René Hurlemann* and Nina Marsh

Deciphering the modulatory role of oxytocin in human altruism

DOI 10.1515/revneuro-2016-0061
Received September 25, 2016; accepted January 6, 2017

Abstract: Unlike any other species, humans frequently engage in altruistic behaviors by which they increase another individual's welfare even if this implies personal costs. The psychological motives underlying altruistic behaviors remain diverse, ranging from the ability to reciprocate trust and cooperation to bonding and empathizing with family members or even genetically unrelated others. This article explores the neuroendocrine architecture of altruism by emphasizing the crucial role of the evolutionarily highly conserved peptide hormone oxytocin as a modulator of cooperative behaviors including empathy-driven altruism. However, accumulating evidence suggests that oxytocin does not invariably facilitate cooperation but also produces protective or even defensive-aggressive responses in specific social contexts. In addition, we highlight the relevance of message frames as critical determinants of whether the peptide promotes altruism toward prosocial ends.

Keywords: altruism; altruistic punishment; empathy; oxytocin; parochial altruism.

Introduction

Over millennia, altruism has been one of the guiding principles in society, but it was only in the 19th century that Auguste Comte first introduced the notion 'vivre pour autrui' (Comte and Fetscher, 1966), a concept which referred to a societal motive superior to egoism. Although studies provided evidence that also microorganisms and plants are able to recognize kin and act altruistically (Lee et al., 2010; Wu et al., 2013), it is only in humans that altruism is being observed between unrelated individuals. By definition, an altruist is a person who increases the welfare of another individual even if it implies a personal disadvantage in terms of health, money, or resources (Fehr and Fischbacher, 2003). Over the years, kin selection (Hamilton, 1964) and parochial altruism (Bernhard et al., 2006) emerged as central concepts to explain human altruism. Insights from the evolution of cooperation suggest that the motivations for human altruism are diverse and deeply rooted in the neuroendocrine architecture of the social brain (Fehr and Fischbacher, 2003, 2004). Specifically, the evolutionarily highly conserved nonapeptide hormone oxytocin (OXT) has a well-established role in human sociality, including altruistic behavior (Young and Wang, 2004; Israel et al., 2012; Hurlemann and Marsh, 2016). Endogenous OXT is synthesized in the paraventricular, supraoptic, and accessory magnocellular nuclei of the hypothalamus which send projections to the posterior pituitary gland where they secrete OXT into systemic circulation. In the periphery, OXT stimulates uterine contraction during parturition and milk let-down during lactation (Carter, 1998; Donaldson and Young, 2008). In addition, OXT is centrally released via volume and wiring transmission and modulates a diverse repertoire of social and reproductive behaviors (Stoop, 2012). This is also demonstrated by a plethora of behavioral and neuroimaging studies in humans, in which exogenous delivery of OXT as a nasal spray alters outcome measures of behavioral and neural response (Meyer-Lindenberg et al., 2011; Striepens et al., 2011; Yamasue et al., 2012), with effect sizes ranging from weak ($d = 0.21$ for face recognition) to moderate ($d = 0.43$ for in-group trust) (van Ijzendoorn and Bakermans-Kranenburg, 2011), and the left insular cortex showing the most robust activation (Wigton et al., 2015). These findings are consistent with studies in humans (Striepens et al., 2013) and non-human primates (Dal Monte et al., 2014; Freeman et al., 2016) that intranasal administration of OXT leads to increased cerebrospinal fluid concentrations of the peptide, although the precise pathways of transnasal brain penetration and dose-response relationships remain to be characterized. The existing evidence from studies in humans suggests that intranasal delivery of OXT promotes positive social behaviors such as trust (Kosfeld et al., 2005; Baumgartner et al., 2008; but see Nave et al., 2015), intra-group cooperation (De Dreu and Kret, 2015), and empathic responding (Domes et al., 2007a,b; Hurlemann et al., 2010; Abu-Akel

***Corresponding author: René Hurlemann,** Department of Psychiatry, University of Bonn Medical Center, D-53105 Bonn, Germany; and Division of Medical Psychology, University of Bonn Medical Center, D-53105 Bonn, Germany, e-mail: renehurlemann@icloud.com
Nina Marsh: Division of Medical Psychology, University of Bonn Medical Center, D-53105 Bonn, Germany

et al., 2015; but see Radke and de Bruijn 2015), most likely by increasing the salience of social cues (Scheele et al., 2015; Shamay-Tsoory and Abu-Akel, 2015). This view is substantiated by evidence of OXT's pivotal role in mother-offspring and partner bonds (Eckstein and Hurlemann, 2013; Hurlemann and Scheele, 2016) as well as social approach behavior (Scheele et al., 2012b; Preckel et al., 2014). It is important to note, though, that the effects of OXT remain highly sensitive to person-specific and contextual factors (Bartz et al., 2011; Olff et al., 2013; Hurlemann, 2017), and thus, might also evoke protective and defensive-aggressive reactions, especially with respect to competing outgroups (Shamay-Tsoory et al., 2009; De Dreu et al., 2010, 2015; Striepens et al., 2012; Samuni et al., 2017). Neural effects of intranasally administered OXT consistently target reward- (Donaldson and Young, 2008; Skuse and Gallagher, 2009; Scheele et al., 2013; but see Striepens et al., 2014) and fear-related circuits (Kirsch et al., 2005; Domes et al., 2007a,b; Meyer-Lindenberg et al., 2011; see also Stoop et al., 2015), which may explain the prosocial and anxiolytic profile of the peptide. Given this empirical background, OXT is hypothesized to significantly contribute to human altruism, including kin-based, parochial, and empathy-based altruism. The rationale of this article is to provide a conceptual and thematic overview of preclinical research specifically examining the modulatory effects of intranasal OXT on altruistic behavior in humans. In the first section, we summarize findings related to kin-based altruism and give a brief overlook of current evolutionary concepts of human parenting and pair-bond formation. In the second section, we focus the peptide's effects on altruism among non-kin, including parochial altruism and altruistic punishment, by capitalizing on motives of reciprocity, fairness, and empathy. A concluding section provides a brief synopsis and discusses future avenues of research into empathy-based altruism.

