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## Research article

# Empathy and mentalizing abilities in relation to psychosocial stress in healthy adult men and women

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## ABSTRACT

Stress has many consequences for our wellbeing, both physically and psychologically, underscoring the need to study markers of differential sensitivity to stressful situations. We examined associations between empathy and mentalizing abilities and psycho-physiological responses to a psychosocial stress task. We conducted two highly comparable studies, the first in men ( $N = 52$ ) and the second in women ( $N = 72$ ). Each study started with a self-report empathy measure and a mentalizing test [Reading the Mind in the Eyes Test (RMET)] followed by the Trier Social Stress Test (TSST) or a control task. Stress reactivity was confirmed in both men and women with significantly higher levels of cortisol, blood pressure, and subjective stress levels in response to the TSST compared to the control task. Higher accuracy on the RMET significantly predicted higher cortisol and heart rate reactivity, while self-reported empathic concern significantly predicted higher subjective stress reactivity. These associations were found in men, and when men and women were analyzed together. This indicates that higher levels of mentalizing and empathic abilities may confer sensitivity to socially stressful situations. While a moderation analysis indicated no gender differences in these associations, the findings could not be directly replicated in women. This suggests that gender may impact such associations and that replication of the findings in larger samples is warranted.

## 1. Introduction

Stress is an increasingly common phenomenon in our ever more technology-driven society. While stress helps us to overcome challenges and to achieve our goals, stress can also have many detrimental health consequences if it continues for a long time (Grippe and Johnson, 2009; Kessler et al., 2010; McEwen, 2003, 2017). When people have to deal with acute stress, this can lead to irritability or aggression (Sandi and Haller, 2015), impulsivity, but also to maladaptive choice behavior (Raio et al., 2020). From earlier studies we know that stress and social behavior are highly interrelated. On the one hand, stress is often activated by social demands and expectations, as it stimulates people's urge to meet these social requirements (Beery and Kaufer, 2015). On the other hand, experiencing feelings of stress often has an impact on how people behave towards others (Raio et al., 2020; Sandi and Haller, 2015). Although several studies looked into the causes and consequences of stress [see e.g. (Gelkopf et al., 2012; Greenberg et al., 2002; Sapolsky, 1994; Schneider et al., 2013)], more knowledge is warranted about differential sensitivity to stressful situations to predict how people will respond to (socially) demanding contexts. The current study will therefore address the

question how individual differences in empathy and mentalizing abilities may lead to differential responses in psychological and physiological stress reactivity to acute psychosocial stress.

When a situation is perceived as threatening – e.g. when having to speak in front of an audience without preparation – multiple hormonal systems come into play. Firstly, (nor)adrenalin is released by the autonomic nervous system, leading to increases in heart rate and blood pressure, to enhance energy and focus to deal with the stressor at hand (Gordan et al., 2015). Secondly, with a slight delay, cortisol is released by the hypothalamic-pituitary-adrenal-axis (HPA-axis) to mobilize energy so that homeostasis can be restored (Russell and Lightman, 2019). In the brain, the amygdala is involved in threat detection leading to the physiological stress responses, but also to subjective stress responses, including feelings of tenseness, anxiety and arousal (Joëls et al., 2018; Rodrigues et al., 2009). Chronic activation of these stress systems can ultimately lead to somatic diseases, such as cardiovascular disease, immune-system dysfunction and metabolic disorders (Grippe and Johnson, 2009; McEwen, 2017). In addition, chronic stress can also enhance the development of anxiety disorders and depression (Kessler et al., 2010; McEwen, 2003). Considering the detrimental effects of chronic

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stress, it is important to elucidate vulnerability and resilience factors to stress, so that interventions can be developed or improved to prevent negative outcomes of prolonged stress exposures.

Empathy and mentalizing abilities are two concepts that play a unique role in enabling successful social interaction. Specifically, the abilities to empathize and mentalize allow us to assess the affective state of another person and help us to understand and adjust to social situations, as well as predict behavior by assessing other people's mental representations (Hooker et al., 2008). Although empathy and mentalizing are beneficial to the development of healthy relationships with the people around us, these abilities may also make us more sensitive to social judgments or critical evaluations by others. That is, high levels of empathy and mentalizing can help us to adjust our behavior in order to, for example, comply with group norms and/or to prevent social rejection (Cialdini and Goldstein, 2004). For these reasons it may be expected that people with high levels of empathy and mentalizing abilities are more sensitive to potentially threatening social situations. For example, in situations where people are being evaluated, a higher stress response may be predicted for individuals who are more aware of, and sensitive to, others' intentions and emotions. However, there is relatively little known about associations between empathy, mentalizing and stress reactivity.

Several studies indicate a possible link between empathy and stress responses (Fairchild et al., 2019, 2008; von Polier et al., 2013). For example, Fairchild and colleagues found that individuals with callous unemotional traits or conduct problems (characterized by antisocial and aggressive behavior) showed low levels of affective empathy and reduced stress responses (Fairchild et al., 2019, 2008; von Polier et al., 2013). A recent study in mice also showed that low empathy-like behavior in male mice was associated with impaired physiological stress reactivity (Laviole et al., 2017). This indicates that reduced sensitivity to others' emotions may be associated with a lower sensitivity to stress. However, it remains unclear whether people with high sensitivity to others' emotions (i.e., high empathic abilities) are inherently more reactive to psychosocial stress. Furthermore, to our knowledge no previous studies have examined whether individual differences in mentalizing abilities can impact stress reactivity. Several studies did examine how acute stress (elicited in a laboratory setting) can influence subsequent social behavior (Buchanan and Preston, 2014; Margittai et al., 2015) and mentalizing (Smeets et al., 2009). However, these studies did not consider potential baseline individual differences in empathy and mentalizing abilities, and how these individual differences may have influenced reactivity to the stressor at hand and possibly post-stressor social behaviors as well.

