Oxytocin and Interpersonal Relationships

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Abstract The neuropeptide oxytocin (OT) has emerged as a potent modulator of diverse aspects of interpersonal relationships. OT appears to work in close interaction with several other neurotransmitter networks, including the dopaminergic reward circuit, and to be dependent on sex-specific hormonal influences. In this chapter, we focus on four main domains of OT and interpersonal relationships, including (1) the protective effect of OT on an individual's ability to withstand stress (i.e., stress buffering), (2) the effect of OT on emotion recognition and empathy, (3) OT's ability to enhance social synchrony and cooperation among individuals, and (4) the effect of OT on an individual's perception of social touch. We then illustrate the connection between OT and loneliness while grieving the loss of a loved one. We finish by discussing the clinical potential of OT, focusing on its potential role as an adjunct to psychotherapy, its enhancement through sex-specific hormonal influences, and the difficulties that present themselves when considering OT as a therapy. Overall, we argue that OT continues to hold strong therapeutic promise, but that it is strongly dependent on internal and external influences, for instance the patient's personal past experiences and interaction with the therapist in order to provide the best possible therapy.

Keywords Oxytocin • Psychotherapy • Social relationship • Social synchrony • Social touch • Stress

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1 The Role of Oxytocin in Non-kin, Interpersonal Relationships

Research surrounding the role of oxytocin (OT) in social neuroscience has exploded in recent years, evolving from initial studies shedding light on OT's contribution to mother–infant bonding (see for instance Fahrbach et al. 1986; Kendrick et al. 1987; Newton and Newton 1967; Pedersen and Prange 1985) and social memory in animals (see for instance Dantzer et al. 1987; Popik and Vetulani 1991). More recent studies have focused on social neuroscience paradigms to explore OT's role on behaviors such as empathy (Hurlemann et al. 2010), or even OT's ability to increase an individual's tendency to anthropomorphize inanimate objects (Scheele et al. 2015). Our current ability to employ OT in an experimental setting is in part due to the ease and harmlessness of its administration and use. By far the most common method of application, intranasal oxytocin spray has been consistently shown to increase cerebrospinal fluid oxytocin levels in both humans (Striepens et al. 2013) and macaques (Freeman et al. 2016; for studies including aerosolized OT, see Chang et al. 2012; Dal Monte et al. 2014; Modi et al. 2014), indicating that OT most likely enters the brain and has a direct effect on central OT levels.

Interestingly, OT effects seem to have a strong reward-based component, as authors consistently show that the dopaminergic and oxytocinergic pathways share several common realms. OT's positive effect on bonding behavior appears to be dependent on a dopaminergic pathway, suggesting a strong reward component in feelings of love and interpersonal relationships (Kendrick 2004). Altogether, findings suggest that arginine-vasopressin/oxytocinergic pathways influence partner preferences, but their specific interactions with other neurotransmitter and hormonal systems such as dopamine, serotonin, and sex steroids are still elusive (Hurlemann and Scheele 2016).

This chapter aims to explore the role of OT in non-kin, interpersonal relationships, with the ultimate goal of examining OT's potential in treating psychiatric

disorders characterized by difficulties in forming or maintaining meaningful bonds. Relationship formation is an innately social process, and while there are cognitive aspects involved, such as a learned evaluation or labeling of another individual's facial emotion (cognitive empathy), there is no aspect that is completely unhinged from a social element. To this end, findings regarding OT's effect on social realms within relationships differ. We focus on four main areas that are most important to inducing and maintaining relationships, including the protective effect of OT on an individual's ability to withstand stress (stress buffering), the effect of OT on emotion recognition and empathy, OT's ability to enhance social synchrony and cooperation among individuals, and the effect of OT on an individual's perception of social touch. Following this, OT's role following the loss of a loved one and in loneliness is outlined. Finally, the potential for OT as an augmentation of psychotherapy, along with the possible modulation of OT via hormonal pathways, and lastly the roadblocks still in place before OT can be considered a viable treatment option are discussed.

1.1 The Effects of Oxytocin in a Social Versus Nonsocial Setting

The exponential amount of social neuroscience literature has allowed an initial differentiation between OT's effects in social versus nonsocial settings. Whereas studies report a plethora of findings surrounding the nasal administration of synthetic OT in social settings, findings of oxytocinergic effects in nonsocial settings are fewer and further between.

Initial literature focused on OT's effects on prosocial behavior, and nasal delivery of OT was found to reduce amygdala activity while viewing emotional faces (Domes et al. 2007a, b; Kanat et al. 2015) and to improve emotion recognition and mind reading (Domes et al. 2007a, b; Lischke et al. 2012; Schulze et al. 2011).

In an early study of OT's effect on learning in a social versus nonsocial feedback setting, we found that while participants performed significantly better under OT when given social feedback (i.e., a smiling or frowning face following a correct or incorrect response during a memory task), they fared no better than participants given placebo when they received nonsocial feedback (i.e., a red or a green light) (Hurlemann et al. 2010). The beneficial effect of OT was therefore specifically limited to the social condition, even given a completely nonsocial task. In this pioneer study, we were able to show an isolated effect of OT on a social setting, therefore providing a basis for further research, in which we showed that OT has a vital influence on the perception of interpersonal relationships, described in the following sections. The finding that OT can augment social but not nonsocial feedback was recently replicated in a functional magnetic resonance imaging (fMRI) study that traced the effect to increased activity in the amygdala, hippocampus, parahippocampal gyrus, and putamen and increased connectivity between the amygdala, insula, and caudate, suggesting that OT increased emotional significance and feelings of reward following social feedback (Hu et al. 2015).

Interestingly, Rimmele and colleagues showed that OT selectively increased participants' feelings of familiarity with a face, but not a nonsocial object, while it did not influence the recollection of the face (Rimmele et al. 2009). Two further studies provide evidence that OT shapes perception of biological, but not non-biological, motion. Alpha/mu and beta electroencephalography (EEG) ranges, which decrease while observing biological motion (Perry et al. 2010; Ulloa and Pineda 2007), were even further reduced when participants were given OT (Perry et al. 2010). Keri and Benedek showed that OT not only modulated perception of biological versus non-biological motion, but also enabled participants to recognize increasingly reduced biological qualities, thereby showing heightened sensitivity to the biological motion. The authors postulate a lack of OT effect on brain regions responsible for non-biological motion (Keri and Benedek 2009). Both studies avoided using an explicitly and immediately recognizable human form, instead employing a type of stick-figure made of up dots on a screen, therefore differentiating between the recognition of human qualities and an effect of motion. Taken together, the studies listed above present a strong case for the role of OT in influencing social and biological stimuli important to strengthening interpersonal bonds.

1.2 Oxytocin and the Mirror Neuron Network

First described in the ventral premotor cortex (PMC) of the monkey brain (di Pellegrino et al. 1992; Gallese et al. 1996), mirror neurons have remained a source of controversy and interest for human social cognition research. In humans, mirror neurons have been described as a system comprising the inferior frontal gyrus (Kilner et al. 2009), inferior parietal cortex (Chong et al. 2008), dorsal PMC (Molenberghs et al. 2012), the supplemental motor area and medial temporal lobe (Mukamel et al. 2010), and the superior parietal lobe (Iacoboni et al. 1999). Collectively, the mirror neuron network (MNN) has been found to respond during social processing, specifically fear processing (Becker et al. 2012; Mihov et al. 2013) and empathy (Brown et al. 2013), for instance.

Initial findings suggest that the MNN is at least in some capacity regulated by the oxytocinergic system. Healthy participants given OT show a reduced ability to control motor imitation (De Coster et al. 2014) as well as a reduced ability to suppress somatosensory regions while viewing biologic motion (Perry et al. 2010). In psychiatric patient populations, reduced OT appears to influence MNN dysfunction, such as in autism spectrum disorder (Odent 2010; Brang and Ramachandran 2010) or anorexia nervosa (Odent 2010).

In support of the effect of OT on MNN activity is the hypothesis that endogenous OT secretion may be increased when a person is being imitated (Aoki and Yamasue 2015; Aoki et al. 2014). Furthermore, both OT (Aoki et al. 2014) and being imitated (Delaveau et al. 2015) activate the right insula, indicating a possibly reciprocal relationship between OT and the MNN to increase prosocial behavior. In a study of patients with autism spectrum disorder, viewing the face of an unfair player during a ball toss game activated the right insula following exogenous OT administration,

suggesting support for the notion that OT is vital to feelings of social judgments (Andari et al. 2016).

In a romantic relationship setting, feelings of love and of understanding are based in part on a reciprocal interaction between two partners who share an extreme familiarity with one another's thoughts and actions. Given OT's role in the MNN, and the MNN's role in increasing feelings of reciprocality, OT modulation on the MNN is an important avenue with which to improve relationship formation and maintenance.

1.3 Oxytocin and Romantic Relationships

A landmark study showed that while OT did not increase total communication during a couple's conflict, it did increase positive communication in relation to negative communication (Ditzen et al. 2009). This suggests that OT changes a person's willingness to communicate, but instead it causes a new evaluation of stimuli to make the person's communication more socially productive. It did not cause participants to handle irrationally, but instead to better direct their communication.

Perhaps because of its utmost importance or its close connection to the mechanisms underlying addiction and reward (Insel and Young 2001), love, pair bonding, and the role of OT in relationships have been a consistent focus of study for the past several years. In one study involving patients with autism spectrum disorder, patients given OT showed increased blood-oxygen-level dependent (BOLD) response in regions important to face processing, including the inferior occipital gyrus and fu-siformgyrus, thereby presenting a response more typical of healthy individuals (Andari et al. 2016). As the authors point out, OT increased social adaptation by improving social judgment. Furthermore, patients in a ball-toss game showed increased mid-orbitofrontal cortex (OFC) response when presented with a fair partner and increased insula response when presented with an unfair partner (Andari et al. 2016).

Increasingly, OT has been shown to have a facilitative effect on interpersonal relationships, correlating with nonverbal affection (Gonzaga et al. 2006) and increasing empathy (Schneiderman et al. 2014a; Hurlemann et al. 2010) and trust (Kosfeld et al. 2005; Baumgartner et al. 2008; Krueger et al. 2012). Findings show that OT may even enable relationship formation with objects (Fürst et al. 2015) and facilitate approach in women by reducing personal space between participants and a male experimenter (Preckel et al. 2014). In a study of OT's effect on male–female attraction, males given OT rated unfamiliar females as being more attractive than under placebo (Striepens et al. 2014). Interestingly, however, this effect was not mirrored by increases in dopaminergic activity, as detailed below. It could therefore be that OT acts as a mediator of approach, making it easier for males and females to build social bonds, but in a less rewarding sense than a romantic or sexual attraction would provide. Support for this notion comes from another study showing that males given OT are affected differently according to whether or not they are in a monogamous relationship, and pair-bonded males keep a greater distance between themselves and an attractive woman (Scheele et al. 2012). Indeed, males who receive OT prior to viewing

their female partner's face in a photograph rate her as more attractive compared to an unfamiliar woman. On the neural level, this effect was paralleled by enhanced activity in the ventral tegmental area and nucleus accumbens (Scheele et al. 2013). Altogether, the findings speak for OT's potential to ease bonding between men and women, but at the same time to maintain and strengthen romantic bonds in an approach and avoidance setting by not jeopardizing an already existing relationship.

One pioneer theory surrounding OT's influence on partnership proposes that OT, along with vasopressin, could be released when an organism feels safe, and therefore increases intimacy among individuals via vagus and sympathetic nerve stimulation (Porges 1998). OT has indeed been suggested to contribute to its own release in a positive feedback loop (Moos et al. 1984). Grewen et al. postulate a kind of cycle of increasing OT levels: where there are high OT levels, there is a greater partner bond, and where there is a greater partner bond, the partners engage in physical contact and show emotional support more often, in turn increasing OT levels. Interestingly, the study shows an isolated effect of OT on physiological parameters, such as systolic blood pressure, in that blood pressure decreased only during the period of increased OT – it was not the direct human contact that improved health, but rather the indirect increase of OT through contact (Grewen et al. 2005).

Other findings support oxytocinergic interaction with further neurotransmitter systems. As mentioned above, the rewarding aspects of loving relationships are likely mediated by dopaminergic pathways (Kendrick 2004) and so far the only positron emission tomography (PET) study to use the d2-receptor radioligand [11C]raclopride found an increased perfusion rate in the striatum but this enhanced striatal activity was not accompanied by an altered endogenous dopamine release in the striatum or pallidum following intranasal administration of OT (Striepens et al. 2014). Instead the authors observed an increased [11C]raclopride binding and thus reduced dopamine release in the right dorsomedial prefrontal gyrus and superior parietal gyrus. The absence of an OT effect on striatal dopamine release could be related to the lack of a salient social context, as highly attractive, but unfamiliar faces instead of bonding-specific stimuli (e.g., the participant's romantic partner or own child) were used in that study. However, it is also conceivable that OT interacts with other neurotransmitter systems to produce the bonding-related effects. The rewarding properties of social interaction could also be mediated by the coordinated activity of OT and serotonin in the nucleus accumbens (Dölen et al. 2013). In fact, another human PET study observed a modulatory impact of OT on serotonin signaling (Mottolese et al. 2014).