Oxytocin and altruism among kin

The relationships we form with our families, friends, and partners are integral to the organization and function of human society. From an evolutionary perspective, altruism toward those most closely related to us is highly beneficial, because it promotes survival in habitats characterized by ubiquitous social and environmental threats (Krebs and Davies, 1993). Although kinship theory is a well-established concept to explain the evolution of human altruism, different researchers formulated contrasting views about it (Nowak et al., 2010). By definition, kin selection relies on mechanisms for identifying, detecting, and bonding with biological kin (Lieberman et al., 2007). A long lineage of research provides evidence that most of these attachment-related behaviors are associated with the OXT system (Insel and Young, 2001; Carter et al., 2008; Hurlemann and Scheele, 2016). The following section reviews the role of OXT in the context of human parenting and pair-bond formation, which have been conceptualized to foster inclusive fitness by forming and maintaining social relationships.

Oxytocin and parental care

From an evolutionary perspective, one of the most fundamental social bonds emerges between parents and their offspring. Human parenting typically requires making costly sacrifices in order to nurse and care for the offspring, so a child has a chance to survive to reproductive age (Kaplan et al., 2000). In women, care-based processes start during gestation and continue throughout an even longer period of nursing, whereas in fathers the care-based phase often is initiated by the time of birth (Krebs and Davies, 1993). The initiation and maintenance of such fundamental social bonds, which create a sense of safety, security, and belonging between parents and their children, has been found to be modulated by OXT (Scheele et al., 2012b; Eckstein and Hurlemann, 2013; Hurlemann and Scheele, 2016; see also Insel and Young, 2001; Rilling and Young, 2014). For example, giving care to infants is associated with increased plasma concentrations of endogenous OXT in both mothers and fathers (Gordon et al., 2010; Mascaro et al., 2014). Furthermore, intranasal administration of OXT reduces hostility in fathers and motivates them to support exploration behavior in their children (Naber et al., 2010). Interestingly, OXT promotes women's responsiveness to infant crying (Riem et al., 2011), whereas in response to child pictures fathers not only exhibit higher OXT plasma concentrations, but also show a stronger activation in brain regions important for the decoding of facial emotion (caudal middle frontal gyrus), mentalizing (temporoparietal junction), and reward processing (medial orbitofrontal cortex) relative to non-fathers (Mascaro et al., 2014). On the neural level, intranasal OXT was found to attenuate amygdala response in women exposed to infant laughter. In contrast, infant crying evokes responses of the insula and inferior frontal gyrus, i.e., brain regions strongly implicated in empathy (Riem et al., 2011, 2012). This resonates well with findings that OXT induces a tendency in mothers to create

a positive social environment for the child, whereas the peptide appears to promote defense-motivated aggression to threat in fathers (Rilling et al., 2014), consistent with or perhaps even driven by changes in social approach and avoidance behaviors (Domes et al., 2007a; Wittfoth-Schardt et al., 2012). Taken together, the data suggest that kin-based altruism is deeply anchored in our evolutionary past, which implies that attachment-related behaviors enable positive parent-offspring relationships, and at the same time evoke defensive responses protecting the offspring toward outside threats (Hahn-Holbrook et al., 2011).

Oxytocin and pair-bond formation

The formation of human pair bonds represents a function of similar relevance for ensuring reproductive success and offspring survival and appears to be closely linked to altruism. For example, Singh Bhogal et al. (2016) reported that men viewing images of attractive women showed an increase in cooperative and altruistic behavior, whereas women associated altruistic behavior in men with greater physical attractiveness (Farrelly et al., 2016).

OXT has a well-established role in forming and maintaining human pair bonds (Insel and Young, 2001; Hurlemann and Scheele, 2016). In a seminal study, Ditzen et al. (2009) videotaped male-female couples during a dispute focused on pre-defined conflicts (e.g. Finances, educational issues, leisure time) and found increased positive relative to negative communication patterns and reduced salivary cortisol levels in those couples who had received intranasal OXT before the argument. In line with these results is another study showing that a warm touch among couples increased salivary concentrations of endogenous OXT and attenuated physiological measures of stress (Holt-Lunstad et al., 2008), which is consistent with OXT's putative influence on the activity of the hypothalamus-pituitary-adrenal axis (Carter, 1998). These findings resonate well with neuroimaging evidence that intranasal OXT stimulates the brain's reward centers (including the ventral tegmental area and the nucleus accumbens) in males viewing the face of their female partners (Scheele et al., 2013). Moreover, intranasal OXT motivates pair-bonded, but not single, men to keep a greater social distance from an unknown female experimenter (Scheele et al., 2012b). It thus appears that OXT has a significant role in promoting monogamous behavior by creating incentives for sexual fidelity via the reward system, which may, in the long run, reduce stress and improve salutogenesis, at least in males.

