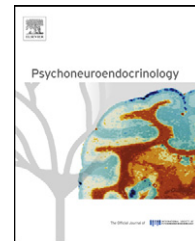




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# Oxytocin buffers cortisol responses to stress in individuals with impaired emotion regulation abilities

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Action orientation

**Summary** Oxytocin facilitates stress regulation but little is known about individual differences in this effect. The present study investigates whether the effect of intranasal oxytocin on stress-contingent cortisol release differs between individuals with high vs. low emotional regulation abilities (ERA). In a double-blind study thirty-six healthy male students with either high or low ERA were randomly assigned to receive intranasally 24 IU oxytocin or placebo. Cortisol was measured at several times before and after a social stressor (public speaking). Individuals with impaired ERA showed a reduced cortisol response to stress after oxytocin but an increased cortisol response after placebo application. The results suggest that healthy individuals with low ERA benefit from intranasal oxytocin application. Neurobiological mechanisms potentially underlying the link between oxytocin, cortisol and ERA are discussed against the background of a neuroendocrinological perspective on personality.

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## 1. Introduction

Healthy individuals typically differ in the degree to which they are able to regulate their emotions and thus to cope with stressful events (e.g., Kuhl, 1981; Lazarus and Folkman, 1984; Gross and John, 2003; Koole, 2009). Notably, individuals with reduced abilities to regulate their emotions are at higher risk to develop psychopathologies such as depression or anxiety disorders (Aldao et al., 2010). In the present work,

we were interested in the neuroendocrinological mechanisms that may differentiate between individuals with efficient vs. inefficient ERA. Specifically, we examined whether application of intranasal oxytocin would dampen cortisol increases to a psychological stressor in individuals with reduced ERA. Such evidence would have relevance for the treatment of (a) subclinical individuals in chronic stress periods to prevent the development of psychopathological disorders and (b) manifest clinical disorders.

The hypothalamus–pituitary–adrenocortical (HPA) system is typically aroused as a reaction to psychological stressors (Dickerson and Kemeny, 2004). Research conducted over the past 15 years or so has demonstrated that cortisol responses to stress vary with personality traits that are linked to abilities to regulate emotions and to cope with stress (Kudielka et al., 2009, for a review). As such, pronounced

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cortisol increases have been found in individuals low in self-esteem (Pruessner et al., 1999), low in subjective controllability beliefs (Pruessner et al., 1999), or high in attachment anxiety (Quirin et al., 2008).

Past research has demonstrated that the neuropeptide oxytocin produced in the hypothalamus and stored in the posterior pituitary (Buijs et al., 1983) counteracts stress-induced activity of the autonomous nervous system (for research using animals, see overviews by Argiolas and Gessa, 1991; Petersson, 2002; for humans, see Light et al., 2000) and the HPA system (for animals, e.g., Windle et al., 1997; Uvnäs-Moberg, 1998; Neumann et al., 2000; for humans, see Heinrichs et al., 2003; Ditzen et al., 2009). With respect to HPA regulation in humans, it has been demonstrated that intranasal oxytocin predicts reduced cortisol levels after experimentally induced couple conflicts (Ditzen et al., 2009). In this study, oxytocin also increased the amount of positive communication during the conflictive situation, a finding that acquiesces in the literature that oxytocin has positive effects on social cognition and behavior in general (Bartz and Hollander, 2006; Heinrichs and Domes, 2008; Kosfeld et al., 2005). Heinrichs et al. (2003) manipulated oxytocin and social support and measured cortisol changes over the course of the Trier Social Stress Test (TSST; Kirschbaum et al., 1993), a demanding public speaking task. The authors found that participants receiving intranasal oxytocin in combination with social support showed the lowest increases in both cortisol and reported anxiety (Heinrichs et al., 2003). However, it should be noted that other research did not find main effects of oxytocin on cortisol responses to speech tasks on cortisol (Taylor et al., 2006) or cardiovascular reactivity (Light et al., 2005).

