



Does cortisol modulate emotion recognition and empathy?



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ABSTRACT

Introduction: Emotion recognition and empathy are important aspects in the interaction and understanding of other people's behaviors and feelings. The Human environment comprises of stressful situations that impact social interactions on a daily basis. Aim of the study was to examine the effects of the stress hormone cortisol on emotion recognition and empathy.

Methods: In this placebo-controlled study, 40 healthy men and 40 healthy women (mean age 24.5 years) received either 10 mg of hydrocortisone or placebo. We used the Multifaceted Empathy Test to measure emotional and cognitive empathy. Furthermore, we examined emotion recognition from facial expressions, which contained two emotions (anger and sadness) and two emotion intensities (40% and 80%).

Results: We did not find a main effect for treatment or sex on either empathy or emotion recognition but a sex × emotion interaction on emotion recognition. The main result was a four-way-interaction on emotion recognition including treatment, sex, emotion and task difficulty. At 40% task difficulty, women recognized angry faces better than men in the placebo condition. Furthermore, in the placebo condition, men recognized sadness better than anger. At 80% task difficulty, men and women performed equally well in recognizing sad faces but men performed worse compared to women with regard to angry faces.

Conclusion: Apparently, our results did not support the hypothesis that increases in cortisol concentration alone influence empathy and emotion recognition in healthy young individuals. However, sex and task difficulty appear to be important variables in emotion recognition from facial expressions.

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1. Introduction

Stressful events activate the hypothalamic-pituitary-adrenal axis (HPA), which leads to an increased secretion of glucocorticoids, i.e., cortisol in humans. Cortisol acts on two different receptors in the brain: mineralocorticoid receptors (MR) are predominantly present in the limbic system (hippocampus & amygdala) and the prefrontal cortex and bind cortisol with high affinity. Glucocorticoid receptors (GR) on the other hand are widely distributed throughout the entire brain and have approximately one tenth the affinity of MRs (de Kloet, 2014; Maggio and Segal, 2012). It has long been known that glucocorticoids have an impact on cognitive abilities such as memory, learning and decision making (for a review, see Wolf, 2009). Brain structures involved in these processes are the

hippocampus (Watzka et al., 2000a), the prefrontal cortex (Watzka et al., 2000b), and the amygdala (Phelps, 2004, 2006). Interestingly, the same brain structures have an important impact on social facets of cognition (e.g., Adolphs, 2010; Gallagher and Frith, 2003; Olsson and Ochsner, 2008; Rubin et al., 2014).

Two essential aspects of social interactions are emotion recognition of faces (Chen, 2014) and empathy (Bernhardt and Singer, 2012; Fiske and Taylor, 2013). Emotion recognition of faces can be seen as a more basic ability which is necessary to interact properly with the environment (Adolphs et al., 1999). However, empathy is a more complex construct and recent research indicates that it might be a multidimensional construct which consists of several separate components (Blair, 2005; Shamay-Tsoory et al., 2009). Two systems are consistently identified: cognitive empathy, the ability to understand another person's perspective and emotional empathy, the ability to feel for another person. Although brain structures, which are important for social cognitive abilities contain a high density of glucocorticoid receptors, little is known about a possible interaction (Amodio and Frith, 2006; Gallese et al., 2004).

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To the best of our knowledge, only one study investigated whether stress influences empathy. Measuring free salivary cortisol Smeets et al. (2009) showed that women with a low cortisol response to a psychosocial stressor showed more cognitive empathy after stress compared to women with a high cortisol response (Trier Social Stress Test, Kirschbaum et al., 1993). In contrast, men with a high cortisol response to stress showed more cognitive empathy than men with a low cortisol response. Thus, sex might modulate the effects of cortisol on cognitive empathy.

In one of our own studies we used a pharmacological approach and tested the influence of a mineralocorticoid agonist (fludrocortisone) on cognitive and emotional empathy (Wingenfeld et al., 2014). In that study, we found greater emotional empathy in healthy young women and female patients with borderline personality disorder after fludrocortisone administration compared to placebo. No beneficial effects emerged for cognitive empathy. Fludrocortisone has a much greater mineralocorticoid than glucocorticoid potency. Thus, these results point to two important aspects: first, stress hormones might have an impact on empathy, and second, this impact could possibly depend on a specific receptor type within the brain.

When looking at emotion recognition performance, Deckers et al. (2015) found an increase of emotion recognition performance in healthy participants and patients with personality disorders after experiencing a psychosocial stressor (TSST). Thus, emotion recognition also seems to be susceptible to psychosocial stress, but it is still unknown if cortisol is the main factor explaining these findings. Importantly, a psychosocial stressor such as the TSST not only leads to an increase of cortisol but also is socially threatening and provokes a release of other hormones (e.g., adrenalin), which might also affect empathy and emotion recognition.