Genetic variations in the OT receptor have been found to contribute to cross-cultural differences in social behavior and relationships. Variants of the OT single nucleotide polymorphisms (SNPs) rs7632287 (Walum et al. 2012), rs53576 (Ditzen et al. 2012), and the cumulative risk of oxytocin receptor (OTR) variants rs13316193, rs2254298, rs1042778, rs2268494, and rs226849 (Schneiderman et al. 2014b), for example, have a negative impact on social relationships.

Studies of endogenous OT levels have found that new lovers show higher levels OT than singles do, and that these levels correlate with positive relationship traits, such as affectionate touch and synchrony (Schneiderman et al. 2012). At the early stage of romantic love, individuals whose partners had higher OT levels also showed greater

empathy (Schneiderman et al. 2014a) and OT concentrations are more tightly coupled with biomarkers of the reward (beta endorphin) and stress-response systems (interleukin-6, IL-6) (Ulmer-Yaniv et al. 2016). Furthermore, positive romantic interactions with a partner could have a cumulative effect on OT levels, both at a resting state but also following physical contact and emotional support (Grewen et al. 2005; Holt-Lunstad et al. 2011). In addition, whereas positive relationships can have a beneficial effect on health, couple conflicts can increase sympathetic activity (Ditzen et al. 2013). OT seems to strengthen the positive aspects of intimate couple relationships, for example by dampening increased sympathetic activity and increasing positive behavior during couple conflict (Ditzen et al. 2009, 2013). Interestingly, participants in romantic relationships who recalled more conflict memories of their current romantic partner under OT compared to placebo were more likely to separate from their partner during the following 18 months (Cardoso et al. 2016a).

Despite the vast evidence supporting a facilitative role of OT in relationships, there are some findings suggesting that this facilitation is strongly dependent on the context of the relationship. For example, Cardoso et al. (2016a) also observed that OT not only decreased the recall of conflict memories of past romantic partners but also reduced affiliation memories of current romantic partners. The authors point out that this effect was more pronounced in individuals in a longer relationship, possibly suggesting that the OT effect is moderated by the relationship duration. Furthermore, in individuals prone to physical aggression, OT increased the probability that they would engage in various aggressive behaviors after two provocation tasks (DeWall et al. 2014). Also, Liu et al. found that even though OT increased participants' preference for someone they were introduced to following OT administration, the effects of OT were limited to participants merely wanting to get to know another person of either sex better – participants did not show an increased heterosexual romantic interest in the person per se (Liu et al. 2013a). These findings may appear to be contradictory at the surface, but as Carter suggests in line with the "calm and connection" model (Uvanas-Moberg et al. 2005), the role of OT and other neuropeptides could lie in paving the way for behaviors beneficial to forming relationships by blocking negative, defensive behaviors that make relationships difficult to create and sustain (Carter 1998). This hypothesis would make relationship formation dependent on the context and external factors, rather than on an intrinsic ability of OT to create bonds. It is noteworthy, however, that there is also an opposing interpretation of OT's function in human pair-bonding. In accordance with observations that elevated plasma OT may index relationship distress in women (Taylor et al. 2010; Tabak et al. 2011), Taylor et al. (2006) put forth a "tend and befriend" model of affiliative responses to stress. This model proposes that social stress due to perceived gaps in positive social relationships is accompanied by elevations in plasma OT to prompt affiliative efforts aimed at restoring positive social contacts. Positive social contacts in turn may lead to a reduction of stress responses.

1.4 The Protective Effects of Oxytocin on Stress Response

Although the common wisdom that married couples live longer is likely based on a multitude of psychological, social, physiological, and epidemiological factors, there is evidence that it is the case, and that being married presents a protective effect on an individual's health (see for instance King and Reis 2012). OT has been found to vary according to relationship quality (Light et al. 2005; Grewen et al. 2005) and according to the element of social support in a stressful context (Heinrichs et al. 2003). The following section will therefore examine the role of OT in enhancing individual ability to withstand stress, and how OT and stress are linked in interpersonal relationships.

Not just limited to the psychological realm, psychosocial stress can have dangerous physiological effects. Consistent with the assumptions of the "tend and befriend" model, some studies have reported that acute stress can induce the release of endogenous OT. For instance, both physical stressors such as heavy exercise (Hew-Butler et al. 2008a, b), uncontrollable noise (Sanders et al. 1990), listening to unpleasant music (Jezova et al. 2013), abdominal surgery (Nussey et al. 1988), or psychosocial stress induced by the Trier Social Stress Test (TSST) (Engert et al. 2016; Jong et al. 2015; Pierrehumbert et al. 2010) have been found to be associated with an increase in peripheral OT concentrations (plasma or saliva).

By contrast, there are also several studies that failed to detect significant changes in OT concentrations following physical (Altemus et al. 1995, 2001; Chicharro et al. 2001; Forsling and Williams 2002) or psychosocial stress (Cyranowski et al. 2008; Ditzen et al. 2007; Doom et al. 2016; Grewen and Light 2011; Heinrichs et al. 2001; Jansen et al. 2006; Moons et al. 2014; Smith et al. 2013). It is currently unclear which factors mediate these divergent findings. One possibility is that these heterogeneous observations are related to methodological problems of the OT measurement (McCullough et al. 2013).

Another explanation is that stress affects OT concentration differently in men and women. In fact, in some studies OT elevations were only evident in women, but not in men (Sanders et al. 1990; Seltzer et al. 2013). An obvious mechanism for these sexual dimorphic effects is differences in gonadal steroids such as estrogen and indeed women using hormonal contraception (Pierrehumbert et al. 2010) and postmenopausal women on estrogen replacement therapy show higher baseline OT plasma concentrations (Light et al. 2005). On the other hand, the hormonal status of women does not unequivocally affect the stress-induced OT response (Altemus et al. 2001; Engert et al. 2016). However, in contrast to the model proposed by Campbell (2010), Taylor et al. (2006) postulate that OT specifically signals relationship distress. In women who were one hormonal therapy, Taylor and colleagues observed no significant changes of OT concentrations after psychosocial stress, but elevated plasma OT was significantly associated with gaps in social relationships (but see also Smith et al. 2013). Along these lines, Tabak et al. (2011) asked women who had recently experienced interpersonal harm to focus their attention on problematic qualities of a single relationship. They found that the task-induced elevated OT reactivity, but not baseline OT levels, were associated with

increased post-conflict anxiety and decreased levels of forgiveness. Thus, relationship distress could sensitize the OT system for subsequent stressful experiences.

Despite the controversies regarding stress-induced OT release, there is strong evidence that OT has a protective effect on health. In animals, OT reduces the risk of artherosclerosis by reducing interleukin (IL)-6 secretion in macrophages and endothelial cells, both in vitro and in mice with greater levels of artherosclerosis due to conditions of social isolation (Szeto et al. 2008; Nation et al. 2010). Moreover, people with higher levels of endogenous OT show faster rates of healing (Gouin et al. 2010). Partner studies show that endogenous OT correlates with greater partner support (Light et al. 2005; Grewen et al. 2005), and with physiological parameters including lower risk of infection and some cancers (Uvnäs-Moberg et al. 2015), lower systolic blood pressure (Light et al. 2005; Grewen et al. 2005), and lower levels of noradrenaline, illustrating a potentially (cardio)protective mechanism of partnerships (Grewen et al. 2005).

Coronary heart disease (Kivimäki et al. 2012), cancer (Cohen et al. 2007), and major depression (Krishnan and Nestler 2008) are among the illnesses most often associated with stress. Increased neural activity in response to psychosocial stress has been found in the cingulate and insular cortices, precuneus, hypothalamus, and frontotemporal regions (Dedovic et al. 2009, 2014; Soliman et al. 2011). Resilience to psychosocial stress tremendously varies between individuals, and has become an increasingly salient focus of stress research. In particular, the role of social support as a counter mechanism to social stress, and the potential augmentation of social support through OT is an interesting therapeutic approach.

Findings in monogamous and highly social prairie voles show that the voles provide social support to stressed conspecifics and even present a similar increase in corticosterone and fear response, paralleled by increased activity in the anterior cingulate cortex (ACC) (Burkett et al. 2016). When given an OT-receptor (OTR) antagonist, the voles showed no such response, suggesting a role of OT in empathy and social support in stressful circumstances (Burkett et al. 2016). In humans, however, findings are somewhat murkier.

Genetic studies demonstrate a link between OTR polymorphisms and stress reactivity. For instance, individuals with one or two copies of the A allele (rs53576) exhibited higher heart rate responses during a startle anticipation task (Rodrigues et al. 2009). Participants with the GG/AG genotypes reported seeking more emotional social support in times of distress (Kim et al. 2010) and during social support interactions (Kanthak et al. 2016) and a stronger attenuation of the cortisol response to psychosocial stress (Chen et al. 2011). However, there are also studies showing that G/G individuals have significantly higher sympathetic cardiac reactivity in response to a psychological stressor (Norman et al. 2012) and are more reactive to ostracism (i.e., higher cortisol response) (McQuaid et al. 2015). These conflicting findings could be reconciled by taking into account moderator variables. It seems that the OTR gene variant interacts with rejection sensitivity (Auer et al. 2015), maltreatment history (Hostinar et al. 2014), as well as gender and poststressor levels of plasma OT (Moons et al. 2014).

Several studies used intranasal OT as a pharmacological probe to examine possible anti-stress effects of OT. It has been found that exogenous OT inhibits the hypothalamic–pituitary–adrenal (HPA) axis and reduces baseline cortisol concentrations, and this effect was attenuated in men with early parental separation (Meinlschmidt and Heim 2007). By contrast, a recent study did not detect any significant effect of OT baseline cortisol in men and women (Wirth et al. 2015), although it should be noted that this study did not assess early lifetime experiences.

Importantly, exogenous OT reduced cortisol stress response during the TSST when participants received social support from a friend (Heinrichs et al. 2003). However, if social support is not available OT may enhance self-referential processing and thereby the subjective awareness of the stressor (Eckstein et al. 2014). In fact, a meta-analysis of the OT effect on cortisol response to laboratory tasks revealed a modest, nonsignificant effect size (Cardoso et al. 2014b). The OT effect was larger in response to challenging laboratory tasks that produced a robust stimulation of the HPA axis. Furthermore, interindividual differences such as emotion regulation abilities (Quirin et al. 2011) and early life stress (Grimm et al. 2014) have been identified as additional moderator variables of the OT effect. Also, one study found a dose-dependent OT effect such that 24 international units (IU) reduced the cortisol response to physical stress, while there was no effect of 48 IU (Cardoso et al. 2013). In line with the "tend and befriend" model, OT given to women in distress increases the motivation to affiliate with the experimenter (Cardoso et al. 2016b). Against this theoretical background, it seems likely that anti-stress and anti-nociceptive effects (Eisenberger et al. 2011; Younger et al. 2010) of social support provided by the romantic partner are mediated by oxytocinergic mechanisms. Future pharmacological studies are warranted to test this hypothesis.

1.5 Oxytocin's Influence on Emotion Recognition and Empathy

At the core of both romantic and unromantic relationship formation is the ability to recognize social signals in the form of emotions in another individual. In a further step, an empathic response to these emotional signals is more likely to maintain and strengthen a bond than an unempathic response. OT's ability to influence emotion recognition and enhance empathy is thus a core building block of healthy interpersonal relationships. In a pioneer study, we found that OT increased emotional empathy in men while they viewed photographs of people in different contexts, but had no effect on their ability to correctly recognize the emotion shown (i.e., cognitive empathy) (Hurlemann et al. 2010). In a recent review, Gonzalez-Liencres et al. (2013) suggest that the difference in OT's effect on the emotional or affective versus the cognitive component of empathy could be explained by interactions with other neurochemical pathways, and that OT is likely more important to emotional empathy, with opioids, dopaminergic, and serotonergic pathways also playing a part. An interaction

between OT and dopamine has been especially present in the literature surrounding social cognitive behavior and interpersonal relationships (Gonzalez-Liencres et al. 2013; Kendrick 2004).

In a meta-analysis of single-dose OT administration and facial emotions, OT was shown to increase emotion recognition, specifically for happy (Marsh et al. 2010; Shahrestani et al. 2013) and fearful faces (Shahrestani et al. 2013; Fischer-Shofty et al. 2010). When presented with a neutral face that morphed to show either a happy or an angry expression, participants given OT gazed at the happy face more than at the angry face (Domes et al. 2013). OT additionally slowed reaction time in participants presented with ambiguous emotions that represented fearful faces, but also increased accuracy overall in terms of correct classification of an ambiguous face showing either positive or negative emotions (Di Simplicio et al. 2009).

