CI[-0.044, 0.015], $t(108.03) = -0.970$, $p = 0.334$. However, as in Experiment-1, we observed a significant conditional effect for contrast-2, $b = 0.029$, 95%CI[0.004, 0.056], $t(108.34) = 2.252$, $p = 0.026$, indicating that, again, OC women performed worse on the empathic accuracy task than RC women across both visits. See Table 1.

Effect of Cortisol on Empathic Accuracy

We then assessed the impact of stress-induced cortisol (AUCi) on Empathic Accuracy during Visit-2. Again, because the previous analyses indicated a differential effect of Visit (i.e., stress) on empathic accuracy for men and women, and a significant difference in cortisol response for men and women, we ran separate models for male and female participants. As predicted, and replicating the findings from Experiment-1, the MEM for men showed a significant effect of cortisol on empathic accuracy: $b = 0.046$, 95% CI[0.013, 0.083], $t(27.28) = 2.501$, $p = 0.019$, whereas the MEM for women did not show a significant association (although the pattern was in the same direction): $b = 0.024$, 95% CI[-0.003, 0.050], $t(77.24) = 1.758$, $p = 0.083$. The inclusion of this curvilinear effect did not result in a significant predictor for either men or women, indicating a linear relationship between cortisol and empathic accuracy for men. As in Experiment-1, there were no effects of sAA or

subjective distress on empathic accuracy for either men or women (see SOM).

In sum, in Experiment-2 we replicate several key findings from Experiment-1. Specifically, acute stress improved empathic accuracy for men, but had no effect on empathic accuracy for women (either RC or OC). Again, it was not that women performed better overall: there was no difference in empathic accuracy between men and women at Visit-1/the baseline testing day; rather, men showed selective gains in empathic accuracy following the stress induction. We also replicated the finding from Experiment-1 that women showed a more blunted cortisol response to the TSST compared to men, and that the effect of stress on empathic accuracy, for men, was related to the magnitude of the stress-induced cortisol response. Finally, we replicate the intriguing oral contraceptives effect observed in Experiment-1: women taking oral contraceptives performed worse on the empathic accuracy task, in general, than did regular cycling women [footnote 3].

6. Discussion

In two independent experiments we show that, for men, acute psychosocial stress improves empathic accuracy—i.e., the ability to accurately track another's emotional experience overtime. Moreover, results show that men's empathic accuracy performance following stress was related to the magnitude of the stress-induced cortisol response. In contrast to men, stress had no effect on empathic accuracy for women (an observation that underscores the importance of including women in stress research). This was not because women were better at the empathic accuracy task as there was no difference between men's and women's empathic accuracy performance in the control condition (Experiment-1) or at baseline

(Experiment-2)(note: other research using the task described here similarly has not reported gender/sex differences in empathic accuracy; Bartz et al., 2019; Zaki et al., 2008, 2009).

These findings are consistent with recent accounts suggesting that acute stress triggers a phasic shift in two large-scale neural networks, prioritizing salience over the executive control network, at least immediately following the stressor (Hermans et al., 2014). If stress facilitates vigilance to salient contextual cues, then one would expect enhanced attention to, and processing of, the emotional experiences conveyed by our empathic accuracy targets. Importantly, our analyses showed that it was *stress-induced* cortisol, not cortisol in general, that facilitates empathic accuracy (i.e., there was no effect of cortisol in the no-stress condition). This is consistent with the hypothesized role of glucocorticoids in the stress-induced shift in information processing, and with prior empirical work (Smeets et al., 2009). Indeed, the lack of an effect of acute stress on empathic accuracy in women may be, at least partly, due to the fact that women did not mount a strong cortisol response to the TSST (even though they reported high levels of psychological distress). In both Experiment-1 and -2, men showed a stronger cortisol response to the TSST compared to women, and the effect of stress on empathic accuracy, in men, was related to stress-induced cortisol. If the re-balancing of the salience and executive networks following acute stress is driven by stress-induced changes in neurotransmitters and hormones (Hermans et al., 2014), then the absence of a strong cortisol response in women may explain the lack of an effect—indeed, the association between cortisol and empathic accuracy for women was positive and, in fact, fell just below our statistical significance threshold in Experiment-2 (see SOM).

Of note, we did not find an association between TSST-induced changes in *subjective* stress and empathic accuracy (nor did we find an association between sAA and empathic accuracy). As outlined before, the human stress response involves multiple signals (e.g., changes in

cortisol, sAA, and subjective stress, as measured here, as well as changes in heart rate variability and even neural activity), that each interact in complex ways to produce functionally nuanced outputs (Ali, Cooperman, et al., 2020; Hermans et al., 2011; Kukulja et al., 2008). Moreover, these signals are often dissociated (e.g., cortisol and subjective distress are often unrelated and may even function to compensate for one another (Ali et al., 2017; Ali, Nitschke, et al., 2020). While the lack of an effect of subjective stress may have been due to measurement (i.e., use of single item self-report measure), it suggests that the effect of our stress manipulation on empathic accuracy was not due to feelings of increased threat in response to the TSST. Indeed, this is further supported by the fact that women—who reported higher levels of subjective stress—did not show improvements in empathic accuracy.

