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The physiological function of oxytocin in humans and its acute response to human-dog interactions: A review of the literature

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ABSTRACT

Oxytocin is increasingly recognized to have a role in human-dog bonding and interactions and a positive influence on various health outcomes including cardiovascular function and stress reactivity. This review summarizes current research investigating human-dog interactions and endogenous oxytocin to highlight the potentially beneficial role of oxytocin within human-dog relationships and overall human health. We discuss progress and challenges for the field, including the assessment of endogenous oxytocin concentrations, and recommend avenues for future research.

Introduction

Oxytocin is a hormone and neuropeptide synthesized in the magnocellular neurosecretory cells of the hypothalamic paraventricular and supraoptic nuclei. Action potentials in these cells trigger the release of oxytocin, primarily from axonal nerve endings into the extracellular space of the posterior pituitary gland, whence it diffuses into the circulation (Brown et al., 2013; Gimpl and Fahrenholz, 2001). Some magnocellular neurons also project into areas in the forebrain, including the amygdala and hippocampus, which allows the release of oxytocin directly into these structures (Knobloch et al., 2012). Once released, oxytocin is bound to oxytocin receptors via activation of G-protein pathways, triggering intracellular calcium release, which then initiates a range of cellular actions (Gimpl and Fahrenholz, 2001; Lambert et al., 1994). The distribution of oxytocin receptors within the brain varies greatly throughout development, with only a small portion of receptors constantly present. Species differences are also apparent (Gimpl and Fahrenholz, 2001). Central oxytocin release can occur independently or in conjunction with the release of peripheral oxytocin (Neumann and Landgraf, 2012) that is synthesized in tissues such as the uterus, placenta, and heart (Gimpl and Fahrenholz, 2001).

Oxytocin has a well-documented role in labor and maternal bonding (Kendrick, 2000). Its release is also associated with various other physiological, psychological, and behavioral effects including positive cardiovascular outcomes such as decreased blood pressure (Gutkowska et al., 2014; Gutkowska and Jankowski, 2008), reduced stress reactivity via inhibition of the hypothalamic-pituitary-adrenal (HPA) axis (Neumann et al., 2000), decreased inflammation (Ross et al., 2011), increased trust (Zak et al., 2005), and reduced fear (Beetz et al., 2012; Ishak et al., 2011).

Recent years have seen growing recognition of the human-like social skills possessed by dogs. Canine social competence, particularly the sensitivity of dogs to human social cues, has regularly been attributed to the release of oxytocin (see Buttner, 2016 for detailed

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review). A recent review by Kis et al. (2017) identified an almost universal increase in endogenous canine oxytocin following human interaction across five studies (Handlin et al., 2011; Mitsui et al., 2011; Nagasawa et al., 2015; Odendaal and Meintjes, 2003; Rehn et al., 2014). A recent study by MacLean et al. (2017) confirmed these results, documenting an estimated mean increase of 39% in salivary oxytocin and 6% in plasma oxytocin after a 10-minute free-form human-dog interaction. To date, only one published study has reported that human-dog interactions did not elicit a significant change in canine oxytocin concentrations (Romero et al., 2014). Exogenous oxytocin has also been shown to influence canine social behavior with intranasal administration increasing human-directed affiliative behaviors, including sniffing, licking, and physical contact (Romero et al., 2014). Several studies have found associations between genetic variation across the eight identified single-nucleotide polymorphisms in the canine oxytocin receptor gene (Bence et al., 2013) and canine human-directed behavior. These behaviors include proximity seeking and friendliness toward strangers in German shepherd dogs and Border collies (Kis et al., 2014a) (see Kis et al., 2017 for detailed review).

Oxytocin has also been proposed as one of the primary systems involved in human-dog interactions and is thought to play a role in some of the positive health outcomes associated with dog ownership (Beetz et al., 2012, Thielke and Udell, 2015). Empirical investigations of the effect of acute human-dog interactions on human oxytocin concentrations are scarce, so this putative role primarily reflects an overlap between the effects of human-animal interaction and oxytocin release (Beetz et al., 2012). Moreover, the few empirical studies that exist are limited by small sample sizes, ranging from 10 to 141 with a mean sample size of $n = 42$ and, often, weak methodologies using between-subjects study designs and a lack of randomization and blinding.