Individual differences in oxytocin plasma levels have been investigated only recently. Specifically, reduced oxytocin plasma levels have been found in individuals with severe symptoms of generalized social anxiety disorder (Hoge et al., 2008), schizophrenic patients with emotional deficits (Goldman et al., 2008), or even in healthy individuals with high as compared to low levels of attachment anxiety (Tops et al., 2007). Intranasal oxytocin application has recently been demonstrated to facilitate social behavior and feelings of trust in autistic individuals (Andaria et al., 2010).

As far as we know, it has not yet been investigated whether the effect of oxytocin on HPA system reactivity to stressors varies with individual differences in ERA in healthy individuals. Whereas emotion regulation processes can be classified at a phenotype level with respect to various strategies employed (e.g., suppression, repression, intellectualization, actionism, aggressive enactment, communication, reappraisal, and self-reflection), at a functional level, they may be classified with respect to low vs. high ERA (Kuhl, 1994b). Low ERA individuals show impairments in downregulating negative affect as aroused by threatening experiences, and, as a consequence, tend to ruminate about these experiences long after. By contrast, high ERA individuals typically are able to downregulate stress and concomitant negative emotions effectively and sustainably, and thus remain functioning and pursue goals in daily life.

It has been argued that whereas individuals with low ERA depend on social support to cope with stress, individuals with high ERA are typically able to reduce stress on their own (Koole et al., 2005). Accordingly, individuals with low ERA as

expressed by a tendency to ruminate about negative experiences indeed seek and benefit more from social support after a traumatic stressor than those with high ERA (Nolen-Hoeksema and Davis, 1999). If oxytocin plays a mediating role between social support and stress regulation (Heinrichs et al., 2003), we expect that individuals with low ERA would benefit more from oxytocin administration than individuals with high ERA.

Notably, previous research has demonstrated that individual differences in ERA can be distinguished from individual differences in emotion sensitivity ("stress reactivity"). Whereas the former refer to the ability to manage stressful situations and concomitant negative affect once present (exit gradient), the latter refers to the sensitivity with which an individual responds to stress (entry gradient) (Kuhl, 1981, 2000; Baumann et al., 2007; Koole, 2009).

The goal of the present study is to investigate effects of oxytocin application on cortisol changes to a stressor as a function of efficient vs. inefficient ERA. We expect that low ERA individuals in the control (placebo) group show a stronger increase in cortisol than high ERA individuals in the control group. Moreover, we expect that low ERA individuals benefit from intranasal oxytocin application by showing a cortisol reaction that is less pronounced than the reaction from low ERA individuals treated with a placebo. Not least, finding a general increase of cortisol over the course of the stressor would speak to the effectiveness of the stressor.

## 2. Methods

### 2.1. Sample and procedure

Thirty-six healthy male students ( $M = 24.8$  years,  $SD = 4.1$  years) from the University of Osnabrück were recruited by an experimenter via flyers and postings and received 20 € for taking part in the study. All participants were subjected to a physical examination to check for diseases or medication that may render oxytocin administration problematic. The study was approved by the ethics committee of the University of Osnabrück.

In a preliminary session, after signing a written informed consent, participants were examined by a medical doctor to screen out chronic diseases, mental disorders, medication, smoking, and drug or alcohol abuse. Participants agreed to abstain from eating and drinking during 2 h before the experimental session, and from exercise, caffeine and alcohol during 24 h before this session. They were informed to be able to withdraw from the study at any time.

All experimental sessions took place between 1300 h and 1600 h and lasted for approximately 2 h. In a double-blind allocation, participants were randomly assigned by the experimenter to one of two groups that either received oxytocin ( $N = 18$ ) or placebo ( $N = 18$ ) intranasally. A dose of 24 IU (Novartis, Basel, Switzerland; 3 puffs each side) was sprayed 45 min before stressor onset. The placebo was produced at a local pharmacy. It contained all ingredients of the oxytocin spray except for oxytocin itself. At the end of the experiment participants were asked to guess whether they received oxytocin or placebo. A chi-square test revealed no significant association between application of oxytocin vs. placebo and detection of substance,  $\chi^2(1, N = 36) = .07, p = .79$ .

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