Oxytocin and altruism beyond family ties

In addition to the bonds with family members and close relatives, human beings need friendship and cooperation not only for survival in hostile environments but also for health, longevity, and life satisfaction. Throughout history, humans cooperate with unrelated others and sacrifice their resources in order to advance and defend the collective fitness of their own group against competing out-groups. This form of altruism is parochial (Bernhard et al., 2006) and thought to support the formation of highly cohesive in-groups, in which individuals share common interests, disseminate knowledge, and learn how to negotiate and trade (Fehr et al., 2002). But why do humans repeatedly engage in behaviors that are costly to themselves in order to provide help for strangers in need (Fehr et al., 2002)? Parochial altruism describes an in-group favoritism (Bernhard et al., 2006) along with the tendency to protect the in-group alliance against outside threat, even if this implies to reject, derogate, or harm out-group members (Choi and Bowles, 2007). Parochial altruism is often associated with motives of reciprocity (Trivers, 1971; Fehr et al., 2002; Fehr and Fischbacher, 2004) or moral-normative principles, such as justice and fairness (Fehr and Gachter, 2002). Interestingly, altruistic behavior can also result from empathic concern and overcome out-group hostility (Preston and de Waal, 2002; de Waal, 2008; Batson, 2011), as illustrated in the biblical parable of the Good Samaritan (Luke 10:25–37). In the following, we elucidate the influence of OXT on altruistic motives in social groups and beyond.

Oxytocin in human cooperation

Cooperation within and between groups requires trust, because cooperative exchanges are often separated in time. In a landmark study, Kosfeld et al. (2005) tested the modulatory effects of intranasal OXT on altruism among unrelated individuals. Specifically, subjects were exposed to a trust game including monetary exchanges between an investor and an anonymous trustee either framed as a computer or an unfamiliar person. Only in the latter condition, the peptide increased the amount of money investors gave to the trustee. Consistent with this are neuroimaging findings that individuals with higher levels of trust exhibit greater neural activity in the subgenual cingulate (Moll et al., 2006), which is rich in OXT receptors and modulates striatal dopamine release (Barberis

and Tribollet, 1996). Furthermore, trusting behavior was found to be sustained in subjects treated with intranasal OXT, even after they learned that their trust had been breached several times (Baumgartner et al., 2008). Another study by Declerck et al. (2010) found that intranasal OXT increased cooperation when social information was provided and subjects had prior contact with an interaction partner (Declerck et al., 2014), suggesting that the prosocial effects of intranasal OXT on cooperation depend on individual person- and context-related factors. The underlying motive of reciprocity, i.e., the repayment of what others have provided us, is thought to be important for the maintenance of social relationships. If favors are not returned, relationships may be short lived (van den Bos et al., 2009). As a consequence, many individuals display a propensity to detect and punish non-cooperation and/or social norm violation, even if this incurs a personal cost (Fehr and Gachter, 2002). Such 'altruistic punishment' is amygdala dependent (Scheele et al., 2012a) and tempered down by intranasal OXT. Instead, intranasal OXT has been shown to enhance empathy for the victim of social norm violations, evident in stronger tendencies to judge criminal offenses as being more harmful for the victim (Krueger et al., 2013) and to support the victim financially (Hu et al., 2016).

Oxytocin and empathy-driven altruism

Empathy has been proposed as a powerful motive for altruism toward distressed and vulnerable strangers (Preston and de Waal, 2002; Batson, 2011; Preston, 2013; Marsh, 2016). Typical examples for empathy-based altruism – also referred to as 'non-reciprocal altruism' – include monetary donations toward homeless people, humanitarian aid for refugees, or living organ donations (Fellner and Schwartz, 1971). Brain areas associated with reward and fear processing (Harbaugh et al., 2007), including the amygdala (Gospic et al., 2014; Marsh et al., 2014; Hein et al., 2016), have been assigned a central role in modulating empathy-driven altruism. Neuroimaging studies have consistently pointed to the reward system (Scheele et al., 2013; Bos et al., 2015) and fear-related circuits (Riem et al., 2011; Rilling et al., 2012; Striepens et al., 2012; Eckstein et al., 2015) as important loci of intranasal OXT action. Furthermore, charitable donations have been associated with differential activity in the subgenual cingulate area (Moll et al., 2006) and the striatum (Harbaugh et al., 2007), two regions dense in OXT receptors (Baberis and Tribollet, 1996; Báez-Mendoza and Schultz, 2013), a region dense in OXT receptors (Barberis and Tribollet, 1996). This empirical background strongly implicates OXT in regulating altruistic behavior driven by empathy.