We believe our findings are consistent with Herman et al.’s theory with respect to stress-induced shifts in information processing (above). An alternative, but not necessarily mutually exclusive, hypothesis is that acute stress increases motivation. Although recent research has linked stress to cognitive effort-avoidance (Bogdanov et al., 2021), it still may augment task engagement more broadly. In this scenario, stress, as indexed by cortisol, may reflect a “challenge” orientation (Dickerson & Kemeny, 2004). Relatedly, it is possible that those highly motivated/challenged participants were trying harder to read the judges faces during the psychosocial stress task, which resulted in a face-reading priming effect that was carried over to the empathic accuracy task. Future research is needed to probe the mechanism by which acute stress and, specifically, cortisol, influences empathic accuracy. For example, using an empathic accuracy task that includes narratives about positive experiences would allow us to address whether the effects observed here are restricted to threat-based processing or social information processing in general (cf. the face reading priming effect alluded to above). Future research could also use other manipulations to induce stress that do not

involve a psychosocial evaluative component to disentangle physiological “stress” from social processes (such as threat perception or social evaluation).

Finally, in addition to providing evidence for our primary aim regarding the effects of stress on empathic accuracy, we also observed, in our exploratory analyses, that women taking oral contraceptives performed worse on the empathic accuracy task than did RC women (regardless of stress), an effect that was replicated in Experiment-2. Evidence regarding oral contraceptive use and social cognition is mixed (Montoya & Bos, 2017), with some studies showing an effect (Hamstra et al., 2014), but not others (Radke & Derntl, 2016; Shirazi et al., 2020). Our findings are consistent with the former. Interestingly, Hamstra and colleagues (2014) found that hormonal contraceptive use impaired emotion recognition abilities particularly for negatively valenced emotions (cf. Pahnke et al., 2018); this is noteworthy given that our task involved negative experiences. Thus, valence may be an important factor to consider in future research. Future research should also include women outside the restricted range of the current sample, and especially women going through naturally occurring hormonal transitions.

In sum, the ability to understand the emotional states of others is a cornerstone of human social-emotional experience. Our findings show that acute psychosocial stress and, specifically, the stress hormone cortisol, facilitates empathic accuracy for men, but has no effect on empathic accuracy for women. This research adds to the growing body of literature showing that cognitive empathy is not only influenced by our psychology but is also tied to our biology.

Footnotes:

[1] We believe that stress-induced glucocorticoids are key, not glucocorticoids in general.

There is little reason to believe that high levels of glucocorticoids, in the absence of stress, should facilitate empathic accuracy: Smeets et al. (2009) found no effect of cortisol on social cognition in the control/no stress condition; moreover, exogenous administration of corticosteroids typically shows no effect of on cognitive empathy (cf. Duesenberg et al., 2016; Nowacki et al., 2020; Schultebrucks et al., 2016). For these reasons, we predicted a moderated effect—i.e., those who show a stronger cortisol response *to the TSST* will be more likely to show improvements in empathic accuracy than those who do not mount a strong cortisol response to the TSST. That said, we also tested for mediation in Experiment-1 but results did not support a mediation model (see SOM).

[2] For an alternative approach to analyze the empathic accuracy data that uses raw scores (perceiver ratings predicting target ratings) rather than aggregated data (correlations) see SOM.

[3] Note: if we only test for the main effect of oral contraception, then the effect only holds for Experiment-2 (see SOM). However, the between-subject design in Experiment-1 may be a culprit as we were unable to control for individual variation in hormones.

Appendix

Figure 1: Study design for both Experiments. Experiment-1, participants were randomly assigned to either an acute stress paradigm or a control condition before doing the EA task. d. In Experiment-2, utilized a within-subject design; participants came to the lab on two separate occasions, separated by a ca. 28 delay (or based on the menstrual cycle), during visit-2 all participants underwent a stress task before doing the same EA task as in Experiment-1.

Figure 2. Experiment-1: Effects of acute psychosocial stress on empathic accuracy in men and women. Group differences between the control and the Stress (TSST) groups. Note, data represents mean participant responses for figure only.

Figure 3: Experiment-2: Effects of acute psychosocial stress on empathic accuracy in men and women. During visit-1 participants did the empathic accuracy task in the absence of stress; during visit-2 all participants did the TSST before re-doing the EA-Task (with different videos, counterbalanced). Note, data represents mean participant responses for figure only.

Tables

Table 1: Mean EA-Scores for each Group

	<i>Experiment 1 (between)</i>			<i>Experiment-2 (within)</i>		
	Control	Stress	d_s	Day-1 (CTL)	Day-2 (TSST)	d_{av}
Men	0.170 (0.31)	0.246 (0.26)	0.27	0.195 (0.28)	0.276 (0.30)	0.26
Women	0.177 (0.30)	0.168 (0.26)	0.03	0.238 (0.31)	0.206 (0.29)	0.11
	RCW	OCW	d_s	RCW	OCW	d_s
	0.190 (0.27)	0.156 (0.29)	0.12	0.235 (0.30)	0.194 (0.30)	0.14

Notes: Mean group-level empathic accuracy scores with standard deviation in parenthesis. Effect size measures were calculated using group-level mean-values and standard deviations: d_s =Cohen's d for two independent samples; d_{av} = Cohen's d for within-subjects designs, averaged standard deviation. RCW= Regular Cycling Women, OCW= Oral Contraceptive Users; both groups' mean values are across groups (Experiment 1) or across days (Experiment-2). Numbers rounded for table only.

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