Significant controversy surrounds the measurement of oxytocin concentrations (Leng and Sabatier, 2016), with the most commonly used fluids, plasma, and saliva, having a variance of 17%-35% (McCullough et al., 2013). Uncertainties also surround the dynamics of central and peripheral oxytocin release. It remains unclear whether the release patterns of oxytocin into each fluid differs and whether possible differences occur in a stimuli-specific manner (Neumann and Landgraf, 2012), with some previous research finding no correlation between cerebrospinal fluid and plasma oxytocin concentrations (Kagerbauer et al., 2013).

We review the literature on acute human-dog interactions and endogenous oxytocin. We also present a model describing oxytocin's role in influencing human-dog relationships, stress reactivity, defined as the biological reaction to exposure to environmental threats (Boyce and Ellis, 2005), social bonding, and cardiovascular parameters. Our review concludes with recommendations for future research directions.

Effects of oxytocin: stress responses and social behavior

Behavioral and endocrine stress responses in humans and other mammals are partially modulated by oxytocin (Brown et al., 2016; Olff et al., 2013). The release of oxytocin decreases arousal to threatening stimuli (Bertsch et al., 2013; Norman et al., 2011a), possibly by attenuating activation of the amygdala (Knobloch et al., 2012) and the HPA axis (Cox et al., 2015; Neumann et al., 2000). Oxytocin also mediates the neurological process of rewarding social information, thereby facilitating learning from social feedback such as happy and sad facial expressions (Hurlemann et al., 2010; Hu et al., 2015). Two possible explanations have been proposed: by increasing the desire for social reward and by influencing sensitivity to the reward value of social information (Bethlehem et al., 2014).

Oxytocin is hypothesized to influence the processing of potential threats, largely through the amygdala, the brain structure primarily responsible for threat processing and social cognition (Ledoux, 2007). Animal models show that magnocellular neurons project from the hypothalamus directly into the amygdala, allowing local release of oxytocin. An oxytocin receptor-dependent pathway then increases activation of GABAergic neurons, inhibiting signaling from neurons in the central nucleus of the amygdala. Local release of endogenous oxytocin has also produced behavioral changes, namely reductions in the freezing response to threatening stimuli in fear-conditioned rats (Knobloch et al., 2012). In humans, functional imaging of the brains of volunteers recruited for a study on amygladic activation associated with presentation of photos of facial expressions found that after nasal oxytocin administration, amygdala activation to angry (Radke et al., 2017) and fearful faces (Domes et al. 2007) is reduced. Oxytocin administration also reduced functional connectivity between the amygdala and the midbrain, providing further evidence of an amygdala-mediated process by which oxytocin reduces fear responses (Kirsch et al., 2005). Interestingly, oxytocin also modulates activation of the amygdala during exposure to happy faces, suggesting an additional effect of mediating arousal to prosocial stimuli (Domes et al., 2007).

The amygdala appears to play a significant role in facilitating oxytocin's influence on social learning (Hu et al., 2015). After exogenous oxytocin administration, increased learning performance has been associated with social reinforces (smiling and angry faces) compared to nonsocial reinforces (green and red lights). Individuals with amygdala damage exhibited poorer learning from this social feedback than individuals with a fully functioning amygdala (Hurlemann et al., 2010). More recently, imaging of the brain has revealed oxytocin administration increased amygdala activation with social feedback during a learning task. Exogenous oxytocin also increased functional connectivity between the amygdala and insula and caudate, brain regions associated with salience and reward, leading the authors to suggest this connection as a possible pathway through which oxytocin enhances social learning (Hu et al., 2015). Animal models are concordant, and impaired social recognition of familiar peers occurs in mice that have undergone amygladic injection of an oxytocin agonist (Ferguson et al., 2001).