The increase in emotion recognition applies to a variety of paradigms, including masked (Schulze et al. 2011) or dynamic faces (Lischke et al. 2012), and participants given OT recognize emotions at a lower intensity and direct more attention to facial stimuli than do those given placebo (Prehn et al. 2013). In a related finding, participants given OT rated emotions (happiness, excitement, sadness, fear, anger, surprise, and disgust) more intensely than under placebo (Cardoso et al. 2014a). Both findings support the notion that OT increases emotional salience. Interestingly, this lowered threshold for recognition could represent a trade-off for accuracy, as participants actually performed worse when it came to emotion identification (Cardoso et al. 2014a).

OT furthermore intensifies the perception of emotion when accompanied by a gentle human touch: researchers found that when given OT and while being touched gently, participants rated frowning faces more negatively and smiling faces more positively (Ellingsen et al. 2014). OT widened the gap between how the positive and negative emotions were perceived, which could be interpreted as being facilitative of group survival – whereas bonds between individuals perceived as friendly grow stronger, the mental distance between perceived adversaries grows farther apart. This notion is supported by findings showing that OT increases ethnocentric, in-group bias and out-group derogation, specifically by increasing in-group favoritism (De Dreu et al. 2011; for a review see De Dreu and Kret 2016). Feelings of in-group favoritism could, in a more general sense, be manifested in altruistic behavior towards someone a person or participant feels pity for, or feels the need to protect compared to someone the participant perceives as a threat. In a recent study, we collaborated to show that participants were more willing to make altruistic monetary decisions following OT administration (Hu et al. 2016). This effect was traced to the temporo-parietal junction, which is important to theory of mind and mentalizing (Schaafsma et al. 2015; Schurz and Perner 2015; Schurz et al. 2014; Frith and Frith 2006).

We additionally showed that the effect of OT's influence on sociality in altruistic settings even extends to more abstract settings, as we found when participants were asked to donate money to either a social or ecological charity. We found that although OT did not cause participants to behave irrationally and donate significantly greater sums of money, it did cause a shift in donations from ecological to social charities, suggesting that OT's effects on prosocial behavior even extend to a more

abstract definition of interpersonal relationships in the form of a charity to help others (Hurlemann and Marsh 2016; Marsh et al. 2015).

Genetic findings suggest that variations in the OTR have crucial effects of empathy in healthy populations. Participants carrying the G allele of the rs53576 polymorphism show greater empathic accuracy (Rodrigues et al. 2009; Laursen et al. 2014) and empathy (Bakermans-Kranenburg and van Ijzendoorn 2008; Tost et al. 2010; Smith et al. 2014), for example, than A allele carriers. The association between the OTR genotype and empathic concern seems to be moderated by gender (Christ et al. 2014) and culture values (Luo et al. 2015). In men, the influence of the OTR gene on cognitive empathy as measured by the "Reading the Mind in the Eyes Test (RMET)" was also dependent on fetal testosterone, indexed by the second-to-forth digit ratio (Weisman et al. 2015). In terms of in-group favoritism, participants with the OTR rs53576 G/G allele activated the ACC and supplementary motor area when viewing members of their own racial group in pain (Luo et al. 2015), both of which regions have been associated with the brain's pain and empathy for pain (Singer et al. 2004). Participants with the A/A allele showed the greatest response in the nucleus accumbens to out-group pain, an area that is associated with feelings of reward (Luo et al. 2015; Pedersen et al. 2011). Furthermore, G/G participants perceived the pain of in-group others more intensely than participants with the A/A allele.

Studies of exogenous OT administration in patient populations have been somewhat mixed. Intranasal OT administration in patients with schizophrenia has been shown to increase ability to comprehend indirect emotion expression (Davis et al. 2013; Guastella et al. 2015; Woolley et al. 2014), as well as emotion recognition, perspective taking, and social cognition (Averbeck et al. 2011; Gibson et al. 2014; Pedersen et al. 2011; for a review see Tan et al. 2016). Patients were also more adept at social perception, including identification of kinship and intimacy following OT (Fischer-Shofty et al. 2013). On the other hand, findings show no effect of OT on emotion recognition (Horta de Macedo et al. 2014). Interestingly, Goldman et al. (2011) found a dose- and subset-dependent relationship between OT and fear recognition: whereas 10 IU of OT in schizophrenic patients actually decreased emotion recognition, it improved following 20 IU OT in polydipsic patients after the authors isolated a fear-identification bias (Goldman et al. 2011). Interestingly, findings suggest that OT most influences higher-order cognitive emotional processing in schizophrenia, as opposed to more basic, affective processes (Guastella et al. 2015; Davis et al. 2013).

1.6 Oxytocin Induces Social Synchrony and Cooperation

Social synchrony and the coordination of the behaviors of different people in a group are often apparent although unconscious (LaFrance 1979; Noy et al. 2011; Schmidt and Richardson 2008; Richardson et al. 2007; Tognoli et al. 2007; Sebanz et al. 2006; Chartrand and Bargh 1999; Bernieri and Rosenthal 1991; Bernieri et al. 1988). Social synchrony can have the effect of increasing reciprocity and feelings

of familiarity, and although the evolutionary benefits to social synchrony revolve in large part around survival in group settings, it is also key building block of modern, interpersonal relationships.

Initial studies show that OT improves paired performance in a computerized drawing task (Arueti et al. 2013) and enhanced alpha-band interbrain neural oscillations during a coordination task (Mu et al. 2016). Findings in military veterans who have been in life-threatening combat situations additionally show synchrony among non-related, non-romantically involved participants presumably highly practiced in working together (Levy et al. 2015). When combat veterans were exposed to short videos of social scenes and of combat scenes, both produced social synchrony in neural regions related to social processing, as measured by magnetoencephalography (MEG). Combat veterans given placebo showed increased response to combat scenes in regions included in the mirror neuron network, but were comparable to controls when given OT. The authors suggest that the MNN "selectively responds to social synchrony pending OT intake and prior social-group experiences," and that OT had an anxiolytic effect on combat veterans (Levy et al. 2015). Further evidence for a close link between OT and social synchrony comes from a recent study showing that synchronous social interactions evoke heightened endogenous OT release in dyadic partners (Spengler et al. 2017). Subsequently, elevated OT levels among highly synchronized interacting partners can enhance emotion transmission of social information since OT made signals of happiness and fear more salient in both facial and vocal expressions.

1.7 Oxytocin Modulates the Experience of Social Touch

Recent research has shown that neural response to human social touch differs remarkably based on the specific type of touch, the person perceived to be doing the touching, and the characteristics of the person being touched. For instance, the sensual caress of the romantic partner is experienced as highly pleasant, while the same touch by a stranger can be aversive. Unsurprisingly, tactile physical affection positively correlates with overall relationship and partner satisfaction (Gulledge et al. 2004). In heterosexual males, being touched by an attractive woman activates the somatosensory cortex differently than by another man (Gazzola et al. 2012). Whereas several different nerve endings can perceive touch, social touch is found to differentially activate the unmyelinated, C-tactile afferents (Löken et al. 2009) and project to the insula. Further areas that are important to processing the emotional value of social touch include the pregenual ACC and the OFC (Scheele et al. 2014a).

Findings support an effect of social touch on OT concentrations and an effect of OT on the perceived touch itself. Studies have found increased endogenous OT release following a massage (Morhenn et al. 2012; Turner et al. 1999; Wikström et al. 2003), and "warm touch" between married participants (Holt-Lunstad et al. 2008). Interestingly, the context of touch seems to be vital to the release of OT: Morhenn and colleagues found that OT was only increased if the participant experienced an act of trust prior to a massaging touch, but not when there was no prior trust question (Morhenn

et al. 2008). Furthermore, the participants who experienced an act of trust and were given a massage following it also showed vast increases in generosity during a game involving monetary sacrifice, leading the authors to postulate that OT increased gratitude in the participants (Morhenn et al. 2008).

The effects of OT on how social touch is perceived seem to be additionally dependent on context factors such as the relationship between the two participants involved in the touch. One study found no OT effect on pleasantness ratings of the touch (Ellingsen et al. 2014). However, this study did not control for gender-related influences. We therefore examined how male participants responded differently to touch delivered from a female versus a male (Scheele et al. 2014a). Overall, the male participants consistently rated the touch as being more pleasant when they believed it was given by a woman than another man, and this effect was magnified in the group given OT. This effect was traced to the pregenual ACC, which has previously been found to be involved in pleasant skin-to-skin touch (Lindgren et al. 2012; Rolls et al. 2003). Interestingly, the OT effect on pleasantness ratings also negatively correlated with autistic traits in the male participants, indicating that those participants with higher levels of autistic traits benefited less from OT, perhaps because they displayed a lower sensitivity to OT's effects in this specific domain. Furthermore, the magnifying effect of OT on pleasantness ratings was only found in response to perceived female touch, and OT had no effect when the male participants thought they were being touched by another male.

The results of the studies detailed above suggest that the effects of OT are strongly dependent on context, including gender but also interactions with other psychological frameworks, such as levels of trust or familiarity with the person giving the touch.

1.8 Oxytocin, Loss of a Loved One, and Loneliness

Despite very early suggestions in the literature that OT could influence psychological illness in the face of loss of a loved one or early dysfunctional relationships (see for example Pedersen and Prange 1985), it is only recently that researchers have placed a stronger focus on the physiological (detrimental) effects of such loss. No longer is there a clear definition between mind and body when it comes to love; whereas the protective effects of relationships were reported above, there are also substantial negative effects of the loss of such a relationship. Acute grief following the loss of a romantic relationship has been linked to the pain network, including the anterior cingulate cortex and insula (Najib et al. 2004), indicating that the suffering following such a loss can have vast physiological consequences. As Carter and Porges write, "a 'broken heart' or a failed relationship can have disastrous effects; bereavement disrupts human physiology and might even precipitate death. Without loving relationships, humans fail to flourish, even if all of their other basic needs are met" (Carter and Porges 2013). Yet it is not only a failure to flourish: several studies have shown that grief following loss can have even damaging effects. For instance, in socially monogamous

prairie voles, isolation leads to physiological, metabolic, and hormonal changes that are commonly found in major depression (Grippo et al. 2007a, b, 2012). Indeed, the unexpected death of a loved one is associated with elevated risk for the onset of multiple psychiatric disorders, in particular major depressive disorder, panic disorder, and posttraumatic stress disorder (Keyes et al. 2014). Loss of a loved one can result in social isolation and chronic feelings of loneliness. In a recent meta-analysis, loneliness and social isolation were shown to result in a 26% increase in morbidity and mortality (Holt-Lunstad et al. 2015). Among its many implications, loneliness leads to increased risk for coronary heart disease and stroke (Valtorta et al. 2016), major depression (Cacioppo et al. 2010), cognitive decline (Shankar et al. 2013), and dementia (Holwerda et al. 2014).

Exogenous OT has been found to counteract the physiological, but not the behavioral, effects of social isolation in prairie voles (Grippo et al. 2012). In a further study building on these findings, both male and female prairie voles were found to respond to chronic social isolation by down-regulation of OTR expression, but in females, OT secretion was also greater, suggesting that females present with a better buffer against the detrimental effects of social isolation (Pournajafi-Nazarloo et al. 2013). Additional findings suggest a role of OTR gene methylation in social anxiety disorder, suggesting a strong epigenetic component in reduced OTR expression in deficient social abilities (Ziegler et al. 2015).

In humans, pathological or dysfunctional relationships show correlations with OT levels. Patients with borderline personality disorder (BPD), an illness characterized in part by disorganized attachment representations and an inability to form stable interpersonal relationships, show lower OT plasma levels (Bertsch et al. 2013; Jobst et al. 2016). In a recent study examining the effect of OT on volitional and emotional ambivalence, participants who were told to imagine their partners' infidelity were less aroused following OT administration (Preckel et al. 2015). This could indicate that OT strengthened perception of the bond with the partner, shown by reduced emotional ambivalence, such that OT could have an overall positive effect on the relationship despite a negative framework.

Interestingly, very recent findings show that plasma OT is actually increased in patients diagnosed with complicated grief compared to bereaved individuals diagnosed with major depressive disorder and bereaved but healthy controls, suggesting that OT plays a specific role in the loss of a social relationship, but not in a general increase in sadness overall (Bui et al. 2016). These findings appear on the surface to be contradictory to what one might expect. However, we suggest two possible explanations: For one, the oxytocinergic pathway could present a mechanism of (over)-compensation via up-regulation following a sudden disruptive social event. Second, it could be that OT response is increased due to the chronic stress involved in complicated grief. The question therefore remains open, what the acute, potentially protective effects of intranasal OT admininstration could be. Indirect evidence in support for the idea that OT could have beneficial effects after the loss of al relationship comes from a recent study showing that OT may enhance the cognitive control of food craving in women (Striepens et al. 2016). Thus, improved emotion regulation abilities could help to cope with the emotional turmoils following the dissolution of relationships.