Hence, in this study we investigate whether individual differences in empathy and mentalizing abilities influence stress reactivity to negative evaluative signals elicited with an often-used psychosocial stress paradigm, the Trier Social Stress Test [TSST (Kirschbaum et al., 1993)]. In the TSST participants are required to perform an unexpected mock job interview and arithmetic task in front of a selection committee giving negative evaluative signals. The TSST allows for assessment of individual differences in both physiological as well as psychological stress reactivity (Frisch et al., 2015). We expect that a better understanding and recognition of social signals from the committee – as measured by self-reported levels of affective and cognitive empathy, and by accuracy on a mentalizing task – are related to increased levels of psychological stress reactivity (measured by changes in anxiety or mood) and physiological stress reactivity (measured by salivary cortisol levels, heart rate, and blood pressure). In sum, we will examine whether the following individual differences are related to psychosocial stress reactivity: 1) the ability to take the perspective of another person (i.e. cognitive empathy; Davis, 1983; Frith and Frith, 2007), 2) one's own feelings in response to others' emotions (i.e. affective empathy; Davis, 1983; Frith and Frith, 2007), and 3) the ability to reason about other peoples' mental state (i.e. mentalizing; Baron-Cohen et al., 2001).

A key factor to be considered in this context is the impact of gender. Gender may impact both the stress response (Kajantie and Phillips, 2006) as well as empathy and mentalizing abilities (Christov-Moore et al., 2014; Overgaauw et al., 2017; Van der Graaff et al., 2014). Several studies using the TSST have shown higher cortisol responses in men compared to women (Liu et al., 2017; Reschke-Hernández et al., 2017; Stephens et al., 2016; Zänkert et al., 2018). These differences may be due to hormonal influences of the menstrual cycle and hormonal contraceptive use (Childs et al., 2010; Kajantie and Phillips, 2006; Kirschbaum et al., 1999). However, other studies (Uhart et al., 2006) indicate these gender differences may also be partly explained by differential HPA-axis stimulation processes, that is, hormonal response patterns may depend on the nature of a stressor. In this regard, Stroud et al. (2002) found that men are more stress sensitive to high-achievement tasks (e.g. cognitive performance), while women are more stress sensitive to social rejection. The TSST includes both cognitive challenge and negative social evaluation (Dickerson and Kemeny, 2004), making it a suitable experimental tool for inducing stress in both men and women. Studies that have investigated gender differences in mentalizing abilities found that women perform slightly better than men (Baron-Cohen et al., 2001; Schiffer et al., 2013). Similarly, men showed lower levels of self-reported empathic abilities than women (Toussaint and Webb, 2005; Van der Graaff et al., 2014). Considering possible gender differences in empathy, mentalizing abilities, and stress reactivity, it is also important to examine associations between these characteristics in both men and women. In this regards, we set out to study whether higher levels of 1) cognitive empathy 2) affective empathy, and 3) mentalizing abilities, are associated with increased psychological and physiological stress reactivity to negative social evaluation as elicited by the TSST in two highly comparable studies in men (study 1) and women (study 2). To our knowledge this is the first study gaining knowledge on whether males and/or females who are being more susceptible to social cues, have a potential higher stress response following acute psychosocial stress.

## 2. Materials and methods

### 2.1. Participants

We conducted two studies, the first in men and the second in women. For both studies, Dutch participants between the ages of 17 and 35 were recruited within and around the Faculty of Social Sciences at Leiden University by means of flyers and active approaching. Inclusion criteria were: at least undergraduate level of study, no recent (<1 year) self-reported major physical or psychological problems, and no medication use that might interfere with cortisol measurements (e.g. corticosteroids, benzodiazepines). Men were actively screened during a telephone call before participation, while women filled in a questionnaire on the inclusion criteria during the lab visit. In both studies a stress and control group were included. Our focus was to examine inter-individual differences in stress reactivity and the stress groups were therefore larger than the control groups, as the latter were only included to confirm the stress reactions. To this end, we included 52 men in the first study (stress group:  $N = 40$ , control group:  $N = 12$ ,  $Mage = 20.7$  yrs,  $SD = 2.8$ ), and 72 women in the second study (stress group:  $N = 45$ , control group:  $N = 27$ ,  $Mage = 20.3$  yrs,  $SD = 2.9$ ). Heart rate and blood pressure data were missing for one male and cortisol data for one female, both in the TSST condition. In the screening questionnaire five women (3 in the stress and 2 in the control group) reported use of corticosteroid or anti-depressant medication, and were therefore excluded from the analyses (final  $n = 67$ ). Forty-three (64%) of these women reported use of hormonal contraceptives (30 in the stress and 13 in the control group), which was included as a possible covariate in the stress reactivity analyses as it may affect cortisol reactivity (Liu et al., 2017). Participants were randomly

assigned to either the TSST or control condition and were not aware of a possible stress test beforehand and during assessment of the empathy questionnaire and mentalizing task.

## 2.2. The psychosocial stress test

The Trier Social Stress Test (TSST) was employed, which is designed to induce psychosocial stress in laboratory settings (Kirschbaum et al., 1993). In both studies the TSST consisted of a 5-minute explanation and anticipation period followed by a 5-minute oral presentation. During the oral presentation participants had to convince a committee composed of two or three psychologists of mixed gender of their suitability for a chosen job while being videotaped and voice-recorded. Next, a 5-minute arithmetic task was performed during which the committee gave negative feedback on performance. The TSST has been shown to reliably induce both physiological and psychological stress responses (Frisch et al., 2015). The control groups were instructed to write a job application letter for 10 min after which the same arithmetic task was performed on paper for 5 min, all without social evaluation. Throughout the rest of the test session they followed the same procedure as the TSST groups.