The oxytocinergic system is also known to inhibit activation of the HPA axis, an effect exerted in part within the paraventricular nucleus (Neumann et al., 2000). Lactating women who commonly display elevated endogenous oxytocin concentrations show lower plasma adrenocorticotrophic hormone (ACTH) and cortisol concentrations when exposed to an exercise stressor compared to nonlactating women (Altemus et al., 1995). Lower cortisol concentrations, attributed to lactation-associated oxytocin release, have also been observed following the Trier Social Stress Test in breastfeeding women (Cox et al., 2015). Similarly, in oxytocin antagonist–treated rats, ACTH and corticosterone concentrations are elevated during basal and stress conditions (Neumann et al., 2000). The attenuating role of oxytocin on the amygdala and HPA axis has potentially significant implications for human health, as chronic stress is commonly associated with compromised immune function and increased risk of chronic disease and premature mortality (Schneiderman et al., 2005).

Animal studies have found that oxytocin increases prosocial behavior in maternal and pair relationships, often assessed in terms of time spent in close proximity to a partner compared to a stranger (Jones et al., 2017). Similar prosocial effects have been observed in humans with oxytocin being regularly cited for its role in promoting social approach. This has been documented using various methodologies, such as measuring the social distance between subjects following intranasal oxytocin administration (Preckel et al., 2014).

Other behavioral outcomes, such as trust, are also influenced by oxytocin, with Zak et al. (2005) reporting an increase in voluntary monetary transfer (as an indicator of trust) with elevated oxytocin concentrations. Frequency of gaze toward the eyes is used as another measure of human social communication, which again increases with exogenous oxytocin administration (Guastella et al., 2008).

However, the effects of oxytocin are not purely prosocial. Several studies have reported disregard and decreased trust toward outgroup members following intranasal oxytocin administration (De Dreu et al., 2010, 2011). In humans, oxytocin administration has also been thought to increase antisocial behaviors such as envy and gloat. These behaviors were measured following a computerized task involving monetary gain/loss and were quantified via a rating scale in which participants indicated how strongly they felt an emotion from 1 (not at all) to 7 (very much) (Shamay-Tsoory et al., 2009). Based on these findings, social salience theory has been suggested, whereby oxytocin may increase the salience of social information (Radke et al., 2017), meaning its effects on social behaviors vary with situational factors.

Effects of oxytocin: cardiovascular system

Oxytocin and its receptors have been identified throughout the heart and large vessels, with the heart serving as a peripheral site of oxytocin synthesis (Gutkowska and Jankowski, 2008, 2012; Gutkowska et al., 2014). Following release in the heart, oxytocin is bound by cardiac oxytocin receptors leading to direct cardiac effects, namely, decreased heart rate and contraction force (Gutkowska and Jankowski, 2008). Oxytocin secretion has also been associated with decreased blood pressure, increased cardiac glucose uptake, modulation of the parasympathetic nervous system, vasodilation, antioxidant actions in the vessels, and reduced cardiac inflammation (Gutkowska and Jankowski, 2012; Gutkowska et al., 2014).

Oxytocin has been proposed as the physiological mediator that links social behavior to improved cardiovascular function (Grewen and Light, 2011; Norman et al., 2011b). However, there is a scarcity of research in this field and studies in humans are rare. Self-reported history of frequent hugs between human partners has been associated with chronically elevated oxytocin concentrations and decreased blood pressure (Light et al., 2005). In oxytocin-deficient mice, Bernatova et al. (2004) reported elevated mean arterial pressure with exposure to stressor tests. Conversely, rats exposed to ventral stroking for 5 days had long-term reductions in blood pressure, presumed to result from increased endogenous oxytocin (Holst et al., 2002).

Heart rate variability (HRV) is also influenced by oxytocin, with exogenous administration producing an increase in high frequency (HF) HRV and attenuated pre-ejection periods, indicative of increased parasympathetic nervous control in humans (Kemp et al., 2012; Norman et al., 2011b). Increased HRV is believed to reflect improved mental well-being and overall health (Laborde et al., 2017; Shaffer and Ginsberg, 2017) and has been associated with decreased risk of cardiovascular disease (CVD) and all-cause mortality (Gerritsen et al., 2001; Kleiger et al., 1987; Thayer et al., 2010). The effect of oxytocin on HRV has shown to be modulated by loneliness, with subjects who report elevated levels of loneliness displaying a reduced HRV response to exogenous oxytocin administration (Norman et al., 2011b). This suggests that oxytocin may play a role in the association between social isolation and CVD. Similarly, in animal models, oxytocin administration has produced a significant increase in canine HF HRV from basal levels (Kis et al., 2014b; Kovács et al., 2016; Romero et al., 2014). Exogenous oxytocin treatment in female prairie voles (*Microtus ochrogaster*) prevented a reduction in HF HRV during exposure to social isolation, compared with untreated controls (Grippo et al., 2009).