2 Translating Nasal Oxytocin to the Clinic

Amidst the multitude of studies that aim to determine OT's effects on interpersonal relationships (and vice versa), the question arises how OT could be used in a clinical context. Unfortunately, methodological issues make efforts to hone in on OT's exact role in the social neuroscience literature difficult to achieve. The relationship between peripheral and central OT concentrations is not clear (Carson et al. 2015; Kagerbauer et al. 2013), and peripheral OT levels are still difficult to measure persuasively (McCullough et al. 2013). Indeed, the implications for a possible enhancement of positive relationship qualities are vast. Given that the threshold for pain is higher given social support, OT could be a valuable add-on therapy in chronic or acute pain situations if its application were to enhance the perception of social support, especially considering its own analgesic qualities (Goodin et al. 2014; Madrazo et al. 1987; Paloyelis et al. 2016).

Findings from the literature show that OT is clearly not a cut and dried monotherapy option, despite OTR polymorphisms being implicated in several psychiatric illnesses characterized by social and interpersonal deficits (for a review, see Aspe-Sanchez et al. 2015). But could OT be used as an add-on, or augmentation, to improve the efficacy of current therapeutic methods? The following section aims to elaborate on how far OT has already begun to establish its role as a viable treatment option in problems of interpersonal relationships, and to explore the most promising avenues for OT's use in the future.

2.1 Oxytocin as a Potential Adjunct to Psychotherapy

So far, studies aiming to augment psychotherapy with OT and improve treatment efficacy have had somewhat mixed results. On the one hand, OT seems to show either no or even detrimental effects when paired with psychotherapy. For instance, OT combined with social cognition training over 6 weeks showed no effect of OT on social cognition, symptom severity, or social functioning in patients with early psychosis (Cacciotti-Saija et al. 2015). Patients with major depression showed increased anxiety during therapy when given OT prior to a "first contact" session (MacDonald et al. 2013), and in a study of exposure therapy for arachnophobia, OT was found to reduce treatment response (Acheson et al. 2015).

On the other hand, OT appears to have a beneficial effect on context- and symptom-specific domains. In patients with schizophrenia, long-term OT daily over 4 months improved emotional processing without concurrent psychotherapy (Brambilla et al. 2016) and when paired with social cognitive training over 6 weeks, OT improved empathic accuracy (Davis et al. 2014). Additionally, OT combined with exposure therapy lead to patients with social anxiety disorder showing improved positive evaluations regarding appearance and speech performance over 5 weeks (Guastella et al. 2009), and

depressed patients showing fewer nonverbal flight behaviors and improved theory of mind over a single therapy session (MacDonald et al. 2013).

One of the most important realms of OT's augmentation of psychotherapy, however, could well be in its potential to enhance therapeutic alliance, or the positive and productive relationship between the therapist and the patient. Successful psychotherapy relies on communication and understanding between the patient and therapist and on the patient's perception of different aspects of the therapist's character, for example trustworthiness (Horvath and Greenberg 1989; Ackermann and Hilsenroth 2003). As OT has been found to enhance trust in others (Baumgartner et al. 2008; Kosfeld et al. 2005), it is highly conceivable that it could enhance therapeutic alliance and therefore positively impact a psychotherapy session by effectively magnifying desirable traits in the therapist as perceived by the patient.

Although the studies above present a foggy picture of OT's potential use in the augmentation of psychotherapy in terms of concrete functions, there is reason to believe that it could have an overlying umbrella function of enhancing therapeutic alliance. There are still too few studies to define clear circumstances and parameters under which OT's mechanisms can best be manipulated in a therapeutic setting. It is probable that OT affects isolated functions, such as emotion recognition, and that this effect is not seen in studies examining a broad category, such as social cognition. It could also be that even these very isolated functions are dependent on an interaction with context, and that OT's effect on exposure therapy in arachnophobia lacked a social element that is per se included in exposure therapy with speech giving. Methodological issues are most likely a large source of conflict between study findings. Overall, the beneficial effects of OT speak for its potential role in psychotherapy augmentation, despite the differing findings in the literature (Hurlemann 2017).

2.2 A Hormonal Boost of Oxytocin Effects?

Several studies have shown sexually dimorphic effects of OT on behavioral and neural changes in various domains ranging from social approach/avoidance behavior (Preckel et al. 2014; Scheele et al. 2012) and social perception (Fischer-Shofty et al. 2012) to moral decision-making (Scheele et al. 2014b). One interesting approach to explaining these differences is the possible influence of hormones on OT's effects. For instance, estrogen has been found to moderate OT activity, availability, and receptor binding (Amico and Hempel 1990; Amico et al. 1981, 1997, 2002; Insel and Young 2001; Light et al. 2005; Petersson et al. 1999). In a recent experiment, Karlsson and colleagues provided evidence for a direct link between androgen and OT receptors and the expression of social behaviors, and that the androgen receptor plays a role in OTR expression (Karlsson et al. 2016).

In humans, sex differences have been found in neural regions associated with empathy and the MNN (Brown et al. 2013; Cheng et al. 2009). Interestingly, in an early study, we showed that males displayed levels of empathy roughly equal to those displayed by females only after males were administered with intranasal OT, suggesting

that not only are there inherent sex differences in empathic behavior, but also that these sex differences are mediated by OT (Hurlemann et al. 2010). Importantly, sex differences in OT binding are dependent on menstrual cycle. Rats in the estrus phase show greater OTR binding levels in several forebrain areas compared to rats in non-estrus phase, and rats with maternal experience showed higher levels of OTR binding in the medial amygdala compared to rats with no previous maternal experience (Dumais et al. 2013).

Previous findings have laid the foundation for newer studies that are increasingly taking sex differences and more specifically female participants' menstrual cycles into account. However, exogenous hormonal modulation, i.e., hormonal contraception, has also been shown to crucially affect bonding-related OT effects (Scheele et al. 2016). Specifically, in women not using hormonal contraception OT enhanced a positive bias in the attractiveness perception of the partner and boosted the neural response to the partner's face in reward-associated brain areas, that is the nucleus accumbens and ventral tegmental area, while there was no such effect in women using hormonal contraception. Given that women using hormonal contraception had lower estradiol plasma levels and that an estrogen pretreatment in female mice enhances anxiolytic OT actions (McCarthy et al. 1996), a combined estradiol-OT treatment could potentially yield more robust prosocial effects.

2.3 Difficulties of Oxytocin Therapy

One of the greatest difficulties in proposing a future clinical, therapeutic role for OT in improving dysfunctional interpersonal relationships and prevent social isolation after loss of a loved one is the current inability to accurately and precisely define risk, for the most part because the exact mechanisms of OT's effects are still unknown (Hurlemann 2017). As discussed above, the potential for negative effects of OT have been increasingly apparent, for example as a function of personality traits of participants (Bartz et al. 2010), in-group/out-group factors (for a review, see De Dreu and Kret 2016), or context (Olff et al. 2013; Scheele et al. 2012).

Reports of decreased cortisol levels following intranasal OT (Cardoso et al. 2013; Ditzen et al. 2009; Meinlschmidt and Heim 2007) are countered by reports of unchanged (Burri et al. 2008; de Oliveira et al. 2012a, b; McRae-Clark et al. 2013; Simeon et al. 2011) or even increased cortisol levels (Weisman et al. 2013). More worrisome are reports of transient anxiogenesis when OT is given as an adjunct to psychotherapy (MacDonald et al. 2013). Interestingly, while OT was shown by our lab to increase initial both feelings of social stress and stress-related response in the cingulate and precuneus, it was not found to increase cortisol levels in our paradigm (Eckstein et al. 2014), providing support for the suggestion that OT serves to increase a processing bias while reflecting on one's own negative feelings (Bryant et al. 2012; Liu et al. 2013b) while not actually increasing cortisol-based stress-response per se. The lack of increased cortisol levels following OT in our study could mean that an increase

in awareness of the stressor on behalf of the participant neutralizes the buffering effects of OT when the participant is given social support (Eckstein et al. 2014).

Despite the plethora of findings suggesting a positive, protective effect of OT in romantic relationships, some findings seem glaringly contradictory. For instance, two studies have found that plasma OT correlates with stress or anxiety in relationships (Marazziti et al. 2006; Taylor et al. 2010), suggesting that romantic relationships in humans are far from clear cut, but rather represent a double-edged sword, resulting in both happiness but also distress in partners. Moreover, increased OT levels following couple conflicts correlate with increased anxiety and reduced willingness to forgive (Tabak et al. 2011). Taylor and colleagues suggest that endogenous OT is a marker of relationship distress and cortisol stress response and with a less positive relationship overall (Taylor et al. 2006). Even in a non-romantic context, participants given OT report feeling less emotional support when faced with a computer, rather than a human experimenter, while relating negative emotional memories (Cardoso et al. 2016b). Indeed, a recent study found that OT facilitates feelings of social stress, mirrored by increases in activity in the precuneus and cingulate cortex, suggesting an increased self-referential processing bias that could have potentially damaging effects during psychotherapy (Eckstein et al. 2014; Hurlemann 2017).

3 Concluding Remarks

The understanding of OT has evolved from having a purely hormonal effect to taking a central role in the social neuroscience of interpersonal relationships via its neurotransmission. It has only begun to be explored as a potential therapeutic option for patients with difficulties in forming and maintaining interpersonal relationships. Methodological issues and conflicting findings in general hamper efforts to clearly define its role in the future of treatment augmentation, although this currently appears to be the most promising use of OT in a clinical setting (for a review, see Striepens et al. 2011). Additionally, the effects of OT seem to be strongly dependent on sex and context, for instance (Hurlemann 2017). Overall, findings speak for OT as a helpful tool for maintaining relationships rather than forming current ones (Hurlemann and Scheele 2016). This speaks for its potential in augmenting a psychotherapeutic relationship, which is strengthened over several therapy sessions. More specifically, OT's potential as an enhancer of therapeutic alliance is not to be overlooked as a core future use of OT in psychotherapy. A therapist's personal qualities as perceived by the patient are of utmost importance to a successful psychotherapy session (Ackermann and Hilsenroth 2003), and an enhancement of this perception could improve psychotherapy efficacy.

Furthermore, OT seems to act as a magnifier of self-referential processing, so that individuals give emotional experiences more salience (Hurlemann and Scheele 2016). OT's effect is therefore less dependent on an intrinsic ability of OT to act as a prosocial or antisocial influence, but more as an enhancer of feelings in social settings (Eckstein and Hurlemann 2013). This helps to explain conflicting findings of both positive and negative effects of OT in social settings. This also means that OT's use in a therapeutic

setting would be necessarily dependent on the patient's previous experiences and thought processes when he or she entered therapy, so as not to exacerbate any tenuous psychiatric conditions he or she may have. It is clear that the clinical perspectives of OT deserve attention and far more research in both healthy and psychiatric populations, as it has already begun to show great potential as a therapeutic agent.

References

Acheson DT, Feifel D, Kamenski M, McKinney R, Risbrough VB (2015) Intranasal oxytocin administration prior to exposure therapy for arachnophobia impedes treatment response. Depress Anxiety 32(6):400–407

Ackermann SJ, Hilsenroth MJ (2003) A review of therapist characteristics and techniques positively impacting the therapeutic alliance. Clin Psychol Rev 23(1):1–33

Altemus M, Deuster PA, Galliven E, Carter CS, Gold PW (1995) Suppression of hypothalmic-pituitary-adrenal axis responses to stress in lactating women. J Clin Endocrinol Metab 80(10):2954–2959

Altemus M, Roca C, Galliven E, Romanos C, Deuster P (2001) Increased vasopressin and adrenocorticotropin responses to stress in the midluteal phase of the menstrual cycle. J Clin Endocrinol Metab 86(6):2525–2530

Amico JA, Hempel J (1990) An oxytocin precursor intermediate circulates in the plasma of humans and rhesus monkeys administered estrogen. Neuroendocrinology 51(4):437–443

Amico JA, Seif SM, Robinson AG (1981) Elevation of oxytocin and the oxytocin-associated neurophysin in the plasma of normal women during midcycle. J Clin Endocrinol Metab 53(6):1229–1232

Amico JA, Thomas A, Hollingshead DJ (1997) The duration of estradiol and progesterone exposure prior to progesterone withdrawal regulates oxytocin mRNA levels in the paraventricular nucleus of the rat. Endocr Res 23(3):141–156

Amico JA, Rauk PN, Cai HM (2002) Estradiol and progesterone regulate oxytocin receptor binding and expression in human breast cancer cell lines. Endocrine 18(1):79–84

Andari E, Richard N, Leboyer M, Sirigu A (2016) Adaptive coding of the value of social cues with oxytocin, an fMRI study in autism spectrum disorder. Cortex 76:79–88

Aoki Y, Yamasue H (2015) Reply: does imitation act as an oxytocin nebulizer in autism spectrum disorder? Brain 138(7):e361