## 2.3. Measures and materials

### 2.3.1. Mentalizing

The Reading the Mind in the Eyes Test (RMET) was originally developed as a measure of adults' understanding of higher order Theory of Mind or mentalizing (Baron-Cohen et al., 2001), assessing the ability to accurately recognize others' intentions and emotions. We used a Dutch computerized version of the RMET (van Honk et al., 2011), administered via E-Prime. Participants had to infer mental states from 36 randomly presented photographs of people's eyes. A choice had to be made between four descriptive words to match the eyes. All correct responses were summed to calculate the accuracy score.

### 2.3.2. Empathy

The Interpersonal Reactivity Index [IRI; (Davis, 1983; De Corte et al., 2007)] is a 28-item self-report measure of empathic abilities. It originally consists of four scales, comprising seven items each. The four scales are: perspective taking (PT; the tendency to adopt another person's perspective), empathic concern (EC; the tendency to experience emotions of warmth, sympathy, and concern), fantasy (FS; the tendency to identify closely with fictitious characters), and personal distress (PD; the tendency to experience discomfort and concern when observing other's negative feelings). Answers are rated on a five point Likert-scale and the maximum sum score per scale is 28, with higher scores reflecting higher empathic abilities. Since we had specific hypotheses on affective and cognitive empathy, we chose to only include the PT and EC scales in this study, as these are most reflective of the affective (EC) and cognitive (PT) aspects of empathy (Davis, 1983). Cronbach's alpha of the EC scale was .77 for men and .68 for women, and of the PT scale .63 for men and .78 for women.

### 2.3.3. Physiological stress measures

Saliva for cortisol analyses was collected with Salivette collection devices (Sarstedt, Germany) and free cortisol levels were determined with a chemiluminescence immuno assay (IBL-Hamburg, Germany) by the Kirschbaum lab (Technical University of Dresden). Heart rate and systolic and diastolic BP were measured from the non-dominant arm with an automatic blood pressure monitor (Omron R5-I).

### 2.3.4. Psychological stress measures

Subjective stress experience was measured by changes in anxiety levels in men with the state version of the State-Trait Anxiety Inventory [STAI; (Spielberger, 1983)], including 20 items indicating either anxiety-related emotions or the opposite that were scored on a scale from 1 (*not at all*) to 4 (*very much*). After recoding, a sum score was calculated

with higher scores reflecting higher anxiety levels. Cronbach's alpha of the STAI before, during, and after the TSST was .78, .95, and .94 respectively. While we intended to replicate the findings on subjective stress reactivity in women, we also wanted to assess a broader spectrum of negative affect than just anxiety. Therefore, in women, the negative affect scale of the Positive and Negative Affect Schedule [PANAS; (Watson et al., 1988)] was used as a subjective stress measure, including 10 items describing negative emotions scored on a scale from 1 (*very slightly or not at all*) to 5 (*extremely*). A sum score was calculated with higher scores reflecting higher levels of negative affect. Cronbach's alpha of the NA scale before, during and after the TSST was .88, .94, and .92 respectively. To compare the subjective stress levels between study 1 and 2, STAI and NA scores were standardized to the group mean within each study.

## 2.4. Procedures

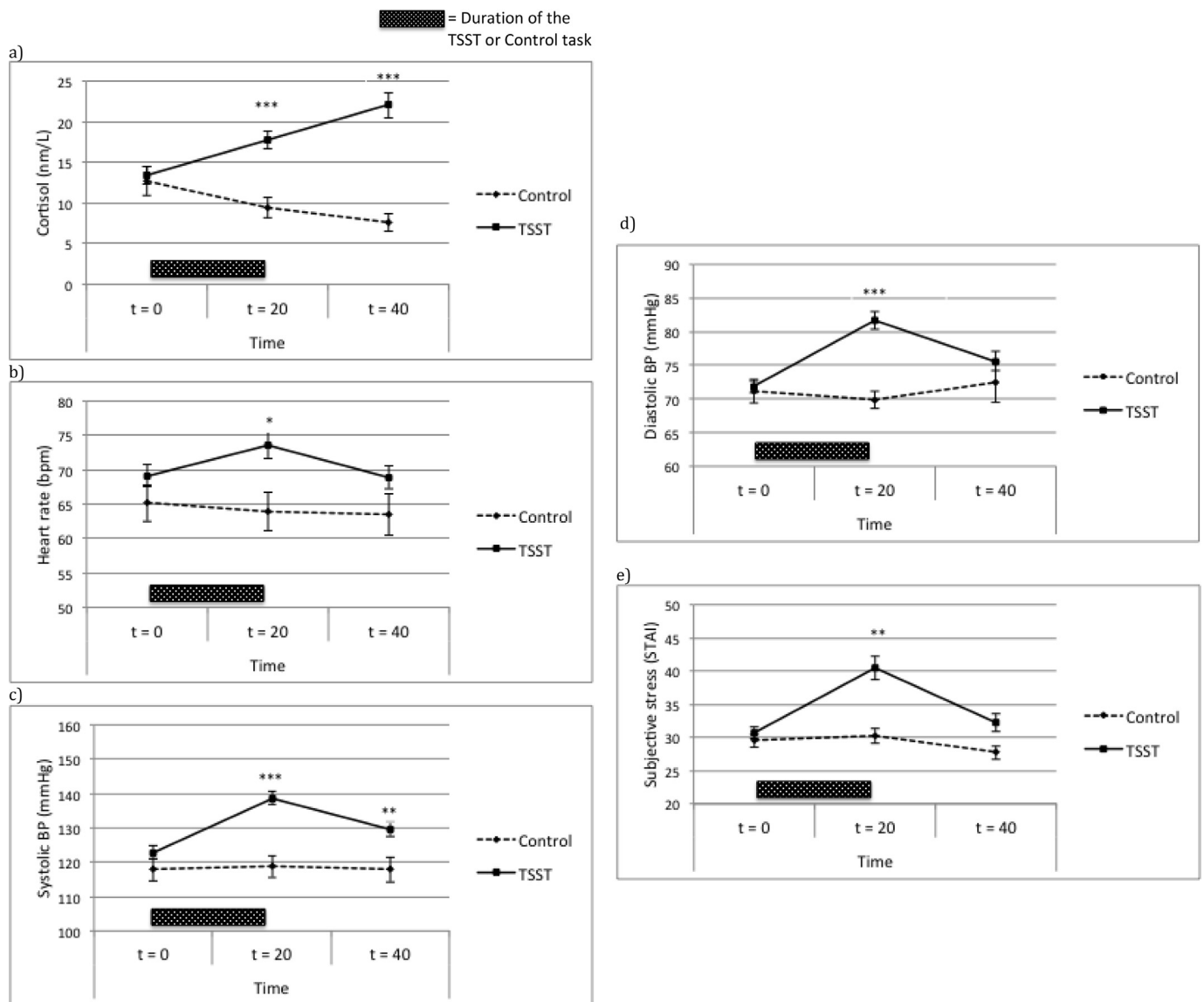
**Study 1.** After a screening by phone, males completed online questionnaires at home (including the IRI) and then visited the lab for a two-hour test session, starting between noon and 4pm to reduce the impact of the circadian cortisol rhythm. At the start of the test session, 40 min before the start of the stress test, the RMET was administered, after which a working memory and a mimicry test were performed. The results of these two additional tests were ultimately not included in the present study, as the working memory test does not address the central concept of empathy and mentalizing, while the mimicry test was not successful due to technical problems. A baseline measurement of the psychophysiological stress measures was taken just before the start of the TSST ( $t = 0$  min, [t is time in minutes]). Directly after the TSST, the psychophysiological stress measures were taken again ( $t = 20$  min), as well as 20 min later ( $t = 40$  min).