Human-dog interactions

Model of oxytocin's role in dog ownership and human health

Despite the general perception that dog ownership has a positive influence on human health, evidence on the mechanism of action is sparse. The literature is further limited by weak research designs and, often, contradictory results (see Herzog, 2011 for review). However, dog ownership has been associated with a variety of positive health outcomes including reduced stress reactivity (Polheber and Matchock, 2014), improved cardiovascular function (Levine et al., 2013) and increased physical activity (Christian et al., 2013). The following paragraphs explore a potential oxytocin-mediated model of how dog ownership may enhance some human health outcomes and then summarize the literature investigating endogenous oxytocin following human-dog interactions.

The stress-attenuating effects of oxytocin in humans, specifically on the amygdala and the HPA axis, present a biological pathway in which human-dog interactions may moderate stress reactivity to produce positive health outcomes. Through imaging of the brain, Stoeckel et al. (2014) observed increased amygdala activity in response to participants viewing photographs of their own dog. Similar brain activation was observed when participants viewed images of their own child but not when viewing an unfamiliar dog or child. This suggests human-dog bond formation uses similar brain networks to maternal bonding and provides evidence for an oxytocin-mediated role of the amygdala in the association between human-dog interactions and health. However, activation in the midbrain, a region containing a high density of oxytocin receptors, was only observed after viewing one's child, indicating that the oxytocin release pattern after exposure to one's dog may differ from that of mother-child interactions (Stoeckel et al., 2014). Human-dog interactions have also been associated with reductions in cortisol concentrations (as an indicator of HPA axis activity). This has been observed after positive human-dog interactions (Handlin et al., 2011, Odendaal and Meintjes, 2003) and during a stressor test in which participants were interviewed by a panel of researchers in the company of either a friend, dog, or on their own (Polheber and Matchock, 2014).

A positive influence of dog ownership on cardiovascular health has also been highlighted. This association exists both cross-sectionally, comparing dog owners and non–dog owners, and longitudinally, after participants acquire a dog, across a variety of health outcomes including blood pressure, HRV, and longevity in sufferers of CVD. However, contradictory results have been documented, and there is a need for further rigorous scientific investigations in the field (see Levine et al., 2013 for full review).

Preliminary research suggests that oxytocin administration over consecutive days has a positive influence on both physical and psychological health outcomes (Barraza et al., 2013). Consequently, it is plausible to hypothesize daily human-dog interactions that influence oxytocin concentrations may deliver similar benefits.

Acute human endogenous oxytocin response

The first experimental evidence suggestive of oxytocin's role in human-animal interactions was documented by Odendaal (2000), who reported an increase in acute human plasma oxytocin after interaction with a dog (Table). Oxytocin concentrations almost doubled from baseline levels and were significantly greater than following the control condition (quiet book reading). Owners interacting with their own dogs displayed a larger increase in oxytocin concentrations than those interacting with an unfamiliar dog, despite all participants reporting feelings of affection toward

Table
Summary of studies on oxytocin responses in humans after human-dog interaction