The decoding of other people's cooperative intentions and the prediction of their underlying attitudes and values is referred to as 'cognitive empathy', whereas 'emotional empathy' is about mirroring or sharing their emotions. Both the emotional and cognitive components of empathy are regulated by OXT, as documented by behavioral studies showing improved performance in the 'Multifaceted Empathy Test' (Hurlemann et al., 2010) and 'Reading the Mind in the Eyes Test' (Domes et al., 2007b; but see Radke and de Bruijn, 2015) following intranasal administration of the peptide. Individuals exhibiting difficulties in empathic responding due to alexithymia (Luminet et al., 2011) or autism spectrum disorders (Guastella et al., 2010) appear to particularly benefit from intranasal OXT treatment. Consistent with these behavioral findings are neuroimaging studies showing that intranasal OXT activates regions within the

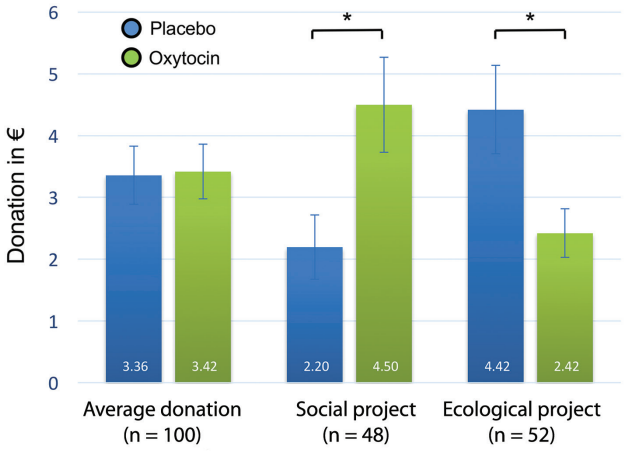

Figure 1: Experimental effects of intranasal oxytocin on human behavior.
One hundred male participants were tested using a sustainability-related monetary donation task, with the option to support either a socially or ecologically framed charity after receiving a 24-IU nasal dose of synthetic oxytocin (OXT) or placebo. The maximum possible donation for each project was EUR 10. The social charity had the aim to help the indigenous people living in an area of the Congo delta, whereas the ecological charity project had the aim to save the rainforest in that preserve. The results show that intranasal OXT more than doubled the sums donated to the social charity (social frame) and substantially decreased donations to the non-social charity (ecological frame), while keeping constant the overall proportion of donated money (numbers indicate the average amount of donated money). Error bars indicate the standard error of the mean. Asterisks indicate statistical significance (p-values < 0.05). (Adapted from Marsh et al., 2015).

empathy network, including the inferior frontal gyrus, the posterior superior temporal sulcus, and the inferior parietal lobe (Levy et al., 2015).

Using game theoretical approaches, previous studies reported an OXT-induced increase in generosity (Zak et al., 2007; see also van Ijzendoorn et al., 2011). However, only recent studies have begun to unravel the contribution of OXT to empathy-driven altruism. In two independent experiments involving a total of 172 volunteers, Marsh et al. (2015) found that intranasal OXT induced a social altruism bias in subjects exposed to a social vs. an ecological charity. Specifically, participants were introduced to a monetary donation task, which was framed as supporting either a social or an ecological charity project. The aim of the social charity was to help indigenous people living in an area of the Congo delta, whereas the aim of the ecological charity was to preserve the rainforest in that particular preserve. The results showed that intranasal OXT reversed the behavioral pattern observed under placebo by increasing donations for the social charity project and decreasing donations to the ecological charity project. Notably, the peptide had no effect on the overall donations, suggesting that the peptide selectively increases sensitivity to socially framed messages rather than increasing generosity *per se* (Figure 1). We thus propose that the prosocial effects of intranasal OXT on human altruism crucially depend on message frames and their interactions with individual person- and context-related factors (Figure 2).

Conclusions

Altruism is a social phenomenon deeply rooted in the evolutionary past of humanity. Across cultures, this form of prosocial behavior is observable both among close relatives and between genetically unrelated individuals. Mounting evidence suggests that the neuropeptide OXT is centrally involved in orchestrating empathy and empathy-based altruism, with recent studies emphasizing the relevance of message frames in determining the direction and magnitude of OXT effects (Marsh et al., 2015; Hurlemann, 2017). However, to date most studies involve male subjects only. Thus, future research involving females is warranted to generalize and further specify the effects of intranasal OXT on human altruism. Another important aspect in OXT-altruism research will be to further elucidate the criteria of message frames under which OXT promotes altruism toward prosocial ends.