Aoki Y, Yahata N, Watanabe T, Takano Y, Kawakubo Y, Kuwabara H et al (2014) Oxytocin improves behavioural and neural deficits in inferring others' social emotions in autism. Brain 137 (11):3073–3086

Arueti M, Perach-Barzilay N, Tsoory MM, Berger B, Getter N, Shamay-Tsoory SG (2013) When two become one: the role of oxytocin in interpersonal coordination and cooperation. J Cogn Neurosci 25(9):1418–1427

Aspe-Sanchez M, Moreno M, Rivera MI, Rossi A, Ewer J (2015) Oxytocin and vasopressin receptor gene polymorphisms: role in social and psychiatric traits. Front Neurosci 9:510

Auer BJ, Byrd-Craven J, Grant DM, Granger DA (2015) Common oxytocin receptor gene variant interacts with rejection sensitivity to influence cortisol reactivity during negative evaluation. Horm Behav 75:64–69

Averbeck BB, Bobin T, Evans S, Shergill SS (2011) Emotion recognition and oxytocin in patients with schizophrenia. Psychol Med 42(2):259–266

Bakermans-Kranenburg MJ, van Ijzendoorn MH (2008) Oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes associated with observed parenting. Soc Cogn Affect Neurosci 3 (2):128–134

Bartz JA, Zaki J, Bolger N, Hollander E, Ludwig NN, Kolevzon A, Ochsner KN (2010) Oxytocin selectively improves empathic accuracy. Psychol Sci 21(10):1426–1428

Baumgartner T, Heinrichs M, Vonlanthen A, Fischbacher U, Fehr E (2008) Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. Neuron 58(4):639–650

Becker B, Mihov Y, Scheele D, Kendrick KM, Feinstein JS, Matusch A et al (2012) Fear processing and social networking in the absence of a functional amygdala. Biol Psychiatry 72(1):70–77

Bernieri FJ, Rosenthal R (1991) Interpersonal coordination: behavior matching and interactional synchrony. In: Stephen R, Rimé B (eds) Fundamentals of nonverbal behavior. Cambridge University Press, New York, pp 401–432

Bernieri FJ, Reznick JS, Rosenthal R (1988) Synchrony, pseudosynchrony, and dissynchrony: measuring the entrainment process in mother-infant interactions. J Pers Soc Psychol 54(2):243–253

Bertsch K, Schmidinger I, Neumann ID, Herpertz SC (2013) Reduced plasma oxytocin levels in female patients with borderline personality disorder. Horm Behav 63(3):424–429

Brambilla M, Cotelli M, Manenti R, Dagani J, Sisti D, Rocchi M et al (2016) Oxytocin to modulate emotional processing in schizophrenia: a randomized, double-blind, cross-over clinical trial. Eur Neuropsychopharmacol 26(10):1619–1628

Brang D, Ramachandran VS (2010) Olfactory bulb dysgenesis, mirror neuron system dysfunction, and autonomic dysregulation as the neural basis for autism. Med Hypotheses 74(5):919–921

Brown LL, Acevedo B, Fisher HE (2013) Neural correlates of four broad temperament dimensions: testing predictions for a novel construct of personality. PLoS One 8(11):e78734

Bryant RA, Hung L, Guastella AJ, Mitchell PB (2012) Oxytocin as a moderator of hypnotizability. Psychoneuroendocrinology 37(1):162–166

Bui THE, Rosencrans P, Hoeppner S, Ross R, Hoge E, Simon N (2016) Circulating levels of oxytocin in complicated grief. Poster presented at the annual meeting for the American College of Neuropsychopharmacology, Orlando, FL

Burkett JP, Andari E, Johnson ZV, Curry DC, de Waal FBM, Young LJ (2016) Oxytocin-dependent consolation behavior in rodents. Science 351(6271):375–378

Burri A, Heinrichs M, Schedlowski M, Kruger TH (2008) The acute effects of intranasal oxytocin administration on endocrine and sexual function in males. Psychoneuroendocrinology 33(5):591–600

Cacciotti-Saija C, Langdon R, Ward PB, Hickie IB, Scott EM, Naismith SL et al (2015) A double-blind randomized controlled trial of oxytocin nasal spray and social cognition training for young people with early psychosis. Schizophr Bull 41(2):483–493

Cacioppo JT, Hawkley LC, Thisted RA (2010) Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago health, aging, and social relations study. Psychol Aging 25(2):453–463

Campbell A (2010) Oxytocin and human social behavior. Personal Soc Psychol Rev 14(3):281–295. [Review]

Cardoso C, Ellenbogen MA, Orlando MA, Bacon SL, Joober R (2013) Intranasal oxytocin attenuates the cortisol response to physical stress: a dose-response study. Psychoneuroendocrinology 38(3):399–407. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]

Cardoso C, Ellenbogen MA, Linnen AM (2014a) The effect of intranasal oxytocin on perceiving and understanding emotion on the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). Emotion 14(1):43–50

Cardoso C, Kingdon D, Ellenbogen MA (2014b) A meta-analytic review of the impact of intranasal oxytocin administration on cortisol concentrations during laboratory tasks: moderation by method and mental health. Psychoneuroendocrinology 49:161–170. [Meta-Analysis Research Support, Non-U.S. Gov't Review]

Cardoso C, Kalogeropoulos C, Brown CA, Orlando MA, Ellenbogen MA (2016a) Memory response to oxytocin predicts relationship dissolution over 18 months. Psychoneuroendocrinology 68:171–176

Cardoso C, Valkanas H, Serravalle L, Ellenbogen MA (2016b) Oxytocin and social context moderate social support seeking in women during negative memory recall. Psychoneuroendocrinology 70:63–69

Carson DS, Berquist SW, Trujillo TH, Garner JP, Hannah SL, Hyde SA et al (2015) Cerebrospinal fluid and plasma oxytocin concentrations are positively correlated and negatively predict anxiety in children. Mol Psychiatry 20(9):1085–1090

Carter CS (1998) Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology 23(8):779–818. doi:10.1016/S0306-4530(98)00055-9
Carter CS, Porges SW (2013) The biochemistry of love: an oxytocin hypothesis. EMBO Rep 14 (1):12–16
Chang SW, Barter JW, Ebitz RB, Watson KK, Platt ML (2012) Inhaled oxytocin amplifies both vicarious reinforcement and self reinforcement in rhesus macaques (Macaca mulatta). Proc Natl Acad Sci U S A 109:959–964
Chartrand TL, Bargh JA (1999) The chameleon effect: the perception–behavior link and social interaction. J Pers Soc Psychol 76(6):893–910
Chen FS, Kumsta R, von Dawans B, Monakhov M, Ebstein RP, Heinrichs M (2011) Common oxytocin receptor gene (OXTR) polymorphism and social support interact to reduce stress in humans. Proc Natl Acad Sci U S A 108(50):19937–19942. [Research Support, Non-U.S. Gov't]
Cheng Y, Chou KH, Decety J, Chen IY, Hung D, Tzeng OJ, Lin CP (2009) Sex differences in the neuroanatomy of human mirror-neuron system: a voxel-based morphometric investigation. Neuroscience 158(2):713–720
Chicharro JL, Hoyos J, Bandres F, Gomez Gallego F, Perez M, Lucia A (2001) Plasma oxytocin during intense exercise in professional cyclists. Horm Res 55(3):155–159. [Research Support, Non-U.S. Gov't]
Chong TTJ, Cunnington R, Williams MA, Kanwisher N, Mattingley JB (2008) fMRI adaptation reveals mirror neurons in human inferior parietal cortex. Curr Biol 18(20):1576–1580
Christ CC, Carlo G, Stoltenberg SF (2014) Oxytocin receptor (OXTR) single nucleotide polymorphisms indirectly predict prosocial behavior through perspective taking and empathic concern. J Pers 84(2):204–213
Cohen S, Janicki-Deverts D, Miller GE (2007) Psychological stress and disease. JAMA 298 (14):1685–1687
Cyranowski JM, Hofkens TL, Frank E, Seltman H, Cai HM, Amico JA (2008) Evidence of dysregulated peripheral oxytocin release among depressed women. Psychosom Med 70 (9):967–975. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]
Dal Monte O, Noble PL, Turchi J, Cummins A, Averbeck BB (2014) CSF and blood oxytocin concentration changes following intranasal delivery in macaque. PLoS One 9(8):e103677
Dantzer R, Bluthe RM, Koob GF, Le Moal M (1987) Modulation of social memory in male rats by neurohypophyseal peptides. Psychopharmacology 91(3):363–368
Davis MC, Lee J, Horan WP, Clarke AD, McGee MR, Green MF, Marder SR (2013) Effects of single dose intranasal oxytocin on social cognition in schizophrenia. Schizophr Res 147(2–3):393–397
Davis MC, Green MF, Lee J, Horan WP, Senturk D, Clarke AD, Marder SR (2014) Oxytocin-augmented social cognitive skills training in schizophrenia. Neuropsychopharmacology 39 (9):2070–2077
De Coster L, Mueller SC, T'Sjoen G, Saedeleer LD, Brass M (2014) The influence of oxytocin on automatic motor simulation. Psychoneuroendocrinology 50:220–226
De Dreu CK, Kret ME (2016) Oxytocin conditions intergroup relations through upregulated in-group empathy, cooperation, conformity, and defense. Biol Psychiatry 79(3):165–173
De Dreu CKW, Greer LL, Van Kleef GA, Shalvi S, Handgraaf MJJ (2011) Oxytocin promotes human ethnocentrism. Proc Natl Acad Sci U S A 108(4):1262–1266
de Oliveira DC, Zuardi AW, Graeff FG, Queiroz RH, Crippa JA (2012a) Anxiolytic-like effect of oxytocin in the simulated public speaking test. J Psychopharmacol 26(4):497–504
de Oliveira DC, Chagas MH, Garcia LV, Crippa JA, Zuardi AW (2012b) Oxytocin interference in the effects induced by inhalation of 7.5% CO(2) in healthy volunteers. Hum Psychopharmacol 27(4):378–385
Dedovic K, D'Aguiar C, Pruessner JC (2009) What stress does to your brain: a review of neuroimaging studies. Can J Psychiatr 54(1):6–15

Dedovic K, Duchesne A, Engert V, Lue SD, Andrews J, Efanov SI et al (2014) Psychological, endocrine and neural responses to social evaluation in subclinical depression. Soc Cogn Affect Neurosci 9(10):1632–1644

Delaveau P, Arzounian D, Rotgé J, Nadel J, Fossati P (2015) Does imitation act as an oxytocin nebulizer in autism spectrum disorder? Brain 138(7):e360

DeWall CN, Gillath O, Pressman SD, Black LL, Bartz JA, Moskovitz J, Stetler DA (2014) When the love hormone leads to violence: oxytocin increases intimate partner violence inclinations among high trait aggressive people. Soc Psychol Personal Sci 5(6):691–697

di Pellegrino G, Fadiga L, Fogassi L, Gallese V, Rizzolatti G (1992) Understanding motor events: a neurophysiological study. Exp Brain Res 91(1):176–180

Di Simplicio M, Massey-Chase R, Cowen PJ, Harmer CJ (2009) Oxytocin enhances processing of positive versus negative emotional information in healthy male volunteers. J Psychopharmacol 23(3):241–248

Ditzen B, Neumann ID, Bodenmann G, von Dawans B, Turner RA, Ehlert U, Heinrichs M (2007) Effects of different kinds of couple interaction on cortisol and heart rate responses to stress in women. Psychoneuroendocrinology 32(5):565–574. [Comparative Study Research Support, Non-U.S. Gov't]

Ditzen B, Schaer M, Gabriel B, Bodenmann G, Ehlert U, Heinrichs M (2009) Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. Biol Psychiatry 65(9):728–731. [Controlled Clinical Trial Research Support, Non-U.S. Gov't]

Ditzen B, Bradley B, Heim CM (2012) Oxytocin and pair bonding: on possible influences during the life course. Biol Psychiatry 72(3):3–4

Ditzen B, Nater UM, Schaer U, La Marca R, Bodenmann G, Ehlert U, Heinrichs M (2013) Sex-specific effects of intranasal oxytocin on autonomic nervous system and emotional responses to couple conflict. Soc Cogn Affect Neurosci 8(8):897–902

Dölen G, Darvishzadeh A, Huang KW, Malenka RC (2013) Social reward requires coordinated activity of accumbens oxytocin and 5HT. Nature 501(7466):179–184

Domes G, Heinrichs M, Glascher J, Buchel C, Braus DF, Herpertz SC (2007a) Oxytocin attenuates amygdala responses to emotional faces regardless of valence. Biol Psychiatry 62(10):1187–1190. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]

Domes G, Heinrichs M, Michel A, Berger C, Herpertz SC (2007b) Oxytocin improves "mind-reading" in humans. Biol Psychiatry 61(6):731–733. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]