**Study 2.** The female participants visited the lab for a two-hour session starting between 9am and 4pm, and completed questionnaires including the IRI and a form regarding inclusion criteria. No women were excluded at that time point, as none reported severe psychological or physical problems that could have interfered with the test procedures. Thirty minutes before the start of the TSST, the RMET was administered, as well as a working memory and attentional bias test. The results of the working memory and attentional bias tests are not included in the present analysis given that neither addresses our core concepts relating to empathy and mentalizing. Again, psychophysiological stress measures were taken at  $t = 0$ ,  $t = 20$  and  $t = 40$  with regards to the TSST. Due to the large range in starting times for women, start time was also included as a possible covariate in the stress reactivity analyses.

All participants gave informed consent before start of the studies, and at the end of their test session participants were debriefed and received a monetary reward (6.50 euros per hour) or study credits for participation. The Psychology Research Ethics Committee of the Faculty of Social and Behavioral Sciences at Leiden University approved the study protocols, which were performed according to the World Medical Association Declaration of Helsinki.

## 2.5. Statistical analyses

We first performed descriptive analyses of the predictors for each study. To examine possible baseline gender differences, datasets of study 1 and 2 were combined and t-tests were performed. To assess whether the TSST was successful in eliciting stress, we first measured stress reactivity in men and women separately by performing Repeated Measures (RM-) MANOVAs with all stress measures (cortisol, heart rate, systolic BP, diastolic BP and subjective stress) as the multivariate outcomes measure, time ( $t = 0$ ,  $t = 20$  and  $t = 40$ ) as within-subjects factor, and group allocation (TSST vs. control) as between-subjects factor in study 1 and 2 (see Figures 1[a-e] and 2[a-e] for the reactivity scores). In case of violations of sphericity, Greenhouse-Geisser corrected values are reported. For women, time of day and oral contraceptive use were examined as



**Figure 1.** Stress measure levels (a–e: Mean  $\pm$  SEM) in the male TSST and control groups over time. Group differences per time point are indicated with \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . TSST = Trier Social Stress Test, BP = Blood Pressure. Duration of the TSST or control task.