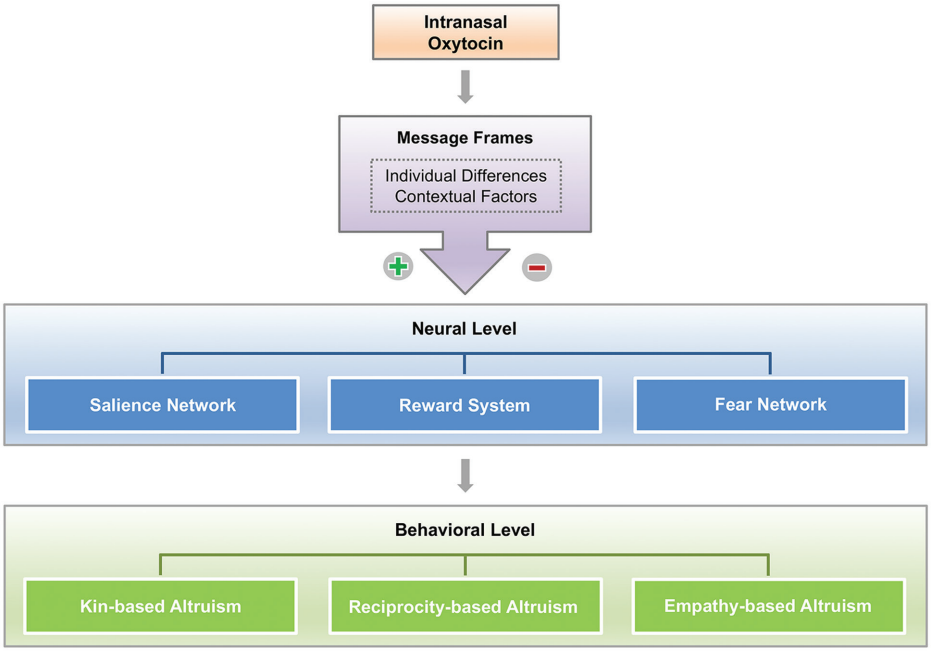

Figure 2: Model of the influence of oxytocin on human altruism.
The behavior-modifying effects of intranasal oxytocin (OXT) appear to be highly sensitive to message frames and their interactions with individual person- and context-related factors. According to our model, intranasal OXT modulates functioning in at least three partially overlapping neural networks, including salience-, reward-, and fear-related circuits. For example, intranasal OXT may promote empathy-driven altruism toward a stranger in need by attenuating amygdala reactivity and increasing the perceived salience of social approach signals.

Acknowledgments: This work was partially supported by a German Research Foundation (DFG) grant (BE 5465/2-1) to RH. The authors thank Johannes Schultz for his comments on an early draft of this manuscript and Alexandra Patin for proofreading the manuscript. They report no biomedical financial interests or potential conflicts of interest.

References

Abu-Akel, A., Palgi, S., Klein E, Decety, J., and Shamay-Tsoory, S. (2015). Oxytocin increases empathy to pain when adopting the other – but not the self-perspective. Soc. Neurosci. *10*, 7–15.

Barberis, C. and Tribollet, E. (1996). Vasopressin and oxytocin receptors in the central nervous system. Crit. Rev. Neurobiol. *10*, 119–154.

Bartz, J.A., Zaki, J., Bolger, N., and Ochsner, K.N. (2011). Social effects of oxytocin in humans: context and person matter. Trends Cogn. Sci. *15*, 301–309.

Batson, C.D. (2011). Altruism in Humans (Oxford, NY: Oxford University Press).

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

Bernhard, H., Fischbacher, U., and Fehr, E. (2006). Parochial altruism in humans. Nature *442*, 912–915.

Bos, P.A., Montoya, E.R., Hermans, E.J., Keysers, C., and van Honk, J. (2015). Oxytocin reduces neural activity in the pain circuitry when seeing pain in others. Neuroimage *113*, 217–224.

Carter, C.S. (1998). Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology *23*, 779–818.

Carter, C.S., Grippo, A.J., Pournajafi-Nazarloo, H., Ruscio, M.G., and Porges, S.W. (2008) Oxytocin, vasopressin and sociality. Prog. Brain. Res. *170*, 331–336.

Choi, J.K. and Bowles, S. (2007). The coevolution of parochial altruism and war. Science *318*, 636–640.

Comte, A. and Fetscher, I. (1966). Rede über den Geist des Positivismus, 2nd ed. (Hamburg, Germany: Meiner).

Dal Monte, O., Noble, P.L., Turchi, J., Cummins, A., and Averbeck, B.B. (2014). CSF and blood oxytocin concentration changes following intranasal delivery in macaque. PLoS One *9*, e103677.

Declerck, C.H., Boone, C., and Kiyonari, T. (2010). Oxytocin and cooperation under conditions of uncertainty: the modulating role of incentives and social information. Horm. Behav. *57*, 368–374.

Declerck, C.H., Boone, C., and Kiyonari, T. (2014). The effect of oxytocin on cooperation in a prisoner's dilemma depends on the social context and a person's social value orientation. Soc. Cogn. Affect. Neurosci. *9*, 802–809.

De Dreu, C.K. and Kret, M.E. (2015). Oxytocin conditions intergroup relations through upregulated in-group empathy, cooperation, conformity, and defense. Biol. Psychiatry *79*, 165–173.

De Dreu, C.K., Greer, L.L., Handgraaf, M.J., Shalvi, S., Van Kleef, G.A., Baas, M., Ten Velden, F.S., Van Dijk, E., Feith, S.W. (2010). The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans. Science *328*, 1408–1411.

De Dreu, C.K., Scholte, H.S., van Winden, F.A., and Ridderinkhof, K.R. (2015). Oxytocin tempers calculated greed but not impulsive defense in predator-prey contests. Soc. Cog. Affect. Neurosci. *10*, 721–728.

de Waal, F.B. (2008). Putting the altruism back into altruism: the evolution of empathy. Ann. Rev. Psychol. *59*, 279–300.

Ditzen, B., Schaer, M., Gabriel, B., Bodenmann, G., Ehlert, U., and Heinrichs, M. (2009). Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. Biol. Psychiatry *65*, 728–731.

Domes, G., Heinrichs, M., Glaescher, J., Buechel, C., Braus, D.F., and Herpertz, S.C. (2007a). Oxytocin attenuates amygdala responses to emotional faces regardless of valence. Biol. Psychiatry *62*, 1187–1190.

Domes, G., Heinrichs, M., Michel, A., Berger, C., and Herpertz, S.C. (2007b). Oxytocin improves "mind-reading" in humans. Biol. Psychiatry *61*, 731–733.

Donaldson, Z.R. and Young, L.J. (2008). Oxytocin, vasopressin, and the neurogenetics of sociality. Science *322*, 900–904.

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

Eckstein, M., Becker, B., Scheele, D., Scholz, C., Preckel, K., Schlaepfer, T.E., Grinevich, V., Kendrick, K.M., Maier, W., and Hurlemann, R. (2015). Oxytocin facilitates the extinction of conditioned fear in humans. Biol. Psychiatry *78*, 194–202.

