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The role of oxytocin in social bonding, stress regulation and mental health: An update on the moderating effects of context and interindividual differences

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Oxytocin; Stress; Emotion; PTSD; Memory; Social support; Self-perception; Attachment; Context; Sex **Summary** In this review we summarize the results and conclusions of five studies as presented in a symposium at the 42nd annual meeting of the International Society for Psychoneuroendocrinology, in New York in September 2012. Oxytocin administration has received increasing attention for its role in promoting positive social behavior and stress regulation, and its potential as a therapeutic intervention for addressing various aspects of psychiatric disorders. However, it has been noted that the observed effects are not uniformly beneficial. In this paper we present five new studies each concluding that contextual and interindividual factors moderate the effects of oxytocin, as well as peripheral oxytocin levels. These findings are in accordance with the recent idea that oxytocin administration may increase sensitivity to social salience cues and that the interpretation of these cues may be influenced by contextual (i.e. presence of a stranger versus friend) or interindividual factors (i.e. sex, attachment style, or the presence of psychiatric symptoms). When social cues in the environment are interpreted as "safe" oxytocin may promote prosociality but when the social cues are interpreted as "unsafe" oxytocin may promote more

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defensive and, in effect, "anti-social" emotions and behaviors. Likewise, oxytocin appears to promote such agonistic tendencies in individuals who are chronically pre-disposed to view the social milieu in uncertain and/or in negative terms (e.g., those with borderline personality disorder, severe attachment anxiety and/or childhood maltreatment). In all, these studies in pre-clinical animal, healthy humans and patients samples further reinforce the importance of considering both contextual and interindividual factors when trying to understand the role of oxytocin as a biological substrate underlying social bonding and stress regulatory processes and when studying the effects of oxytocin administration in particular in patients with (increased risk for) psychiatric disorders. © 2013 Published by Elsevier Ltd.

1. Introduction

Recently oxytocin has received increasing attention, both scientifically for its role in social bonding, stress regulation, and mental health, as well as in the more popular media. It has been advertised as a universal "love hormone", as the remedy against loneliness, fears, partner relationship and sexual problems. In this review, we will briefly discuss evidence for oxytocin's role in social bonding, stress regulation and mental health. Specifically, it has been argued that the social effects of oxytocin are, more often than not, moderated by features of the context in which oxytocin is administered and/or the individuals to whom it is administered (Bartz et al., 2011b). Here, we review more recent data supporting this hypothesis, and highlight findings from five studies as presented at the 42nd annual meeting of the International Society for Psychoneuroendocrinology (ISPNE), New York, September 2012. The goal of the symposium was to gain more insight in the influence of a broad variety of contextual and interindividual factors on the effects of exogenous oxytocin administration as well as peripheral oxytocin levels. Finally, the findings of these new studies will be integrated and discussed. Taken together, the integrated results and discussion further support the idea that oxytocin is not simply a "love hormone", but instead that oxytocin may increase sensitivity to social salience and subsequent effects of oxytocin administration depend on the attributed salience of the situation (Bartz et al., 2011b).

1.1. Oxytocin and social bonding

Work in a wide variety of mammalian and non-mammalian species contributed important insights into the critical involvement of oxytocin in the formation and continuation of social bonds. Oxytocin is physiologically primarily involved in events associated with reproduction, including stimulation of uterine contraction and lactation (Fuchs et al., 1984). These physiological effects are likely mechanistically linked to regulating attachment behaviors, since these early critical periods represent privileged times during which mothers bond with their offspring, and newly born infants collect information about safety and threat in their environment (for review see Carter, 1998). Early work in animals demonstrated oxytocin's ability to induce maternal behavior (e.g. Pedersen and Prange, 1979) and its role in forming pair-bonds (e.g. Insel, 1997; Williams et al., 1994), setting the stage for investigations of oxytocin's role in social bonding and attachment more generally. In humans, markers of the oxytocinergic system have been linked to parental behavior and parent—infant bonding. For example, high endogenous oxytocin levels peripartum are associated with increased mother—infant bonding (Feldman et al., 2007). In line with this finding, higher plasma and salivary oxytocin levels in mothers and fathers were positively associated with the parent's and child's social engagement, affect synchrony, as well as positive communicative sequences between parent and child (Feldman et al., 2011).

Moreover, early experiences seem to influence the oxytocin system later in life. It has been observed that experiencing childhood trauma, which is a major predisposing factor for the development of insecure attachment and mental health problems, may dysregulate functioning of the oxytocin system. For example, it was shown that adult women who were exposed to any form of childhood maltreatment had lower oxytocin levels in the cerebrospinal fluid compared to controls (Heim et al., 2009). Furthermore, intranasal oxytocin administration studies in humans confirm the overall idea that oxytocin is involved in a broad variety of other processes that are associated with social bonding in healthy individuals, including elevation of (in-group) trust (van Ijzendoorn and Bakermans-Kranenburg, 2012) and improved recognition of facial emotions (Shahrestani et al., 2013).

1.2. Oxytocin and stress regulation

The formation of enduring bonds may play an important role in structuring adaptive responses to stressors, since the mechanisms that arose to facilitate their development likely evolved in environments that presented numerous survival challenges. A large body of evidence links oxytocin to stress regulation in rodents. Central and peripheral oxytocin levels have been found to increase in response to a wide variety of stressful stimuli, such as conditioned fear stimuli and restraint stress (Neumann et al., 2000; Onaka, 2004). In humans an increase in plasma oxytocin was found after exposure to uncontrollable noise in women (Sanders et al., 1990) and in response to several types of psychosocial stressors (Hoge et al., 2008; Marazziti et al., 2006; Taylor et al., 2010). It has been hypothesized that oxytocin release during stressful situations serves to dampen physiological stress levels, for it has also been observed that high basal plasma oxytocin levels are associated with low norepinephrine levels, blood pressure and heart rate (Light et al., 2004). In addition, in lactating women, i.e. women with high oxytocin levels, cortisol and ACTH responses to a physical exercise stressor were attenuated compared to nonbreastfeeding women (Altemus et al., 1995). It was shown that oxytocin administration has stress-regulating effects in

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