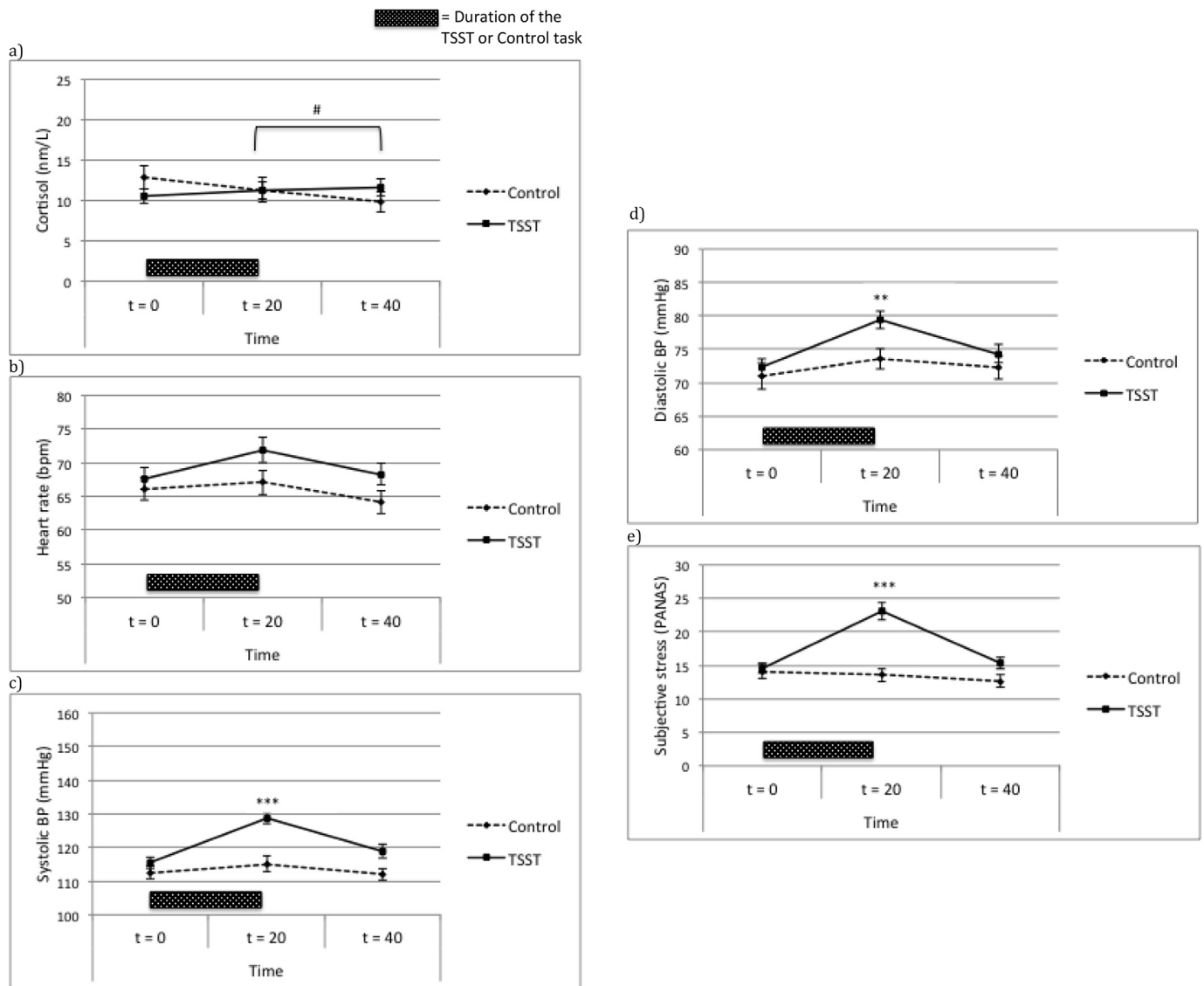
possible covariates in the RM-ANOVAs. Cortisol values were log transformed before analyses due to skewness of the data, but raw values are shown in the figures. Afterwards a RM-MANOVA including gender as a between-subjects factor was performed to examine possible gender differences in stress reactivity.

Next, to test our hypotheses that higher levels of mentalizing abilities (RMET accuracy) and higher levels of self-reported cognitive (PT scale of the IRI) and affective empathy (EC scale of the IRI) would predict increased stress reactivity, we performed multivariate regression analyses to test the predictive value of the RMET and the two IRI scales on stress reactivity using cortisol, heart rate, systolic BP, diastolic BP, and subjective stress reactivity as the multivariate outcome measures in study 1 ( $n = 52$ ) and 2 ( $n = 67$ ) separately. Reactivity scores were calculated by regressing the highest post-TSST stress levels (based on the group means for each stressor, i.e.,  $t = 40$  for cortisol and  $t = 20$  for the other four stress measures) on pre-TSST stress levels and group allocation, and then saving the standardized regression residuals. By using these regression residuals we control for initial baseline differences between participants and their effect on reactivity (Ramsay and Lewis, 2003), and the

standardized values reflect deviations in reactivity from the estimated group average (Tollenaar et al., 2011).

In case of differences in associations between empathy, mentalizing abilities, and stress reactivity between men and women, we combined the datasets from study 1 and 2 to examine whether gender statistically moderated the effect of empathy and mentalizing abilities on stress reactivity. This was done because conclusions about differences between males and females require the presence of an interaction between the independent variable (the two IRI scales and RMET accuracy) and gender (Nieuwenhuis et al., 2011).

All analyses were performed in IBM SPSS 24 and alpha was set at .05. Because three predictors were included within each regression analyses (the RMET and 2 IRI scales), the alpha for the individual predictors was Bonferroni corrected to .017 (.05/3) in the multivariate regression analyses. In the univariate post-hoc analyses for the five stress measures, the alpha for the individual outcome measures was Bonferroni corrected to .01 (.05/5). Partial eta squared ( $\eta^2$ ) is given as a measure of effect size where applicable.



**Figure 2.** Stress measure levels (a–e: Mean  $\pm$  SEM) in the female TSST and control groups over time. Group differences per time point are indicated with \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . The significant increase in cortisol levels over time in the TSST group is indicated with # $p < 0.05$ . TSST = Trier Social Stress Test, BP = Blood Pressure. Duration of the TSST or control task.

### 3. Results

#### 3.1. Descriptive statistics

Table 1 shows the means, SDs, and ranges on the predictor variables and start time for male participants (study 1) and female participants

(study 2). Independent t-tests show that women scored significantly higher than men on both the PT and EC scales of the IRI ( $ps < .05$ ), but not on the RMET ( $p = .091$ ). Furthermore, the start time for women was on average earlier in the day ( $p < .001$ ). Interrelations amongst the predictors were low enough ( $rs < .27$ ,  $ps > .05$ ), excluding the possibility of collinearity.