First author	Year	Population	Protocol	Sample type	Timing of sample	Measurement	Findings
Odendaal	2000	n = 18 (8 m, 10 f)	Positive interaction with unfamiliar dog compared to book reading	Plasma	Pre-post 0 min, 5-24 mins	High-performance liquid chromatography	↑Oxytocin
Handlin	2011	n = 10 (0 m, 10 f)	3-min verbal, tactile interaction with their own male dogs or no interaction	Plasma	Repeated 0, 1, 3, 5, 15, 30 and 60 min	Enzyme immunoassay	↑Oxytocin at 1, 3 and 5 min
Curry	2015	n = 141(50% m, 50% f)	10-min interaction with unfamiliar dog or cat or no interaction	Plasma	Pre-post 0 min, 10-12 min	Enzyme immunoassay	↓Average percentage change in oxytocin Positive correlation with oxytocin and number of dogs, cats, and total number of pets resided with ↑Oxytocin associated with dog lying down away from person + eye contact between participant and dog
Miller	2009	n = 20 (10 m, 10 f)	≤25-min tactile, verbal, and play-based interaction with their own dog after separation during the day compared to book reading	Serum	Pre-post 0 min, 25 min	Enzyme immunoassay	↑oxytocin in female ↓Oxytocin in male
Nagasawa	2009	n = 55 (21 m, 34 f)	30-min interaction with dog. Human remained sitting, but dog could move freely. Human asked dog to sit every 3 mins for 5 times. Compared to similar interaction but participant forbidden to gaze directly at dog.	Urine	Pre-post 0 min, 50 min	Radioimmunoassay	↑Oxytocin in group 1 but not group 2[a]
Nagasawa	2015	n = 30 (6 m, 24 f)	30-min stationary interaction with dog. Human remained sitting, but dog could move freely.	Urine	Pre-post 0 min, 60 min	Radioimmunoassay	↑Oxytocin in group 1 but not group 2 or human-wolf pairs ↑Human oxytocin when dogs were administered oxytocin, potentially due to ↑ dog-human gaze
Nagasawa	2017	n = 21 (11 m, 10 f) n dogs = 22 (10 m, 12 f)	30-min stationary interaction. Human remained sitting (changed chair every 10 minutes) but dog could move freely. Human could not voluntarily interact with dog but could respond if dog initiated interaction.	Urine	Pre-post 0 min, 60 min	Radioimmunoassay	↑Oxytocin in owners of female dogs compared to male dogs ↑Oxytocin in owners of female dogs treated with oxytocin compared to saline ↑Oxytocin with shorter dog-human touch duration

[a] Group 1: longer duration of dog-owner gaze during interaction; Group 2: shorter duration of dog-owner gaze during interaction.

dogs. This suggests an additional role of oxytocin in long-term human-dog bonding. Compared to the control condition, human-dog interaction also had a significant influence on β-endorphin and prolactin concentrations, both of which are neurochemicals associated with social bonding.

Handlin et al. (2011) observed a significant increase in oxytocin from baseline concentrations in 10 female dog owners after a 3-minute verbal and tactile interaction with their own male dogs. Plasma oxytocin concentrations peaked between 1 and 5 minutes after commencing the interaction. No effect was observed in control participants who sat quietly in the same room with no dog present. In a further study, the mean oxytocin concentrations of owners were associated with several indicators of the long-term quality of the human-dog bond (Handlin et al., 2012), measured via the Monash Dog Owner Relationship Scale (Dwyer et al., 2006). A positive association was found with the frequency of owners kissing their dog and a trending toward significant negative association with the perceived difficulty to care for dog (Handlin et al., 2012). More recently, associations have been identified between owners' oxytocin concentrations and the behaviors displayed by both the owner and dog. Specifically, owners with lower baseline and maximum concentrations of oxytocin initiated touch with their dogs more frequently, possibly due to an increased desire for physical contact. A negative correlation was identified between the owners' maximum oxytocin concentrations and the number of times the dog changed position during the interaction. A positive association was also apparent between a greater increase in oxytocin and reduced use of verbal reprimands. The authors hypothesize that high concentrations of oxytocin may lead to an owner exhibiting friendly behavior toward their dog, thereby producing a calming effect in the dog (Petersson et al., 2017).

Miller et al. (2009) proposed a slight variation to the hypothesis; oxytocin release in humans after human-dog interactions is dependent on the sex of the owner. This dissertation documented a significant increase of 58.4% from baseline serum values in female dog owners following a 25-minute interaction with their own dog, compared to a 26% decrease after the control condition (book reading). These findings were not replicated in male dog owners who demonstrated an unexpected decrease of 21.5% in oxytocin concentrations after dog interaction and a decrease of 56.3% after book reading. Both male and female owners reported similar levels of attachment to the dog, measured via the Lexington Attachment to Pets Scale (Johnson et al., 1992), with no overall correlation emerging between attachment and oxytocin change ratio, directly contradicting previous findings. The notion of sex-dependent oxytocin expression is supported by exogenous oxytocin literature, which has documented variations in behavioral responses between males and females following intranasal administration (Ditzen et al., 2013).