Domes G, Steiner A, Porges SW, Heinrichs M (2013) Oxytocin differentially modulates eye gaze to naturalistic social signals of happiness and anger. Psychoneuroendocrinology 38(7):1198–1202

Doom JR, Doyle CM, Gunnar MR (2016) Social stress buffering by friends in childhood and adolescence: effects on HPA and oxytocin activity. Soc Neurosci 25:1–14

Dumais KM, Bredewold R, Mayer TE, Veenema AH (2013) Sex differences in oxytocin receptor binding in forebrain regions: correlations with social interest in brain region- and sex-specific ways. Horm Behav 64(4):693–701

Eckstein M, Hurlemann R (2013) Oxytocin: evidence for a therapeutic potential of the social neuromodulator. Nervenarzt 84(11):1321–1328

Eckstein M, Scheele D, Weber K, Stoffel-Wagner B, Maier W, Hurlemann R (2014) Oxytocin facilitates the sensation of social stress. Hum Brain Mapp 35(9):4741–4750

Eisenberger NI, Master SL, Inagaki TK, Taylor SE, Shirinyan D, Lieberman MD, Naliboff BD (2011) Attachment figures activate a safety signal-related neural region and reduce pain experience. Proc Natl Acad Sci U S A 108(28):11721–11726

Ellingsen D-M, Wessberg J, Chelnokova O, Olausson H, Laeng B, Leknes S (2014) In touch with your emotions: oxytocin and touch change social impressions while others' facial expressions can alter touch. Psychoneuroendocrinology 39:11–20

Engert V, Koester AM, Riepenhausen A, Singer T (2016) Boosting recovery rather than buffering reactivity: higher stress-induced oxytocin secretion is associated with increased cortisol reactivity and faster vagal recovery after acute psychosocial stress. Psychoneuroendocrinology 74:111–120

Fahrbach SE, Morrell JI, Pfaff DW (1986) Effect of varying the duration of pre-test cage habituation on oxytocin induction of short-latency maternal behavior. Physiol Behav 37(1):135–139
Fischer-Shofty M, Shamay-Tsoory SG, Harari H, Levkovitz Y (2010) The effect of intranasal administration of oxytocin on fear recognition. Neuropsychologia 48(1):179–184
Fischer-Shofty M, Levkovitz Y, Shamay-Tsoory SG (2012) Oxytocin facilitates accurate perception of competition in men and kinship in women. Soc Cogn Affect Neurosci 8(3):313–317
Fischer-Shofty M, Brüne M, Ebert A, Shefet D, Levkovitz Y, Shamay-Tsoory SG (2013) Improving social perception in schizophrenia: the role of oxytocin. Schizophr Res 146(1–3):357–362
Forsling ML, Williams AJ (2002) The effect of exogenous melatonin on stimulated neurohypophysial hormone release in man. Clin Endocrinol 57(5):615–620. [Clinical Trial Randomized Controlled Trial]
Freeman SM, Samineni S, Allen PC, Stockinger D, Bales KL, Hwa GG, Roberts JA (2016) Plasma and csf oxytocin levels after intranasal and intravenous oxytocin in awake macaques. Psychoneuroendocrinology 66:185–194
Frith CD, Frith U (2006) The neural basis of mentalizing. Neuron 50(4):531–534
Fürst A, Thron J, Scheele D, Marsh N, Hurlemann R (2015) The neuropeptide oxytocin modulates consumer brand relationships. Sci Rep 5:14960
Gallese V, Fadiga L, Fogassi L, Rizzolatti G (1996) Action recognition in the premotor cortex. Brain 119:593–609
Gazzola V, Spezio ML, Etzel JA, Castelli F, Adolphs R, Keysers C (2012) Primary somatosensory cortex discriminates affective significance in social touch. Proc Natl Acad Sci U S A 109 (25):1657–1666
Gibson CM, Penn DL, Smedley KL, Leserman J, Elliott T, Pedersen CA (2014) A pilot six-week randomized controlled trial of oxytocin on social cognition and social skills in schizophrenia. Schizophr Res 156(2–3):261–265
Goldman M, Marlow-O'Connor M, Torres I, Carter CS (2008) Diminished plasma oxytocin in schizophrenic patients with neuroendocrine dysfunction and emotional deficits. Schizophr Res 98(1–3):247–255
Goldman MB, Gomes AM, Carter CS, Lee R (2011) Divergent effects of two different doses of intranasal oxytocin on facial affect discrimination in schizophrenic patients with and without polydipsia. Psychopharmacology 216(1):101–110
Gonzaga GC, Turner RA, Keltner D, Campos B, Altemus M (2006) Romantic love and sexual desire in close relationships. Emotion 6:163–179
Gonzalez-Liencres C, Shamay-Tsoory SG, Brüne M (2013) Towards a neuroscience of empathy: ontogeny, phylogeny, brain mechanisms, context and psychopathology. Neurosci Biobehav Rev 37(8):1537–1548
Goodin BR, Anderson AJ, Freeman EL, Bulls HW, Robbins MT, Ness TJ (2014) Intranasal oxytocin administration is associated with enhanced endogenous pain inhibition and reduced negative mood states. Clin J Pain. doi:10.1097/AJP.0000000000000166
Gouin J-P, Carter CS, Pournajafi-Nazarloo H, Glaser R, Malarkey WB, Loving TJ et al (2010) Marital behavior, oxytocin, vasopressin, and wound healing. Psychoneuroendocrinology 35(7):1082–1090
Grewen KM, Light KC (2011) Plasma oxytocin is related to lower cardiovascular and sympathetic reactivity to stress. Biol Psychol 87(3):340–349. [Research Support, N.I.H., Extramural]
Grewen KM, Girdler SS, Amico J, Light KC (2005) Effects of partner support on resting oxytocin, cortisol, norepinephrine, and blood pressure before and after warm partner contact. Psychosom Med 67(4):531–538
Grimm S, Pestke K, Feeser M, Aust S, Weigand A, Wang J et al (2014) Early life stress modulates oxytocin effects on limbic system during acute psychosocial stress. Soc Cogn Affect Neurosci 9(11):1828–1835
Grippo AJ, Lamb DG, Carter CS, Porges SW (2007a) Cardiac regulation in the socially monogamous prairie vole. Physiol Behav 90(2–3):386–393

Grippo AJ, Cushing BS, Carter CS (2007b) Depression-like behavior and stressor-induced neuroendocrine activation in female prairie voles exposed to chronic social isolation. Psychosom Med 69(2):149–157

Grippo AJ, Trahanas DM, Zimmerman RR, Porges SW, Carter CS (2009) Oxytocin protects against negative behavioral and autonomic consequences of long-term social isolation. Psychoneuroendocrinology 34(10):1542–1553

Grippo AJ, Pournajafi-Nazarloo H, Sanzenbacher L, Trahanas DM, McNeal N, Clarke DA et al (2012) Peripheral oxytocin administration buffers autonomic but not behavioral responses to environmental stressors in isolated prairie voles. Stress 15(2):149–161

Guastella AJ, Howard AL, Dadds MR, Mitchell P, Carson DS (2009) A randomized controlled trial of intranasal oxytocin as an adjunct to exposure therapy for social anxiety disorder. Psychoneuroendocrinology 34(6):917–923

Guastella AJ, Ward PB, Hickie IB, Shahrestani S, Hodge MAR, Scott EM, Langdon R (2015) A single dose of oxytocin nasal spray improves higher-order social cognition in schizophrenia. Schizophr Res 168(3):628–633

Gulledge AK, Stahmann RF, Wilson CM (2004) Seven types of nonsexual romantic physical affection among Brigham young university students. Psychol Rep 95:609–614

Heinrichs M, Meinlschmidt G, Neumann I, Wagner S, Kirschbaum C, Ehlert U, Hellhammer DH (2001) Effects of suckling on hypothalamic-pituitary-adrenal axis responses to psychosocial stress in postpartum lactating women. J Clin Endocrinol Metab 86(10):4798–4804. [Clinical Trial Randomized Controlled Trial]

Heinrichs M, Baumgartner T, Kirschbaum C, Ehlert U (2003) Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. Biol Psychiatry 54(12):1389–1398

Hew-Butler T, Jordaan E, Stuempfle KJ, Speedy DB, Siegel AJ, Noakes TD et al (2008a) Osmotic and nonosmotic regulation of arginine vasopressin during prolonged endurance exercise. J Clin Endocrinol Metab 93(6):2072–2078. [Clinical Trial Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]

Hew-Butler T, Noakes TD, Soldin SJ, Verbalis JG (2008b) Acute changes in endocrine and fluid balance markers during high-intensity, steady-state, and prolonged endurance running: unexpected increases in oxytocin and brain natriuretic peptide during exercise. Eur J Endocrinol 159 (6):729–737. [Comparative Study Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]

Holt-Lunstad J, Birmingham WA, Light KC (2008) Influence of a "warm touch" support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol. Psychosom Med 70(9):976–985

Holt-Lunstad J, Birmingham WA, Light KC (2011) The influence of depressive symptomatology and perceived stress on plasma and salivary oxytocin before, during and after a support enhancement intervention. Psychoneuroendocrinology 36(8):1249–1256

Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D (2015) Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci 10(2):227–237

Holwerda TJ, Deeg DJ, Beekman AT, van Tilburg TG, Stek ML, Jonker C, Schoevers RA (2014) Feelings of loneliness, but not social isolation, predict dementia onset: results from the Amsterdam Study of the Elderly (AMSTEL). J Neurol Neurosurg Psychiatry 85(2):135–142

Horta de Macedo LR, Zuardi AW, Machado-de-Sousa JP, Chagas MHN, Hallak JEC (2014) Oxytocin does not improve performance of patients with schizophrenia and healthy volunteers in a facial emotion matching task. Psychiatry Res 220(1–2):125–128

Hostinar CE, Cicchetti D, Rogosch FA (2014) Oxytocin receptor gene polymorphism, perceived social support, and psychological symptoms in maltreated adolescents. Dev Psychopathol 26:465–477. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]

Horvath AO, Greenberg LS (1989) Development and validation of the Working Alliance Inventory. J Couns Psychol 36(2):223–233

Hu J, Qi S, Becker B, Luo L, Gao S, Gong Q et al (2015) Oxytocin selectively facilitates learning with social feedback and increases activity and functional connectivity in emotional memory and reward processing regions. Hum Brain Mapp 36(6):2132–2146
Hu Y, Scheele D, Becker B, Voos G, David B, Hurlemann R, Weber B (2016) The effect of oxytocin on third-party altruistic decisions in unfair situations: an fMRI study. Sci Rep 6:20236
Hurlemann R (2017) Oxytocin-augmented psychotherapy: beware of context. Neuropsychopharmacology 42(1):377
Hurlemann R, Marsh N (2016) New insights into the neuroscience of human altruism. Nervenarzt 87(11):1131–1135. [English abstract]
Hurlemann R, Scheele D (2016) Dissecting the role of oxytocin in the formation and loss of social relationships. Biol Psychiatry 79(3):185–193
Hurlemann R, Patin A, Onur OA, Cohen MX, Baumgartner T, Metzler S et al (2010) Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. J Neurosci 30(14):4999–5007
Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G (1999) Cortical mechanisms of human imitation. Science 286(5449):2526–2528
Insel TR, Young LJ (2001) The neurobiology of attachment. Nat Rev Neurosci 2:129–136
Jansen LM, Gispen-de Wied CC, Wiegant VM, Westenberg HG, Lahuis BE, van Engeland H (2006) Autonomic and neuroendocrine responses to a psychosocial stressor in adults with autistic spectrum disorder. J Autism Dev Disord 36(7):891–899. [Research Support, Non-U.S. Gov't]
Jezova D, Hlavacova N, Makatsori A, Duncko R, Loder I, Hinghofer-Szalkay H (2013) Increased anxiety induced by listening to unpleasant music during stress exposure is associated with reduced blood pressure and ACTH responses in healthy men. Neuroendocrinology 98:144–150. [Research Support, Non-U.S. Gov't]
Jobst A, Padberg F, Mauer MC, Daltrozzo T, Bauriedl-Schmidt C, Sabass L et al (2016) Lower oxytocin plasma levels in borderline patients with unresolved attachment representations. Front Hum Neurosci 10:125
Jong TR, Menon R, Bludau A, Grund T, Biermeier V, Klampfl SM et al (2015) Salivary oxytocin concentrations in response to running, sexual self-stimulation, breastfeeding and the TSST: the Regensburg oxytocin challenge study. Psychoneuroendocrinology 62:381–388. [Research Support, Non-U.S. Gov't]
Kagerbauer SM, Martin J, Schuster T, Blobner M, Kochs EF, Landgraf R (2013) Plasma oxytocin and vasopressin do not predict neuropeptide concentrations in human cerebrospinal fluid. J Neuroendocrinol 25(7):668–673
Kanat M, Heinrichs M, Mader I, van Elst LT, Domes G (2015) Oxytocin modulates amygdala reactivity to masked fearful eyes. Neuropsychopharmacology 40(11):2632–2638
Kanthak MK, Chen FS, Kumsta R, Hill LK, Thayer JF, Heinrichs M (2016) Oxytocin receptor gene polymorphism modulates the effects of social support on heart rate variability. Biol Psychol 117:43–49
Karlsson SA, Studer E, Kettunen P, Westberg L (2016) Neural androgen receptors modulate gene expression and social recognition but not social investigation. Front Behav Neurosci 10:41
Kendrick KM (2004) The neurobiology of social bonds. J Neuroendocrinol 16(12):1007–1008
Kendrick KM, Keverne EB, Baldwin BA (1987) Intracerebroventricular oxytocin stimulates maternal behaviour in the sheep. Neuroendocrinology 46(1):56–61. [Research Support, Non-U.S. Gov't]
Keri S, Benedek G (2009) Oxytocin enhances the perception of biological motion in humans. Cogn Affect Behav Neurosci 9(3):237–241
Keyes KM, Pratt C, Galea S, McLaughlin KA, Koenen KC, Shear MK (2014) The burden of loss: unexpected death of a loved one and psychiatric disorders across the life course in a national study. Am J Psychiatry 171(8):864–871
Kilner JM, Neal A, Weiskopf N, Friston KJ, Frist CD (2009) Evidence of mirror neurons in human inferior frontal gyrus. J Neurosci 29(32):10153–10159

Kim HS, Sherman DK, Sasaki JY, Xu J, Chu TQ, Ryu C et al (2010) Culture, distress, and oxytocin receptor polymorphism (OXTR) interact to influence emotional support seeking. Proc Natl Acad Sci U S A 107(36):15717–15721. [Research Support, U.S. Gov't, Non-P.H.S.]