**Table 1.** Descriptive statistics of study 1 (men) and study 2 (women).

	Study 1 Men (N = 52)			Study 2 Women (N = 67)			Gender difference
	Mean	SD	Range	Mean	SD	Range	p-value
Start time	14:34	1:08	12:41–16:36	12:46	2:21	9:05–16:33	<.001
RMET	26.6	3.0	22–33	27.6	3.4	20–34	.091
EC	16.9	5.0	6–28	19.9	3.7	8–27	<.001
PT	16.8	4.3	7–26	18.6	4.4	6–27	.022

Notes. RMET = Reading the Mind in the Eyes Test, EC = Empathic Concern Scale of the Interpersonal Reactivity Index, PT = Perspective Taking Scale of the Interpersonal Reactivity Index.



**Table 2.** Univariate beta coefficients of the RMET and IRI scales in predicting cortisol, heart rate, BP, and subjective stress reactivity, and the multivariate *F*-values per predictor.

Study 1	Males										
	Cortisol reactivity		Heart rate reactivity		Systolic BP reactivity		Diastolic BP reactivity		Subjective stress <sup>a</sup> reactivity		<i>F</i> (5,44)
	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	
RMET	.133	.005**	.110	.023*	.003	.958	.018	.720	.026	.568	2.82*
EC	-.013	.630	.023	.426	.009	.763	-.017	.568	.076	.009**	2.00
PT	-.031	.354	-.036	.289	-.013	.710	.027	.442	-.045	.180	.669
Study 2	Females										
	Cortisol reactivity		Heart rate reactivity		Systolic BP reactivity		Diastolic BP reactivity		Subjective stress <sup>a</sup> reactivity		<i>F</i> (5,58)
	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	Beta	<i>p</i>	
RMET	.036	.316	.067	.061	.041	.246	-.012	.728	-.054	.138	1.51
EC	-.022	.552	.006	.858	-.021	.556	-.027	.445	.043	.235	.468
PT	-.039	.198	-.050	.102	-.041	.175	-.064	.034*	-.036	.236	1.74

Notes: Reactivity scores are post-stressor levels (based on highest group mean) regressed on pre-stressor levels and group allocation (TSST versus control). TSST = Trier Social Stress Test, BP = Blood Pressure, EC = Empathic Concern Scale of the Interpersonal Reactivity Index, PT = Perspective Taking Scale of the Interpersonal Reactivity Index, RMET = Reading the Mind in the Eyes Test, \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

<sup>a</sup> State anxiety in men; Negative Affect in women.

### 3.2. Manipulation check of the TSST: stress reactivity

The RM-MANOVA in study 1 indicated that men in the TSST responded with higher stress levels than men in the control condition [time\*condition effect:  $F(10, 190) = 9.82$ ,  $p < .001$ ,  $\eta^2 = .34$ ]. Univariate post-hoc tests showed the interaction between time and condition was significant for cortisol [ $F(1.7, 84.3) = 30.27$ ,  $p < .001$ ,  $\eta^2 = .38$ ], systolic BP [ $F(2, 98) = 10.18$ ,  $p < .001$ ,  $\eta^2 = .17$ ], diastolic BP [ $F(1.8, 6.0) = 9.50$ ,  $p < .001$ ,  $\eta^2 = .16$ ], and subjective stress [ $F(1.7, 83.5) = 3.95$ ,  $p = .030$ ,  $\eta^2 = .073$ ], but not heart rate [ $F(2, 98) = 2.80$ ,  $p = .066$ ,  $\eta^2 = .054$ ]. The interaction between time and condition was due to the findings that cortisol and systolic blood pressure were significantly increased at  $t = 20$  and  $t = 40$  in the stress group compared to the control group (all  $ps < .01$ ) while they were similar at baseline. Diastolic blood pressure, heart rate and subjective stress levels were significantly higher in the stress group compared to the control group at  $t = 20$  (all  $ps < .05$ ), while they were similar at baseline. Hence, the TSST successfully elicited a response on all psychophysiological outcomes in the male participants compared to the control group, although the effect in heart rate was least pronounced; see Figure 1(a-e).

The RM-MANOVA in study 2 indicated that women in the TSST responded with higher stress levels than women in the control condition [time\*condition effect:  $F(10, 242) = 7.90$ ,  $p < .001$ ,  $\eta^2 = .25$ ]. Univariate post-hoc tests showed the interaction between time and condition was significant for cortisol [ $F(1.4, 84.0) = 15.54$ ,  $p < .001$ ,  $\eta^2 = .20$ ], systolic BP [ $F(2, 126) = 11.86$ ,  $p < .001$ ,  $\eta^2 = .16$ ], diastolic BP [ $F(1.8, 114.6) = 3.97$ ,  $p = .025$ ,  $\eta^2 = .059$ ], and subjective stress:  $F(2, 126) = 14.46$ ,  $p < .001$ ,  $\eta^2 = .19$ ], but not for heart rate [ $F(1.73, 108.87) = 2.34$ ,  $p = .108$ ,  $\eta^2 = .036$ ]. The interaction between time and condition was due to the findings that systolic blood pressure was significantly increased at  $t = 20$  and  $t = 40$  in the stress group compared to the control group ( $ps < .05$ ), while similar at baseline. Diastolic blood pressure and subjective stress were significantly higher in the stress group compared to the control group at  $t = 20$  ( $ps < .05$ ), while similar at baseline. No differences between the stress and control group were found in cortisol level and heart rate levels at any of the time points (all  $ps > .05$ ). However, paired sample *t*-tests showed significant decreases in cortisol levels over time from  $t = 0$  to  $t = 20$  and from  $t = 20$  to  $t = 40$  ( $t(24) = 5.25$ ,  $p < .001$  and  $t(24) = 4.03$ ,  $p < .001$  respectively) in the control group. In contrast, the stress group showed a significant increase in cortisol levels from  $t = 20$  to  $t = 40$  [ $t(40) = 2.36$ ,  $p = .023$ ]. Overall, the TSST successfully elicited a psychophysiological stress response in the female participants compared to the control group on all stress measures except heart rate; see Figure 2(a-e). Time of day and contraceptive use did not

significantly affect psychophysiological responses over time (all interactions with time;  $p > .05$ ), and were hence not included as covariates in the regression analyses.

