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Oxytocin administration and emotion recognition abilities in adults with a history of childhood adversity

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ABSTRACT

Adverse childhood experience such as neglect or abuse can lead to long-term deficits in emotion processing abilities. Animal studies indicate that oxytocin production and/or sensitivity are influenced by variation in early nurturing experiences. The goal of this study was to test whether emotion recognition abilities and empathy might be improved via intranasal oxytocin administration in adults with a history of childhood maltreatment. We assessed a total of 80 healthy participants, half with and half without a history of childhood adversity. Participants performed the Reading the Mind in the Eyes Test (RMET) and an emotion recognition task under 24 IU intranasal oxytocin and placebo, using a double-blind crossover study design. In the first of two sessions, both groups profited equally form oxytocin administration and showed greater accuracy under oxytocin compared to placebo in the RMET ($p = .049$). In the emotion recognition task, only the early adversity group benefited significantly from oxytocin administration in the first session ($p = .035$), mainly due to more accurate recognition of angry and fearful facial expression. Our findings show that emotion processing abilities might be improved via oxytocin administration in adults reporting adverse childhood experiences.

1. Introduction

It is well established that adverse early life experiences can predispose individuals to mental and physical disease in adulthood (Gilbert et al., 2009; Repetti et al., 2002) raising the question of how the long-lasting health consequences of unfavorable early environments are sustained. A large body of research has shown that early adversity can lead to altered regulation of the hypothalamus-pituitary-adrenal (HPA) axis (Heim et al., 2008) and to deficits in social behavior and social cognitive skills such as emotion processing (Young and Widom, 2014). Facial emotion recognition is essential for social cognition and the early learning environment plays animportant role in how facial expressions are interpreted and which expressions are particularly relevant to the individual (Pollak and Kistler, 2002). Several studies with maltreated children have reported increased sensitivity for negative emotions (Curtis and Cicchetti, 2011; Masten et al., 2008; Pollak et al., 2000). Furthermore, impairments in emotion recognition in clinical samples of adults reporting childhood trauma have been reported (Nicol et al., 2014; Russo et al., 2015). A potential neurobiological mechanism underlying the link between childhood adversity and social and emotional difficulties observed in adulthood involves the central oxytocin system (Heim et al., 2008): the neuropeptide oxytocin modulates the activity of various brain areas (including limbic structures such as the amygdala, hippocampus, striatum, and midbrain; (Meyer-Lindenberg et al., 2011) involved in social behavior and cognition. Intranasal application of oxytocin in humans has been shown to have beneficial effects on complex social cognitive functions (Heinrichs et al., 2009; Kanat et al., 2014). There is evidence suggesting that adverse experiences in childhood, like maltreatment or neglect, can have long-lasting effects on the developing oxytocin system. Due to its role in mediating caregiver-child attachment and trust (Feldman, 2015; Rilling and Young, 2014), disruptions in the relationship to attachment figures during early-life – a phase of heightened plasticity – may influence the development of the oxytocin system (Heim et al., 2008). Animal studies revealed that central oxytocin receptor expression was influenced by early nurturing experiences in rats, and that these changes persisted over time (Francis et al., 2000). In rhesus monkeys, a lower concentration of oxytocin in cerebrospinal fluid (CSF) was found in nursery-reared male monkeys than in mother-reared controls (Winslow et al., 2003). In humans, children raised in deprived orphanages showed less responsivity of the

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oxytocin system after physical interaction with their adoptive mothers as compared to family-reared control children (Fries et al., 2005). Meinlschmidt and Heim (2007) reported a decreased sensitivity to intranasally applied oxytocin in men who experienced early life stress in the form of parental separation. A lower concentration of oxytocin in CSF was observed in women with a history of childhood abuse or neglect, most notably in those who experienced emotional abuse (Heim et al., 2009).

Given the evidence of deficits in social cognitive skills in adults with adverse childhood experiences, and given the association between childhood adversity and alterations in the oxytocin system, we sought to test in adults with early adverse experiences whether intranasal oxytocin administration might lead to an improvement in the performance of tasks involving the recognition of basal emotions and complex mental states. We hypothesized that the ability to recognize basic emotions as well as complex mental states would improve after oxytocin administration in adults reporting childhood adversity.