King KB, Reis HT (2012) Marriage and long-term survival after coronary artery bypass grafting. Health Psychol 31(1):55–62

Kivimäki M, Nyberg ST, Batty GD, Fransson EI, Heikkilä K, Alfredsson L et al (2012) Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. Lancet 380(9852):1491–1497

Kosfeld M, Heinrichs M, Zak PJ, Fischbacher U, Fehr E (2005) Oxytocin increases trust in humans. Nature 435(7042):673–676

Krishnan V, Nestler EJ (2008) The molecular neurobiology of depression. Nature 455(7215):894–902

Krueger F, Parasuraman R, Iyengar V, Thornburg M, Weel J, Lin M et al (2012) Oxytocin receptor genetic variation promotes human trust behavior. Front Hum Neurosci 6:4

LaFrance M (1979) Nonverbal synchrony and rapport: analysis by the cross-lag panel technique. Soc Psychol Q 42(1):66–70

Laursen HR, Siebner HR, Haren T, Madsen K, Grønlund R, Hulme O, Henningsson S (2014) Variation in the oxytocin receptor gene is associated with behavioral and neural correlates of empathic accuracy. Front Behav Neurosci 8:423

Levy J, Goldstein A, Zagoory-Sharon O, Weisman O, Schneiderman I, Eidelman-Rothman M, Feldman R (2015) Oxytocin selectively modulates brain response to stimuli probing social synchrony. NeuroImage 124(Pt A):923–930

Light KC, Grewen KM, Amico JA, Brownley KA, West SG, Hinderliter AL, Girdler SS (2005) Oxytocinergic activity is linked to lower blood pressure and vascular resistance during stress in postmenopausal women on estrogen replacement. Horm Behav 47(5):540–548. [Clinical Trial Randomized Controlled Trial Research Support, N.I.H., Extramural Research Support, U.S. Gov't, P.H.S.]

Lindgren L, Westling G, Brulin C, Lehtipalo S, Andersson M, Nyberg L (2012) Pleasant human touch is represented in pregenual anterior cingulate cortex. NeuroImage 59(4):3427–3432

Lischke A, Berger C, Prehn K, Heinrichs M, Herpertz SC, Domes G (2012) Intranasal oxytocin enhances emotion recognition from dynamic facial expressions and leaves eye-gaze unaffected. Psychoneuroendocrinology 37(4):475–481. [Research Support, U.S. Gov't, Non-P.H.S.]

Liu Y, Sheng F, Woodcock KA, Han S (2013a) Oxytocin effects on neural correlates of self-referential processing. Biol Psychol 94(2):380–387

Liu JC, Guastella AJ, Dadds MR (2013b) Exploring the role of intra-nasal oxytocin on the partner preference effect in humans. Psychoneuroendocrinology 38(4):587–591

Löken LS, Wessberg J, McGlone F, Olausson H (2009) Coding of pleasant touch by unmyelinated afferents in humans. Nat Neurosci 12(5):547–548

Luo S, Li B, Ma Y, Wenxia Z, Rao Y, Han S (2015) Oxytocin receptor gene and racial ingroup bias in empathy-related brain activity. NeuroImage 110:22–31

MacDonald K, MacDonald TM, Brune M, Lamb K, Wilson MP, Golshan S, Feifel D (2013) Oxytocin and psychotherapy: a pilot study of its physiological, behavioral and subjective effects in males with depression. Psychoneuroendocrinology 38(12):2831–2843

Madrazo I, Franco-Bourland RE, Leon-Meza VM, Mena I (1987) Intraventricular somatostatin-14, arginine vasopressin, and oxytocin: analgesic effect in a patient with intractable cancer pain. Appl Neurophysiol 50(1–6):427–431

Marazziti D, Dell'Osso B, Baroni S, Mungai F, Catena M, Rucci P et al (2006) A relationship between oxytocin and anxiety of romantic attachment. Clin Pract Epidemiol Ment Health 2:28

Marsh AA, Yu HH, Pine DS, Blair RJR (2010) Oxytocin improves specific recognition of positive facial expressions. Psychopharmacology 209(3):225–232

Marsh N, Scheele D, Gerhardt H, Strang S, Enax L, Weber B et al (2015) The neuropeptide oxytocin induces a social altruism bias. J Neurosci 35(47):15696–15701

McCarthy MM, McDonald CH, Brooks PJ, Goldman D (1996) An anxiolytic action of oxytocin is enhanced by estrogen in the mouse. Physiol Behav 60(5):1209–1215
McCullough ME, Churchland PS, Mendez AJ (2013) Problems with measuring peripheral oxytocin: can the data on oxytocin and human behavior be trusted? Neurosci Biobehav Rev 37(8):1485–1492
McQuaid RJ, McInnis OA, Matheson K, Anisman H (2015) Distress of ostracism: oxytocin receptor gene polymorphism confers sensitivity to social exclusion. Soc Cogn Affect Neurosci 10(8):1153–1159. [Research Support, Non-U.S. Gov't]
McRae-Clark AL, Baker NL, Maria MM, Brady KT (2013) Effect of oxytocin on craving and stress response in marijuana-dependent individuals: a pilot study. Psychopharmacology 228 (4):623–631
Meinlschmidt G, Heim C (2007) Sensitivity to intranasal oxytocin in adult men with early parental separation. Biol Psychiatry 61(9):1109–1111. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]
Mihov Y, Kendrick KM, Becker B, Zschernack J, Reich H, Maier W et al (2013) Mirroring fear in the absence of a functional amygdala. Biol Psychiatry 73(7):e9–e11
Modi ME, Connor-Stoud F, Landgraf R, Young LJ, Parr LA (2014) Aerosolized oxytocin increases cerebrospinal fluid oxytocin in rhesus macaques. Psychoneuro 45:49–57
Molenberghs P, Cunnigton R, Mattingley JB (2012) Brain regions with mirror properties: a meta-analysis of 125 human fMRI studies. Neurosci Biobehav Rev 36(1):341–349
Moons WG, Way BM, Taylor SE (2014) Oxytocin and vasopressin receptor polymorphisms interact with circulating neuropeptides to predict human emotional reactions to stress. Emotion 14(3):562–572. [Clinical Trial Research Support, N.I.H., Extramural Research Support, U.S. Gov't, Non-P.H.S.]
Moos F, Freund-Mercier MJ, Guerne Y, Guerne JM, Stoeckel ME, Richard P (1984) Release of oxytocin and vasopressin by magnocellular nuclei in vitro: specific facilitatory effect of oxytocin on its own release. J Endocrinol 102(1):63–72
Morhenn VB, Park JW, Piper E, Zak PJ (2008) Monetary sacrifice among strangers is mediated by endogenous oxytocin release after physical contact. Evol Hum Behav 29(6):375–383
Morhenn V, Beavin LE, Zak PJ (2012) Massage increases oxytocin and reduces adrenocorticotropin hormone in humans. Altern Ther Health Med 18(6):11
Mottolese R, Redouté J, Costes N, Bars DL, Sirigu A (2014) Switching brain serotonin with oxytocin. Proc Natl Acad Sci U S A 111(23):8637–8642
Mu Y, Guo C, Han S (2016) Oxytocin enhances inter-brain synchrony during social coordination in male adults. Soc Cogn Affect Neurosci 11(12):1882–1893
Mukamel R, Ekstrom AD, Kaplan J, Iacoboni M, Fried I (2010) Single neuron responses in humans during execution and observation of actions. Curr Biol 20(8):750–756
Najib A, Lorberbaum JP, Kose S, Bohning DE, George MS (2004) Regional brain activity in women grieving a romantic relationship breakup. Am J Psychiatry 161(12):2245–2256
Nation DA, Szeto A, Mendez AJ, Brooks LG, Zaias J, Herderick EE et al (2010) Oxytocin attenuates atherosclerosis and adipose tissue inflammation in socially isolated ApoE−/− mice. Psychosom Med 72(4):376
Newton N, Newton M (1967) Psychologic aspects of lactation. N Engl J Med 277(22):1179–1188
Norman GJ, Hawkley L, Luhmann M, Ball AB, Cole SW, Berntson GG, Cacioppo JT (2012) Variation in the oxytocin receptor gene influences neurocardiac reactivity to social stress and HPA function: a population based study. Horm Behav 61(1):134–139
Noy L, Dekel E, Alon R (2011) The mirror game as a paradigm for studying the dynamics of two people improvising motion together. Proc Natl Acad Sci U S A 108(52):20947–20952
Nussey SS, Page SR, Ang VT, Jenkins JS (1988) The response of plasma oxytocin to surgical stress. Clin Endocrinol 28(3):277–282. [Research Support, Non-U.S. Gov't]
O'Connor M-F, Wellisch DK, Stanton AL, Eisenberger NI, Irwin MR, Lieberman MD (2008) Craving love? Enduring grief activates brain's reward center. NeuroImage 42(2):969–972
Odent M (2010) Autism and anorexia nervosa: two facets of the same disease? Med Hypotheses 75 (1):79–81

Olff M, Frijling JL, Kubzansky LD, Bradley B, Ellenbogen MA, Cardoso C et al (2013) The role of oxytocin in social bonding, stress regulation and mental health: an update on the moderating effects of context and interindividual differences. Psychoneuroendocrinology 38(9):1883–1894

Paloyelis Y, Krahe C, Maltezos S, Williams SC, Howard MA, Fotopoulou A (2016) The analgesic effect of oxytocin in humans: a double-blind, placebo-controlled cross-over study using laser-evoked potentials. J Neuroendocrinol 28(4). doi:10.1111/jne.12347

Pedersen CA, Prange AJ Jr (1985) Oxytocin and mothering behavior in the rat. Pharmacol Ther 28 (3):287–302

Pedersen CA, Gibson CM, Rau SW, Salimi K, Smedley KL, Casey RL et al (2011) Intranasal oxytocin reduces psychotic symptoms and improves theory of mind and social perception in schizophrenia. Schizophr Res 132(1):50–53

Perry A, Bentin S, Shalev I, Israel S, Uzefovsky F, Bar-On D, Ebstein RP (2010) Intranasal oxytocin modulates EEG mu/alpha and beta rhythms during perception of biological motion. Psychoneuroendocrinology 35(10):1446–1453

Petersson M, Lundeberg T, Uvnas-Moberg K (1999) Short-term increase and long-term decrease of blood pressure in response to oxytocin-potentiating effect of female steroid hormones. J Cardiovasc Pharmacol 33(1):102–108

Pierrehumbert B, Torrisi R, Laufer D, Halfon O, Ansermet F, Beck Popovic M (2010) Oxytocin response to an experimental psychosocial challenge in adults exposed to traumatic experiences during childhood or adolescence. Neuroscience 166(1):168–177. [Research Support, Non-U.S. Gov't]

Popik P, Vetulani J (1991) Opposite action of oxytocin and its peptide antagonists on social memory in rats. Neuropeptides 18(1):23–27

Porges S (1998) Love: an emergent property of the mammalian autonomic nervous system. Psychoneuroendocrinology 23(8):837–861

Pournajafi-Nazarloo H, Kenkel W, Mohsenpour SR, Sanzenbacher L, Saadat H, Partoo L et al (2013) Exposure to chronic isolation modulates receptors mRNAs for oxytocin and vasopressin in the hypothalamus and heart. Peptides 43:20–26