In addition, a RM-MANOVA was performed on the dataset combining both study 1 and 2, to examine the impact of gender on stress reactivity. The three-way interaction between time, condition and gender was significant [ $F(10, 446) = 2.67$ ,  $p = .003$ ,  $\eta^2 = .057$ ], which was due to the impact of gender on cortisol reactivity only (univariate test for cortisol:  $F(1.60, 180.6) = 10.14$ ,  $p < .001$ ,  $\eta^2 = .082$ ).

### 3.3. The role of empathy and mentalizing in stress reactivity

A multivariate regression analysis was first performed in men (Study 1), with the RMET and the PT and EC scales as predictors and the five stress reactivity scores as dependent variables. The overall multivariate model including all three predictors and five stress reactivity scores as outcome did not reach significance,  $F(15, 138) = 1.57$ ,  $p = .089$ ,  $\eta^2 = .146$ . Within this model, the EC and PT scale did not predict stress reactivity,  $F(5,44) = 2.00$ ,  $p = .097$ ,  $\eta^2 = .185$  and  $F(5,44) = .67$ ,  $p = .65$ ,  $\eta^2 = .071$ , respectively. RMET accuracy did predict stress reactivity [ $F(5,44) = 2.82$ ,  $p = .027$ ,  $\eta^2 = .242$ ], although this effect was no longer significant after correction for multiple testing ( $p > .017$ ). We did explore the univariate tests per stress reactivity outcome, to assess whether specific stress measures would be more sensitive to mentalizing or empathy than others. Post-hoc univariate tests showed that higher accuracy on the RMET predicted higher levels of cortisol reactivity (beta = .33,  $t = 2.92$ ,  $p = .005$ ) and heart rate reactivity (beta = .11,  $t = 2.26$ ,  $p = .023$ ), although the latter effect did not survive correction for multiple testing ( $p > .01$ ). Furthermore, higher scores on the EC scale significantly predicted higher subjective stress reactivity (beta = .076,  $t = 2.73$ ,  $p = .009$ ), see Table 2.

The multivariate regression analysis was repeated in women (Study 2). The overall multivariate model including all three predictors and five stress reactivity scores as outcome was not significant,  $F(15, 180) = 1.39$ ,  $p = .16$ ,  $\eta^2 = .140$ . Within this model, neither the EC or PT scale, nor the RMET predicted stress reactivity [ $F(5,58) = 1.51$ ,  $p = .202$ ,  $\eta^2 = .105$ ,  $F(5,58) = .47$ ,  $p = .80$ ,  $\eta^2 = .039$ , and  $F(5,58) = 1.74$ ,  $p = .14$ ,  $\eta^2 = .13$ , respectively]. While explorative univariate posthoc analyses indicated that higher scores on the PT scale predicted reduced diastolic blood pressure reactivity, this effect did not survive correction for multiple testing (beta = -.064,  $t = -2.17$ ,  $p = .034$ ), see Table 2.

Different effects were found in men and women with regard to the predictive value of the RMET and IRI scales on stress reactivity. We therefore also performed a multivariate regression analysis on the





system. We know from animal studies that oxytocin, i.e. a triggering hormone in approaching behavior within social situations, is also released within the brain when facing threatening situations (Heinrichs et al., 2009; Neumann and Slattery, 2015). A prior study, including only men, found that oxytocin administration increased males' accuracy on the RMET (Domes et al., 2007). Higher levels of endogenous oxytocin may possibly be related to higher trait levels of mentalizing, as well as behavioral and physiological responses during socially stressful situations (Bartz et al., 2011; Heinrichs et al., 2009), and may hence explain associations between mentalizing, empathy, and stress reactivity during a stressful situation.

In addition, a study by Tomova et al. (2017) measuring the association between acute stress and empathy for pain, showed that under the stress of solving difficult tasks, participants showed enhanced neural activation in the affective empathy brain network (anterior insula, anterior midcingulate cortex) when empathizing with unknown others suffering from physical pain. The findings of our present study add to this knowledge by demonstrating that this association also works in the opposite direction; being more stress sensitive because of higher levels of mentalizing abilities may lead to higher psychological and physiological stress reactivity, and should therefore be taken into account as a possible risk factor for stress-related symptomatology. Likewise, the influence of baseline or trait empathy and mentalizing abilities should be taken into account in studies looking at the impact of acute stress on social behavior and cognition. Individual differences in trait empathy and mentalizing may influence the reactivity to a laboratory-induced stressor, and thereby both directly (due to their underlying abilities) and indirectly (via the stress response) influence post-stressor performance on tasks that require mentalizing or empathic responses. It is yet unknown whether the ability to estimate and feel the intentions and emotions of evaluators during a social evaluative stressor like the TSST is related to a person's ability to handle the stressful situation and how they may adjust their behavior afterwards accordingly. Future studies in this area are warranted.

Interestingly, accuracy on the RMET was not related to either self-reported affective empathy or cognitive empathy in our study. A prior study (Melchers et al., 2015) also demonstrated absent correlations between self-reported empathy and indirectly measured empathy (i.e. by using tasks). It could be that indirect measures give more information about biological mechanisms like stress reactivity. This may also explain why the RMET is a better predictor for physiological stress reactivity compared to self-reported empathy in our study. Additionally, mentalizing abilities might be more relevant to stress reactivity, as both the TSST and the RMET require – although with a different purpose – the ability to read other people's intentions and emotions. In contrast, self-reported empathy may more closely relate to self-reported emotions during stress, which may explain the association we found between affective empathy and subjective stress.