Farrelly, D., Clemson, P., and Guthrie, M. (2016). Are women's mate preferences for altruism also influenced by physical attractiveness? Evol. Psychol. *14*, 1–6.

Fehr, E. and Gachter, S. (2002). Altruistic punishment in humans. Nature *415*, 137–140.

Fehr, E. and Fischbacher, U. (2003). The nature of human altruism. Nature *425*, 785–791.

Fehr, E. and Fischbacher, U. (2004). Social norms and human cooperation. Trends Cogn. Sci. *8*, 185–190.

Fehr, E., Fischbacher, U., and Gachter, S. (2002). Strong reciprocity, human cooperation, and the enforcement of social norms. Hum. Nat. *13*, 1–25.

Fellner, C.H. and Schwartz, S.H. (1971). Altruism in disrepute. Medical versus public attitudes toward the living organ donor. N. Engl. J Med. *284*, 582–585.

Freeman, S.M., Samineni, S., Allen, P.C., Stockinger, D., Bales, K.L., Hwa, G.G., and Roberts, J.A. (2016). Plasma and CSF oxytocin levels after intranasal and intravenous oxytocin in awake macaques. Psychoneuroendocrinology *66*, 185–194.

Gordon, I., Zagoory-Sharon, O., Leckman, J.F., and Feldman, R. (2010). Oxytocin and the development of parenting in humans. Biol. Psychiatry *68*, 377–382.

Gospic, K., Sundberg, M., Maeder, J., Fransson, P., Petrovic, P., Isacsson, G., Karlstrom, A., and Ingvar, M. (2014). Altruism costs-the cheap signal from amygdala. Soc. Cog. Affect. Neurosci. *9*, 1325–1332.

Guastella, A.J., Einfeld, S.L., Gray, K.M., Rinehart, N.J., Tonge, B.J., Lambert, B.J., and Hickie, I.B. (2010). Intranasal oxytocin improves emotion recognition for youth with autism spectrum disorders. Biol. Psychiatry *67*, 692–694.

Hahn-Holbrook, J., Holt-Lunstad, J., Holbrook, C., Coyne, S.M., and Lawson, E.T. (2011). Maternal defense: breast feeding increases aggression by reducing stress. Psychol. Sci. *22*, 1288–1295.

Hamilton, W.D. (1964). The genetical evolution of social behaviour: I. J. Theor. Biol. *7*, 1–16.

Harbaugh, W.T., Mayr, U., and Burghart, D.R. (2007). Neural responses to taxation and voluntary giving reveal motives for charitable donations. Science *316*, 1622–1625.

Hein, G., Morishima, Y., Leiberg, S., Sul, S., and Fehr, E. (2016). The brain's functional network architecture reveals human motives. Science *351*, 1074–1078.

Holt-Lunstad, J., Birmingham, W.A., and Light, K.C. (2008). Influence of a "warm touch" support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, α amylase, and cortisol. Psychosom. Med. *70*, 976–985.

Hu, Y., Scheele, D., Becker, B., Voos, G., David, B., Hurlemann, R., and 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*, 377.

Hurlemann, R. and Scheele, D. (2016). Dissecting the role of oxytocin in the formation and loss of social relationships. Biol. Psychiatry *79*, 185–193.

Hurlemann, R. and Marsh, N. (2016). New insights into the neuroscience of human altruism. Der Nervenarzt *87*, 1131–1135.

Hurlemann, R., Patin, A., Onur, O.A., Cohen, M.X., Baumgartner, T., Metzler, S., Dziobek, I., Gallinat, J., Wagner, M., Maier, W., et al. (2010). Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. J Neurosci. *30*, 4999–5007.

Insel, T.R. and Young, L.J. (2001). The neurobiology of attachment. Nat. Rev. Neurosci. *2*, 129–136.

Israel, S., Weisel, O., Ebstein, R.P., and Bornstein, G. (2012). Oxytocin, but not vasopressin, increases both parochial and universal altruism. Psychoneuroendocrinology *37*, 1341–1344.

Kaplan, H., Hill, K., Lancaster, J., and Hurtado, A.M. (2000). A theory of human life history evolution: diet, intelligence, and longevity. Evol. Anthropol. *9*, 156–185.

Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., Gruppe, H., Mattay, V. S., Gallhofer, B., and Meyer-Lindenberg, A. (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. J. Neurosci. *25*, 11489–11493.

Kosfeld, M., Heinrichs, M., Zak, P.J, Fischbacher, U., and Fehr, E. (2005). Oxytocin increases trust in humans. Nature *435*, 673–676.

Krebs, J.R. and Davies, N.B. (1993). An introduction to Behavioural Ecology, 3rd ed. (Oxford, Cambridge, MA: Blackwell Scientific Publications).

Krueger, F., Parasuraman, R., Moody, L., Twieg, P., de Visser, E., McCabe, K., O'Hara, M., and Lee, M.R. (2013). Oxytocin selectively increases perceptions of harm for victims but not the desire to punish offenders of criminal offenses. Soc. Cog. Affect. Neurosci. *8*, 494–498.

Lee, H.H., Molla, M.N., Cantor, C.R., and Collins, J.J. (2010). Bacterial charity work leads to population-wide resistance. Nature *467*, 82–85.