2. Methods and materials

2.1. Participants

A total of 80 healthy adults (54 females, 26 males) were recruited from the Freiburg (Germany) region. We used articles in local newspapers as well as community-posted flyers to advertise a study looking for adults with adverse childhood experiences. The control group was recruited by the same means, advertising a study on „Stress and Emotions“. Inclusion criteria were age between 40 and 60 years, and experience of childhood adversity for the early adversity group (and absence thereof for the control group). The German 28-item version of the Childhood Trauma Questionnaire (CTQ, Bernstein et al., 1994, 2003; Rodewald, 2005) was used to assess five categories of childhood adversities (sexual, physical and emotional abuse, as well as physical and emotional neglect). In order to classify subjects as positive for a history of childhood adversity, CTQ cut-off scores for moderate to severe exposure to traumatic experiences were used (> 12 for emotional abuse; > 9 for physical abuse; > 7 for sexual abuse; > 14 for emotional neglect; and > 9 for physical neglect). Experience of adversity was validated in a structured interview with the Early Trauma Inventory (ETI, Bremner et al., 2000; Heim, 2000). Acute mental disorders were screened for by a psychologist using the German version of the Structured Clinical Interview for DSM-IV Disorders (SKID I & II; Wittchen et al., 1996). None of the participants fulfilled the criteria for mental disorders at the time of assessment or during the preceding twelve months. The control group participants scored below cut-off on all CTQ subscales, and were matched using a matched-pair procedure to the early adversity group according to sex, age, and socioeconomic status (SES) at present, and SES during childhood. Current and childhood SES were assessed in reference to current and childhood family income as well as the participants' and their parents' educational level. The Brief Symptom Inventory (Franke, 2000) was used to assess subclinical psychopathological symptoms at the time of testing. For both groups, the use of psychoactive medication or hormone intake (e.g. oral contraceptives) led to study exclusion. The participants gave written informed consent to the study procedures, approved by the Ethics Committee of the Albert-Ludwigs University of Freiburg (183/11). The study was part of a larger project investigating the long-term consequences of childhood adversity, which also included the assessment of hormonal and genomic responses to stress (Schwaiger et al., 2016). Experiments reported here were conducted at least one week after the stress session.

2.2. Study procedure

A double-blind, placebo-controlled, within-subject design was used to investigate the effect of a single dose of intranasal oxytocin on social cognitive abilites. Participants first completed a multidimensional mood-questionnaire (MDBF, Steyer et al., 1997) at each experimental session, followed by the intranasal application of the oxytocin or placebo spray via self-administration. In accordance with a standardized protocol and under investigator supervision, the participants administered three puffs of oxytocin (Syntocinon-Spray Novartis, Switzerland; 4 IU oxytocin per puff, total dose of 24 IU oxytocin) or placebo (containing all ingredients except for the neuropeptide) per nostril (Spengler et al., 2017). After a 45 min loading period, during which the participants watched a movie with non-social content, the MDBF was completed a second time and then the tests were carried out. Dosage and test latency were chosen based on the results by Spengler et al. (2017) who systematically varied dose-test latencies and doses of oxytocin and identified a time window between 45 and 70 min after administration of a dose of 24 international units as most effective. After each experimental session, participants were asked if they thought they had received oxytocin or placebo. The self-report indicated that they were unable to guess beyond the chance level. Two tests were applied to assess emotion processing ability, the “Reading the Mind in the Eyes Test” (RMET`, Baron-Cohen et al., 2001) and a “Gradual Emotion Recognition Test” (Chen et al., 2015; based on Lischke et al., 2012). Whereas the RMET calls for high sensitivity to emotional cues and requires the participant to infer complex mental states from solely the eye region, the “Gradual Emotion Recognition Test” requires the individual to swiftly and accurately detect basic emotions form naturalistic, animated stimuli. Both tests were conducted twice on two separate sessions, with the RMET preceding the emotion recognition task on both sessions. Block randomization was used to ensure that an equal number of participants in the two groups would receive oxytocin and placebo in the two sessions. The experimental sessions took place in the afternoon and lasted about two hours. Tests were implemented on a computer and each participant was seated in an individual cubicle. At any given time, there was a maximum of four subjects participating in the experiments. Participants did not communicate with each other before, during or after the experimental sessions.

To account for fluctuations in gonadal steroids over the menstrual cycle and their possible interactions with exogenous oxytocin, female participants with regular menstrual cycles were tested in the mid-luteal phase. The cycle-phase was assessed as a self-report by participants and validated by saliva assays of estradiol and progesterone taken on both sessions. All values were in the typical range for the second cycle phase for both hormones. To take the menstrual cycle phase into account and reduce learning effects, there was a four-week time period between the two experimental sessions for all participants. After completion of the second sessions, subjects received monetary compensation for study participation (total of 100 €).

2.2.1. Experiment 1: reading the mind in the eyes test

The RMET was used to assess participants' ability to infer complex mental states from the eye region. During the test, 36 pictures of the eye region are shown on a computer screen with four alternative labels describing what the person is thinking or feeling. Participants have to decide which of the four labels accurately describes the person's mental state (Baron-Cohen et al., 2001). Performance on the RMET was calculated as the percentage of items rated correctly.

2.2.2. Experiment 2: emotion recognition task

The task to determine emotion recognition ability of the subjects corresponds to the task used by Chen et al. (2015). The task requires that subjects evaluate a person's emotional state from the display of a face gradually changing from a neutral expression towards one of the emotions sadness, anger, happiness or fear. Participants were instructed to respond as quickly and accurately as possible. As soon as they recognized the displayed emotion, they were supposed to press a stop button. After stopping the presentation, they had to indicate which of the four emotions they had identified. There were 24 test trials