Also important to address are the limitations of the present study. Men and women were tested within 2 different studies, including similar tests and protocols but also with slight differences in set-up (e.g. other committee members, different measures of subjective stress). It is therefore possible that the gender differences we observed in the separate analyses could be study dependent. When the samples were merged, gender did not moderate the associations between empathy, mentalizing ability, and stress reactivity, and the association between the RMET and heart rate reactivity was even significant including corrections for multiple testing. This may be due to the larger sample size when combining the studies, and thus to higher power to detect such associations. However, from a more conservative point of view, the results from our first study in men could not be replicated in our second study in women, stressing the need for replication of these findings in a study including both men and women. Also of note, all participants performed the RMET shortly before the TSST and a direct influence of such an emotion-focused test on TSST reactivity cannot be directly ruled out. Ideally, a stress group should be included that did not receive this test beforehand. In addition, our choice to include the IRI and the RMET was predominantly based on

the fact that both measures are well validated and often used. However, using self-reports to measure empathy, like the IRI, has often led to gender differences that were not found in studies testing empathy in a more indirect way (Rueckert, 2011). The RMET is a more indirect measure of mentalizing abilities, which has its benefits when it comes to possible gender differences as a result of using self-reports and demand characteristics. However, the RMET also has its disadvantage because it does not include contextual information as it only presents the eye region of faces. Future studies might consider using more ecologically valid mentalizing measures (Achim et al., 2013) and implement paradigms like the one designed by Dziobek et al. (2006: the Movie Assessment for Social Cognition) in order to test the broader concept of mentalizing. Furthermore, with regards to the subjective stress measures, the STAI and negative affect scale of the PANAS may not optimally reflect a stressed state. While the STAI measures anxiety levels, which are expected to increase in response to stress, it is conceptually not a perfect stress measure. The PANAS includes a broader range of negative states, e.g. also representing feelings of anger in addition to anxiety and distress. Little consensus is found in the literature on how to best measure state levels of stress and a possible alternative is the use of Visual Analogue Scales (Lesage et al., 2012).

Our goal was to examine individual differences in stress reactivity and for this reason we chose to include most participants in the experimental stress conditions with relatively small groups in the control conditions. This may have resulted in low power to detect stress reactivity in the TSST compared to the control group and a higher influence of possible outliers. However, except for heart rate measures in females, we showed statistically significant reactivity of our stress measures to the TSST in both men and women, with heart rate reactivity still variable enough to be used as a stress outcome. Furthermore, due to the multiple stress measures, chances for type 1 errors are possible and replication is needed in larger samples, including both men and women, to further establish gender differences in the association between empathy, mentalizing abilities, and stress. Also, generalizability beyond students is limited, because students may possibly perform higher on a mentalizing task than the general population, while psychology students may specifically over-report on empathic abilities. Inclusion of participants with broader educational levels would be of interest.

Additionally, because we did not manipulate empathy or mentalizing abilities, we cannot necessarily conclude that higher levels of these traits cause stress sensitivity. That is, empathy, mentalizing abilities, and stress sensitivity may be expressions of underlying un-examined traits. Such traits include possible genetic variations (in e.g. the oxytocin system) or neural mechanisms implicated in social behavior, such as the amygdala and anterior insula (Petrovic et al., 2008; Singer et al., 2008). Finally, differences in stress sensitivity might also be explained by the biosychosocial model, which postulates that individuals tend to make a trade-off between their level of competence (e.g. empathic skills) and the situational demands in case of acute stress. This situational appraisal influences physiological responses and subsequently individuals' performance and could be susceptible to individual and/or gender differences (Blascovich et al., 1999; Folkman et al., 1986). Future studies should further address these underlying mechanisms.

This is the first study to examine associations between empathy, mentalizing abilities, and stress reactivity in men and women. In future studies, it will be of interest to study the mechanisms through which mentalizing abilities are associated with reactivity to social stress, while taking gender differences into consideration. Potential mediators could be: differences in emotion regulation and coping strategies, situational appraisal, and fear of negative evaluation. Furthermore, investigating how empathy, mentalizing abilities, and stress reactivity in chronic stressful situations change over time could provide further insight into cause-effect relationships. Moreover, it would be interesting to deepen our understanding of stress in relation to hypo- and hypermentalizing (Sharp and Vanwoerden, 2014). Hypomentalizing can be explained as less Theory of Mind (ToM), which characterizes individuals having an

insufficient mental state reasoning resulting in incorrect mental state attributions. Hypermentalizing can be interpreted as an excessive form of ToM where individuals make assumptions about a person's mental state that go far beyond what can be observed, and which often leads to a misinterpretation of the other person's behavior. Based on our results, it seems that hypermentalizing could play a role in how stress sensitive people are. It would be interesting to specifically test this, and also whether individuals who have a tendency towards hypomentalizing would be better protected against a stress-inducing environment.

To conclude, while sensitivity to social signals is generally considered a good social quality, it may also indicate a vulnerability to social evaluations, especially in men, which could become problematic in chronically stressful situations (Grippe and Johnson, 2009; Kessler et al., 2010; McEwen, 2017). Therefore, our findings should be further investigated in order to explore whether empathy, mentalizing abilities, and gender should be taken into account when training people in how to cope with stressful situations. Such insights are likely to be of relevance in creating healthy psychological work environments in a world of continually rising expectations and demands. With this study, we have taken an important step towards a better understanding of the role of empathy and mentalizing abilities, i.e. a more socially sensitive constitution, in psychological and physiological stress reactivity.

## Declarations

### Author contribution statement

M. Tollenaar: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

S. Overgaauw: Analyzed and interpreted the data; Wrote the paper.

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### Competing interest statement

The authors declare no conflict of interest.

### Additional information

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