Preckel K, Scheele D, Kendrick KM, Maier W, Hurlemann R (2014) Oxytocin facilitates social approach behavior in women. Front Behav Neurosci 8:191

Preckel K, Scheele D, Eckstein M, Maier W, Hurlemann R (2015) The influence of oxytocin on volitional and emotional ambivalence. Soc Cogn Affect Neurosci 10(7):987–993

Prehn K, Kazzer P, Lischke A, Heinrichs M, Herpertz SC, Domes G (2013) Effects of intranasal oxytocin on pupil dilation indicate increased salience of socioaffective stimuli. Psychophysiology 50(6):528–537

Quirin M, Kuhl J, Dusing R (2011) Oxytocin buffers cortisol responses to stress in individuals with impaired emotion regulation abilities. Psychoneuroendocrinology 36(6):898–904. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]

Richardson MJ, Marsh KL, Isenhower RW, Goodman JRL, Schmidt RC (2007) Rocking together: dynamics of intentional and unintentional interpersonal coordination. Hum Mov Sci 26(6):867–891

Rimmele U, Hediger K, Heinrichs M, Klaver P (2009) Oxytocin makes a face in memory familiar. J Neurosci 29(1):38–42

Rodrigues SM, Saslow LR, Garcia N, John OP, Keltner D (2009) Oxytocin receptor genetic variation relates to empathy and stress reactivity in humans. Proc Natl Acad Sci U S A 106 (50):21437–21441

Rolls ET, O'Doherty J, Kringelbach ML, Francis S, Bowtell R, McGlone F (2003) Representations of pleasant and painful touch in the human orbitofrontal and cingulate cortices. Cereb Cortex 13(3):308–317

Sanders G, Freilicher J, Lightman SL (1990) Psychological stress of exposure to uncontrollable noise increases plasma oxytocin in high emotionality women. Psychoneuroendocrinology 15 (1):47–58

Schaafsma SM, Pfaff DW, Spunt RP, Adolphs R (2015) Deconstructing and reconstructing theory of mind. Trends Cogn Sci 19(2):65–72

Scheele D, Striepens N, Güntürkün O, Deutschlander S, Maier W, Kendrick KM, Hurlemann R (2012) Oxytocin modulates social distance between males and females. J Neurosci 32(46):16074–16079
Scheele D, Wille A, Kendrick KM, Stoffel-Wagner B, Becker B, Güntürkün O et al (2013) Oxytocin enhances brain reward system responses in men viewing the face of their female partner. Proc Natl Acad Sci U S A 110(50):20308–20313
Scheele D, Kendrick KM, Khouri C, Kretzer E, Schlapfer TE, Stoffel-Wagner B et al (2014a) An oxytocin-induced facilitation of neural and emotional responses to social touch correlates inversely with autism traits. Neuropsychopharmacology 39(9):2078–2085
Scheele D, Striepens N, Kendrick KM, Schwering C, Noelle J, Wille A et al (2014b) Opposing effects of oxytocin on moral judgment in males and females. Hum Brain Mapp 35(12):6067–6076
Scheele D, Schwering C, Elison JT, Spunt R, Maier W, Hurlemann R (2015) A human tendency to anthropomorphize is enhanced by oxytocin. Eur Neuropsychopharmacol 25(10):1817–1823
Scheele D, Plota J, Stoffel-Wagner B, Maier W, Hurlemann R (2016) Hormonal contraceptives suppress oxytocin-induced brain reward responses to the partner's face. Soc Cogn Affect Neurosci 11 (5):767–774
Schmidt RC, Richardson MJ (2008) Dynamics of interpersonal coordination. In: Coordination: neural, behavioral and social dynamics. Springer, Berlin, pp 281–308
Schneiderman I, Zagoory-Sharon O, Leckman JF, Feldman R (2012) Oxytocin during the initial stages of romantic attachment: relations to couples' interactive reciprocity. Psychoneuroendocrinology 37(8):1277–1285
Schneiderman I, Kanat-Maymon Y, Zagoory-Sharon O, Feldman R (2014a) Mutual influences between partners' hormones shape conflict dialog and relationship duration at the initiation of romantic love. Soc Neurosci 9(4):337–351
Schneiderman I, Kanat-Maymon Y, Ebstein RP, Feldman R (2014b) Cumulative risk on the oxytocin receptor gene (OXTR) underpins empathic communication difficulties at the first stages of romantic love. Soc Cogn Affect Neurosci 9(10):1524–1529
Schulze L, Lischke A, Greif J, Herpertz SC, Heinrichs M, Domes G (2011) Oxytocin increases recognition of masked emotional faces. Psychoneuroendocrinology 36(9):1378–1382. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]
Schurz M, Perner J (2015) An evaluation of neurocognitive models of theory of mind. Front Psychol 6:1610
Schurz M, Radua J, Aichhorn M, Richlan F, Perner J (2014) Fractionating theory of mind: a meta-analysis of functional brain imaging studies. Neurosci Biobehav Rev 42:9–34
Sebanz N, Knoblich G, Prinz W, Wascher E (2006) Twin peaks: an ERP study of action planning and control in coacting individuals. J Cogn Neurosci 18(5):859–870
Seltzer LJ, Ziegler T, Connolly MJ, Prososki AR, Pollak SD (2013) Stress-induced elevation of oxytocin in maltreated children: evolution, neurodevelopment, and social behavior. Child Dev 85(2):501–512
Shahrestani S, Kemp AH, Guastella AJ (2013) The impact of a single administration of intranasal oxytocin on the recognition of basic emotions in humans: a meta-analysis. Neuropsychopharmacology 38(19):1929–1936
Shankar A, Hamer M, McMunn A, Steptoe A (2013) Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English longitudinal study of ageing. Psychosom Med 75(2):161–170
Simeon D, Bartz J, Hamilton H, Crystal S, Braun A, Ketay S, Hollander E (2011) Oxytocin administration attenuates stress reactivity in borderline personality disorder: a pilot study. Psychoneuroendocrinology 36(9):1418–1421
Singer T, Seymore B, O'Doherty J, Kaube H, Dolan RJ, Frith CD (2004) Empathy for pain involves the affective but not sensory components of pain. Science 303(5661):1157–1162
Smith TW, Uchino BN, MacKenzie J, Hicks AM, Campo RA, Reblin M et al (2013) Effects of couple interactions and relationship quality on plasma oxytocin and cardiovascular reactivity: empirical findings and methodological considerations. Int J Psychophysiol 88(3):271–281. [Research Support, N.I.H., Extramural]

Smith KE, Porges EC, Norman GJ, Connelly JJ, Decety J (2014) Oxytocin receptor gene variation predicts empathic concern and autonomic arousal while perceiving harm to others. Soc Neurosci 9(1):1–9

Soliman A, O'Driscoll GA, Pruessner J, Joober R, Ditto B, Streicker E et al (2011) Limbic response to psychosocial stress in schizotypy: a functional magnetic resonance imaging study. Schizophr Res 131(1):184–191

Spengler FB, Scheele D, Marsh N, Kofferath C, Flach A, Schwarz S, Stoffel-Wagner B, Maier W, Hurlemann R (2017) Oxytocin facilitates reciprocity in social communication. Soc Cogn Affect Neurosci. doi:10.1093/scan/nsx061

Striepens N, Kendrick KM, Maier W, Hurlemann R (2011) Prosocial effects of oxytocin and clinical evidence for its therapeutic potential. Front Neuroendocrinol 32(4):426–450. [Research Support, Non-U.S. Gov't Review]

Striepens N, Kendrick KM, Hanking V, Landgraf R, Wullner U, Maier W, Hurlemann R (2013) Elevated cerebrospinal fluid and blood concentrations of oxytocin following its intranasal administration in humans. Sci Rep 3:3440

Striepens N, Matusch A, Kendrick KM, Mihov Y, Elmenhorst D, Becker B et al (2014) Oxytocin enhances attractiveness of unfamiliar female faces independent of the dopamine reward system. Psychoneuroendocrinology 39:74–87

Striepens N, Schroter F, Stoffel-Wagner B, Maier W, Hurlemann R, Scheele D (2016) Oxytocin enhances cognitive control of food craving in women. Hum Brain Mapp 37(12):4276–4285

Szeto A, Nation DA, Mendez AJ, Dominguez-Bendala J, Brooks LG, Scheiderman N, McCabe PM (2008) Oxytocin attenuates NADPH-dependent superoxide activity and IL-6 secretion in macrophages and vascular cells. Am J Physiol Endocrinol Metab 295(6):1495–1501

Tabak BA, McCullough ME, Szeto A, Mendez AJ, McCabe PM (2011) Oxytocin indexes relational distress following interpersonal harms in women. Psychoneuroendocrinology 36(1):115–122. [Controlled Clinical Trial Research Support, N.I.H., Extramural]

Tan BL, Lee SA, Lee J (2016) Social cognitive interventions for people with schizophrenia: a systematic review. Asian J Psychiatr. doi:10.1016/j.ajp.2016.06.013

Taylor SE, Gonzaga GC, Klein LC, Hu P, Greendale GA, Seeman TE (2006) Relation of oxytocin to psychological stress responses and hypothalamic-pituitary-adrenocortical axis activity in older women. Psychosom Med 68:238–245. [Research Support, N.I.H., Extramural Research Support, U.S. Gov't, Non-P.H.S.]

Taylor SE, Saphire-Bernstein S, Seeman TE (2010) Are plasma oxytocin in women and plasma vasopressin in men biomarkers of distressed pair-bond relationships? Psychol Sci 21(1):3–7

Tognoli E, Lagarde J, DeGuzman GC, Kelso JAS (2007) The phi complex as a neuromarker of human social coordination. Proc Natl Acad Sci U S A 104(19):8190–8195

Tost H, Kolachana B, Hakimi S, Lamaitre H, Verchinski BA, Mattay VS et al (2010) A common allele in the oxytocin receptor gene (OXTR) impacts prosocial temperament and human hypothalamic-limbic structure and function. Proc Natl Acad Sci U S A 107(31):13936–13941

Turner RA, Altemus M, Enos T, Cooper B, McGuinness T (1999) Preliminary research on plasma oxytocin in normal cycling women: investigating emotion and interpersonal distress. Psychiatry 62(2):97–113

Ulloa ER, Pineda JA (2007) Recognition of point-light biological motion: mu rhythms and mirror neuron activity. Behav Brain Res 183:188–194

Ulmer-Yaniv A, Avitsur R, Kanat-Maymon Y, Schneiderman I, Zagoory-Sharon O, Feldman R (2016) Affiliation, reward, and immune biomarkers coalesce to support social synchrony during periods of bond formation in humans. Brain Behav Immun 56:130–139

Uvanas-Moberg K, Arn I, Magnusson D (2005) The psychobiology of emotion: the role of the oxytocinergic system. Int J Behav Med 12:59–65

Uvnäs-Moberg K, Handlin L, Petersson M (2015) Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory simulation. Front Psychol 5(2015):1529

Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty B (2016) Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. Heart 102(13):1009–1016

Walum H, Lichtenstein P, Neiderhiser JM, Reiss D, Ganiban JM, Spotts EL et al (2012) Variation in the oxytocin receptor gene (OXTR) is associated with pair-bonding and social behavior. Biol Psychiatry 71(5):419–426

Weisman O, Zagoory-Sharon O, Feldman R (2013) Oxytocin administration alters HPA reactivity in the context of parent-infant interaction. Eur Neuropsychopharmacol 23(12):1724–1731

Weisman O, Pelphrey KA, Leckman JF, Feldman R, Lu Y, Chong A et al (2015) The association between 2D: 4D ratio and cognitive empathy is contingent on a common polymorphism in the oxytocin receptor gene (OXTR rs53576). Psychoneuroendocrinology 58:23–32

Wikström S, Gunnarsson T, Nordin C (2003) Tactile stimulus and neurohormonal response: a pilot study. Int J Neurosci 113(6):787–793

Wirth MM, Gaffey AE, Martinez BS (2015) Effects of intranasal oxytocin on steroid hormones in men and women. Neuropsychobiology 71(4):202–211. [Research Support, Non-U.S. Gov't]

Woolley JD, Chuang B, Lam O, Lai W, O'Donovan A, Rankin KP, Mathalon DH, Vinogradov S (2014) Oxytocin administration enhances controlled social cognition in patients with schizophrenia. Psychoneuroendocrinology 47:116–125

Younger J, Aron A, Parke S, Chatterjee N, Mackey S (2010) Viewing pictures of a romantic partner reduces experimental pain: involvement of neural reward systems. PLoS One 5(10):e13309. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]

Ziegler C, Dannlowski U, Brauer D, Stevens S, Laeger I, Wittmann H et al (2015) Oxytocin receptor gene methylation: converging multilevel evidence for a role in social anxiety. Neuropsychopharmacology 40(6):1528–1538