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

Lieberman, D., Tooby, J., and Cosmides, L. (2007). The architecture of human kin detection. Nature *445*, 727–731.

Luminet, O., Grynberg, D., Ruzette, N., and Mikolajczak, M. (2011). Personality-dependent effects of oxytocin: greater social benefits for high alexithymia scorers. Biol. Psychol. *8*, 401–406.

Marsh, A.A. (2016). Neural, cognitive, and evolutionary foundations of human altruism. Wiley Interdiscip. Rev. Cogn. Sci. *7*, 59–71.

Marsh, A.A., Stoycos, S.A., Brethel-Haurwitz, K.M., Robinson, P., VanMeter, J.W., and Cardinale, E.M. (2014). Neural and cognitive characteristics of extraordinary altruists. Proc. Natl. Acad. Sci. USA *111*, 15036–15041.

Marsh, N., Scheele, D., Gerhardt, H., Strang, S., Enax, L., Weber, B., Maier, W., and Hurlemann, R. (2015). The neuropeptide oxytocin induces a social altruism bias. J. Neurosci. *35*, 15696–15701.

Mascaro, J.S., Hackett, P.D., and Rilling, J.K. (2014). Differential neural responses to child and sexual stimuli in human fathers and non-fathers and their hormonal correlates. Psychoneuroendocrinology *46*, 153–163.

Meyer-Lindenberg, A., Domes, G., Kirsch, P., and Heinrichs, M. (2011). Oxytocin and vasopressin in the human brain: social neuropeptides for translational medicine. Nat. Rev. Neurosci. *12*, 524–538.

Moll, J., Krueger, F., Zahn, R., Pardini, M., de Oliveira-Souza, R., and Grafman, J. (2006). Human fronto-mesolimbic networks guide decisions about charitable donation. Proc. Natl. Acad. Sci. USA *103*, 15623–15628.

Naber, F., van Ijzendoorn, M.H., Deschamps, P., van Engeland, H., and Bakermans-Kranenburg, M.J. (2010). Intranasal oxytocin increases fathers' observed responsiveness during play with their children: a double-blind within-subject experiment. Psychoneuroendocrinology *35*, 1583–1586.

Nave, G., Camerer, C., and McCullough, M. (2015). Does oxytocin increase trust in humans? A critical review of research. Perspect. Psychol. Sci. *10*, 772–789.

Nowak, M.A., Tarnita, C.E., and Wilson, E.O. (2010). The evolution of eusociality. Nature *466*, 1057–1062.

Olff, M., Frijling, J.L., Kubzansky, L.D., Bradley, B., Ellenbogen, M.A., Cardoso, C., Bartz, J. A., Yee, J.R., and van Zuiden, M. (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*, 1883–1894.

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

Preston, S.D. (2013). The origins of altruism in offspring care. Psychol. Bull. *139*, 1305–1341.

Preston, S.D. and de Waal, F.B. (2002). Empathy: its ultimate and proximate bases. Behav. Brain Sci. *25*, 1–20.

Radke, S. and de Bruijn, E.R. (2015). Does oxytocin affect mindreading? A replication study. Psychoneuroendocrinology *60*, 75–81.

Riem, M.M., Bakermans-Kranenburg, M.J., Pieper, S., Tops, M., Boksem, M.A., Vermeiren, R.R., van Ijzendoorn, M.H., and Rombouts, S.A. (2011). Oxytocin modulates amygdala, insula, and inferior frontal gyrus responses to infant crying: a randomized controlled trial. Biol. Psychiatry *70*, 291–297.

Riem, M.M., van Ijzendoorn, M.H., Tops, M., Boksem, M.A., Rombouts, S.A., and Bakermans-Kranenburg, M.J. (2012). No

laughing matter: intranasal oxytocin administration changes functional brain connectivity during exposure to infant laughter. Neuropsychopharmacology *37*, 1257–1266.

Rilling, J.K. and Young, L.J. (2014). The biology of mammalian parenting and its effect on offspring social development. Science *345*, 771–776.

Rilling, J.K., DeMarco, A.C., Hackett, P.D., Thompson, R., Ditzen, B., Patel, R., and Pagnoni, G. (2012). Effects of intranasal oxytocin and vasopressin on cooperative behavior and associated brain activity in men. Psychoneuroendocrinology, *37*, 447–461.

Rilling, J.K., Demarco, A.C., Hackett, P.D., Chen, X., Gautam, P., Stair, S., Haroon, E., Thompson, R., Ditzen, B., Patel, R., et al. (2014). Sex differences in the neural and behavioral response to intranasal oxytocin and vasopressin during human social interaction. Psychoneuroendocrinology *39*, 237–248.

Samuni, L., Preis, A., Mundry, R., Deschner, T., Crockford, C., and Wittig, R.M. (2017). Oxytocin reactivity during intergroup conflict in wild chimpanzees. Proc. Natl. Acad. Sci. USA *114*, 268–273.

Scheele, D., Mihov, Y., Kendrick, K.M., Feinstein, J.S., Reich, H., Maier, W., and Hurlemann, R. (2012a). Amygdala lesion profoundly alters altruistic punishment. Biol. Psychiatry *72*, e5–7.

Scheele, D., Striepens, N., Güntürkün, O., Deutschlander, S., Maier, W., Kendrick, K.M., and Hurlemann, R. (2012b). Oxytocin modulates social distance between males and females. J. Neurosci. *32*, 16074–16079.