Other research suggests the change in oxytocin concentration after human-dog interactions is influenced by previous exposure to dogs. Curry et al. (2015) documented an unexpected decrease in plasma oxytocin concentrations of −5.3% after interaction with an unfamiliar dog (n = 62). The results showed considerable variation, with change in oxytocin concentration ranging from −40% to +81%. This variation was explained by previous pet exposure, with a significant, positive association identified between the oxytocin response and the number of dogs a participant had previously resided with. It is interesting to note that the authors did not conduct further subgroup analysis based on gender. Considering the findings of Miller et al. (2009), it can be hypothesized that the sex of the owner may also explain the above variation in results.

Focusing on eye contact as an interaction type, Nagasawa et al. (2009) identified a significant association between the duration of human-dog gaze and owner-reported satisfaction and communication with the dog. Cluster analysis showed that, based on these variables, human-dog dyads could be separated into two groups, group 1; "long gaze" (n = 13) and group 2; "short gaze" (n = 42). A significant increase in human urinary oxytocin concentration was observed after the 30-minute interaction in participants clustered in group 1, whereas those in group 2 showed no change. However, when the interactions were controlled to prevent gazing, there was no significant effect on oxytocin concentration, suggesting that dog-human gaze was the primary interaction behavior responsible for the increase in oxytocin.

Nagasawa et al. (2015) replicated these findings, demonstrating a significant association between dog-to-owner gaze duration and the urinary oxytocin change ratio in long-gaze dyads (n = 8). No such association was found between wolf-owner dyads (n = 5) or short-gaze dog-owner dyads (n = 22), suggesting that oxytocin concentrations in humans may be associated with specific social cues representative of attachment in dogs. Supporting this link, the owners of dogs (n = 27) that were administered oxytocin intranasally displayed a significant increase in urinary oxytocin, most likely due to increased human-directed gazing behavior from the dog. However, in both experiments, most participants were clustered in the short-gaze group, meaning the interaction did not significantly influence their oxytocin concentrations, thereby raising questions regarding the generalizability of these findings. Further critique has been cited regarding the omission of the sex of the owners in data analysis. Reanalysis of the data by Kekecs et al. (2016) identified an increase in human oxytocin concentrations in female owners only, compared to no variation in male owners, providing support for the hypothesis of Miller et al. (2009).

On the contrary, a more recent study by Nagasawa et al. (2017) found that the duration of dog-human gaze was not associated with oxytocin change ratio in owners of Japanese breeds of dog (n = 21). In this sample, urinary oxytocin increased significantly after interaction in the owners of female (n = 12) but not male dogs (n = 10). Oxytocin concentrations were also significantly higher in the owners of female dogs when treated with oxytocin compared to saline. The sex of the owner did not significantly affect oxytocin. These findings suggest that breed may influence a dog's interaction style, in turn altering the owners' oxytocin response to interaction. The authors also investigated HRV during dog-human gaze, as an indicator of emotional state, which highlighted reduced overall variability and parasympathetic nervous activity in the owners of female dogs and dogs treated with oxytocin.

Overall, the literature demonstrates a positive association between human-dog interactions and endogenous oxytocin concentrations. However, the relationship is complex with various factors, such as the sex of the owner and previous pet exposure suggested to influence oxytocin secretion. Nonetheless, these findings support an oxytocin-mediated model in which optimal human-dog interactions may enhance human health.

Future research

There is a significant need for further empirical investigations of the immediate and long-term effects of human-dog interactions on oxytocin. Substantial differences in methodologies across the literature make cross-study comparisons difficult. These methodological differences include the type of biological samples acquired, timing of sample collection, location, length and type of interaction, or the relationship of human and dog. To allow pooling of data and future comparisons between studies to, in turn, strengthen our understanding of human-dog interactions, a valid and reliable experimental approach to the measurement of oxytocin is required.