To further examine the association between stress hormones, emotion recognition and empathy, we assessed the effects of a pharmacological challenge with 10 mg hydrocortisone on the named social variables. The second aim of our study was to obtain a better understanding of a possible impact of sex in the context of cortisol and empathy, thus we counterbalanced the number of male and female participants to systematically examine sex effects and sex by treatment interactions.

Based on the findings of Deckers et al. (2015), we expected an increase in emotion recognition performance after hydrocortisone intake compared to placebo, independent of sex. For empathy, sex differences related to the effects of cortisol are described in the literature (Smeets et al., 2009). In line with their findings, we based our hypothesis on high cortisol responders after a psychosocial stressor as a proxy for exogenous cortisol administration. Thus, we expected an increase in cognitive and emotional empathy performance for men after hydrocortisone, whereas women should show decreased cognitive and emotional empathy after hydrocortisone intake.

2. Method

2.1. Participants

The study took place at the Department of Psychiatry, Charité—Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany. In total, 80 healthy participants (40 women and 40 men) with an average age of 24.5 years ($SD = 3.4$) and a completed German-university entrance diploma took part in the study. All participants were free of medication and were excluded if any of the following medical conditions were present: CNS diseases or severe somatic diseases, metabolic or endocrine diseases, autoimmune diseases, current infections, or pregnancy. In addition, participants were screened for axis I disorders according to DSM-IV (based on

SCID I Screening Questionnaire) and were excluded if psychiatric illness was present. All participants signed a written informed consent and received financial remuneration (20€). The study was approved by the national ethic committee of the German Psychology Association (DGPs).

2.2. Procedure

We conducted a placebo-controlled, double-blind study and randomized participants via computerized randomization to either 10 mg hydrocortisone or placebo, both given orally. A dose of 10 mg hydrocortisone was used in several other studies in different laboratories, reliably increasing salivary cortisol concentration (e.g., Entringer et al., 2009; Henckens et al., 2011; Terfehr et al., 2011; van Ast et al., 2013; Wingenfeld et al., 2013).

A priori, men and women were equally recruited into both treatment groups to allow systematic examination of sex effects. Participants arrived at 1 p.m., signed the informed consent and received hydrocortisone or placebo. Testing started 45 min after drug intake. The study was performed in a quiet surrounding. Salivary cortisol was collected immediately prior to administering hydrocortisone or placebo (0) and 45, 75 and 105 min after drug intake using neutral Salivettes® (blue cap; Sarstedt, Germany). After collection, which took place at room temperature, saliva was kept at -80°C until biochemical analysis.

Cortisol concentration was determined in the Neurobiology Laboratory of the Department of Psychiatry, Charité—Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany.

Free cortisol was analyzed using an adapted homogenous time-resolved fluorescence resonance energy transfer (HTR-FRET)-based competitive immunoassay, which is based on an anti-cortisol antibody labeled with Europium 3+-cryptate as the donor dye, and authentic cortisol conjugated with a second generation acceptor dye (D2) (Cisbio International, Codolet, France). In brief, 2 parts of the sample were subjected to a fluorescence microtiter plate and 1 part of D2-conjugated cortisol was added immediately thereafter. Both components (saliva and D2-conjugate) were thoroughly mixed using a multi-channel pipette and centrifuged for 2 min at $1000 \times g$ using a microtiter plate centrifuge (Heracus Biofuge, Thermo Fisher Scientific, Braunschweig, Germany). After centrifugation, 1 part of Eu3+-cryptate-labeled anti-cortisol antibody was added, again thoroughly mixed, centrifuged (2 min at $1000 \times g$) and allowed to incubate for at least 2 h. Appropriate authentic standards, negative, positive and blank controls were included according to the manufacturer's instructions. After incubation, time-resolved fluorescence was measured at 620 nm and 665 nm using a Clariostar multimode plate reader (BMG Labtech, Ortenberg, Germany). Increase in fluorescence at 665 nm (acceptor fluorescence of D2) was normalized to fluorescence at 620 nm (donor fluorescence of Eu3+-cryptate) to account for differences in plating volumes or micro bubbles, and calculated as relative increase in fluorescence over Eu3+-cryptate-only containing blanks. Intra-assay coefficients of variation were below 8%, inter-assay coefficients of variation were below 10%. The limit of detection of free cortisol was 0.2 nM. All samples and standards were measured in duplicates.

2.2.1. Multifaceted Empathy Test (MET)

The MET is a PC-assisted test which assesses cognitive and emotional empathy (Dziobek et al., 2008). 30 pictures displaying people in different emotionally charged situations are presented.

The images represent everyday life scenes including a particular emotional state and serve as valid stimuli (Dziobek et al., 2011; Wingenfeld et al., 2014). To assess cognitive empathy the participants had to answer the question: "What is the person feeling?"

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