Scheele, D., Wille, A., Kendrick, K.M., Stoffel-Wagner, B., Becker, B., Güntürkün, O., Maier, W., and Hurlemann, R. (2013). Oxytocin enhances brain reward system responses in men viewing the face of their female partner. Proc. Natl. Acad. Sci. USA *110*, 20308–20313.

Scheele, D., Schwering, C., Elison, J.T., Spunt, R., Maier, W., and Hurlemann, R. (2015). A human tendency to anthropomorphize is enhanced by oxytocin. Eur. Neuropsychopharmacol. *25*, 1817–1823.

Shamay-Tsoory, S.G. and Abu-Akel, A. (2015). The social salience hypothesis of oxytocin. Biol. Psychiatry *79*, 194–202.

Shamay-Tsoory, S.G., Fischer, M., Dvash, J., Harari, H., Perach-Bloom, N., and Levkovitz, Y. (2009). Intranasal administration of oxytocin increases envy and schadenfreude (gloating). Biol. Psychiatry *66*, 864–870.

Singh Bhogal, M., Galbraith, N., and Manktelow, K. (2016). Sexual selection and the evolution of altruism: males are more altruistic and cooperative towards attractive females. Lett. Evol. Behav. Sci. *7*, 10–13.

Skuse, D.H. and Gallagher, L. (2009). Dopaminergic-neuropeptide interactions in the social brain. Trends Cogn. Sci. *13*, 27–35.

Stoop, R. (2012). Neuromodulation by oxytocin and vasopressin. Neuron *76*, 142–159.

Stoop, R., Hegoburu, C., and van den Burg, E. (2015). New opportunities in vasopressin and oxytocin research: a perspective from the amygdala. Annu. Rev. Neurosci. *38*, 369–388.

Striepens, N., Kendrick, K.M., Maier, W., and Hurlemann, R. (2011). Prosocial effects of oxytocin and clinical evidence for its therapeutic potential. Front. Neuroendocrinol. *32*, 426–450.

Striepens, N., Scheele, D., Kendrick, K.M., Becker, B., Schafer, L., Schwalba, K., Reul, J., Maier, W., and Hurlemann, R. (2012). Oxytocin facilitates protective responses to aversive social stimuli in males. Proc. Natl. Acad. Sci. USA *109*, 18144–18149.

Striepens, N., Kendrick, K.M., Hanking, V., Landgraf, R., Wüllner, U., Maier, W., and Hurlemann, R. (2013). Elevated cerebrospinal fluid and blood concentrations of oxytocin following its intranasal administration in humans. Sci. Rep. *3*, 440.

Striepens, N., Matusch, A., Kendrick, K.M., Mihov, Y., Elmenhorst, D., Becker, B., Lang, M., Coenen, H.H., Maier, W., Hurlemann, R., et al. (2014). Oxytocin enhances attractiveness of unfamiliar female faces independent of dopamine reward system. Psychoneuroendocrinology *39*, 74–87.

Trivers, R.L. (1971). Evolution of reciprocal altruism. Q. Rev. Biol. *46*, 35–57.

van den Bos, W., van Dijk, E., Westenberg, M., Rombouts, S.A.R.B., and Crone, E.A. (2009). What motivates repayment? Neural correlates of reciprocity in the trust game. Soc. Cogn. Affect. Neurosci. *4*, 294–304.

van Ijzendoorn, M.H. and Bakkermans-Kranenburg, M.J. (2011). A sniff of trust: meta-analysis of the effect of intranasal oxytocin administration on face recognition, trust to in-group, and trust to out-group. Psychoneuroendocrinology *37*, 438–443.

van Ijzendoorn, M.H., Huffmeijer, R., Alink, L.R., Bakkermans-Kranenburg, M.J., and Tops, M. (2011). The impact of oxytocin administration on charitable donating is moderated by experiences of parental love-withdrawal. Front. Psychol. *2*, 258.

Wigton, R., Radua, J., Allen, P., Averbeck, B., Meyer-Lindenberg, A., McGuire, P., Shergill, S. S., and Fusar-Poli, P. (2015). Neurophysiological effects of acute oxytocin administration: systematic review and meta-analysis of placebo-controlled imaging studies. J. Psychiatry Neurosci. *40*, E1–22.

Wittfoth-Schardt, D., Gründing, J., Wittfoth, M., Lanfermann, H., Heinrichs, M., Domes, G., Buchheim, A., Gündel, H., and Waller, C. (2012). Oxytocin modulates neural reactivity to children's faces as a function of social salience. Neuropsychopharmacology *37*, 1799–1807.

Wu, C.C., Diggle, P.K., and Friedman, W.E. (2013). Kin recognition within a seed and the effect of genetic relatedness of an endosperm to its compatriot embryo on maize seed development. Proc. Natl. Acad. Sci. USA *110*, 2217–2222.

Yamasue, H., Yee, J.R., Hurlemann, R., Rilling, J.K., Chen, F.S., Meyer-Lindenberg, A., and Tost, H. (2012). Integrative approaches utilizing oxytocin to enhance prosocial behavior: from animal and human social behavior to autistic social dysfunction. J. Neurosci. *32*, 14109–14117.

Young, L.J. and Wang, Z. (2004). The neurobiology of pair bonding. Nat. Neurosci. *7*, 1048–1054.

Zak, P.J., Stanton, A.A., and Ahmadi, S. (2007). Oxytocin increases generosity in humans. PLoS One *2*, e1128.