As previously suggested, there is substantial debate across the literature surrounding the measurement of peripheral oxytocin,

first, due to our limited understanding of its release patterns (McCullough et al., 2013; Neumann and Landgraf, 2012) and second due to variations in the use of extraction and assay methodologies (Leng and Sabatier, 2016). Most human-animal interaction studies, to date, have investigated the concentrations of oxytocin in plasma, although several have reported concentrations in urine (Nagasawa et al., 2009, 2015). Concerns regarding the validity of human urinary oxytocin are common, with some research reporting no evidence for an association between urinary oxytocin concentrations and plasma or salivary oxytocin concentrations (Feldman et al. 2011). Another study has suggested that peripheral oxytocin release patterns may differ based on stimuli (De Jong et al., 2015). Therefore, reliance on urinary oxytocin measurements represents a significant methodological flaw that, in turn, limits the validity of findings.

Immunoassays, the most commonly used method of measuring oxytocin, are susceptible to interference from plasma factors and therefore, sample extraction is highly recommended (Leng and Sabatier, 2016). Previous research has shown that without sample extraction, radioimmunoassay and enzyme-linked immunosorbent assay (ELISA) cannot accurately recover spiked oxytocin concentrations. The use of ELISA to measure unextracted samples also produces high variance between duplicates, with a mean coefficient of variation of 20% (Christensen et al., 2014). Hence, it has been suggested that unextracted samples return oxytocin concentrations that are entirely erroneous (Leng and Sabatier, 2016). Studies including those of Curry et al. (2015) have relied on the use of ELISA to measure unextracted plasma samples. Other methods of measuring plasma oxytocin concentrations, such as liquid chromatography, used by Odendaal (2000), are also affected by interference concerns. Such interference represents a major challenge to research in the field, as it raises doubts about the accuracy of past findings. Therefore, a standardized method of extracting and assaying plasma oxytocin is urgently required for future research.

Oxytocin has a short half-life of 4-10 minutes in humans (Leng and Sabatier, 2016). Therefore, the use of presampling and postsampling techniques, seen in Nagasawa et al. (2009); Nagasawa et al. (2015); Miller et al. (2009), and Odendaal (2000), entail a higher risk of missing the peak in oxytocin concentration. The magnitude of the effect of human-dog interactions on oxytocin concentrations may differ between these studies and others that used repeated sampling methods, for example, Handlin et al. (2011) who collected 7 samples across a 60-minute period.

To date, the effects of environment, familiarity of testing facilities, and interaction type on human endogenous oxytocin concentrations remain undocumented. We must consider the possibility that standardized human-dog interactions in clinical settings for research purposes are not indicative of authentic, everyday interactions between human-dog dyads and the effect of experimental interactions on oxytocin concentration may vary from “real-world” situations. An unfamiliar interaction type performed in a novel setting may produce stress in an owner and/or dog, potentially negating the influence of interaction on oxytocin concentrations. All aforementioned studies, with the exception of Miller et al. (2009), were performed in unfamiliar clinical settings, with no empirical evidence regarding the possible influence this may have had on oxytocin concentrations. Protocols incorporating active interaction types, such as dog-walking, rather than inactive interactions, remain negligible. This represents a major gap in the literature, with the potentially cumulative effect of human-dog interactions and environment on the oxytocin response presenting a novel direction for future investigation.

To the authors’ knowledge, no studies have used intranasal administration of human oxytocin to examine the influence on canine-directed behavior, which presents another exciting opportunity for future research. However, the use of exogenous oxytocin is not without issue (Guastella and Macleod, 2012). Intranasal administration has been shown to elevate plasma oxytocin concentrations at a greater and more rapid rate compared to cerebrospinal fluid oxytocin (Striepens et al., 2013), which may be explained by direct absorption of oxytocin from the nasal cavity into the blood stream (Guastella et al., 2013). Peripheral organs, such as the cardiovascular system, may then bind the exogenous oxytocin, in turn influencing the autonomic functioning of an individual and producing anxiolytic effects due to increased parasympathetic control. This may ultimately influence one’s behavior toward their dog.

To further our understanding of the oxytocin response to human-dog interaction, data need to be collected in a valid, reliable, and repeatable manner using standardized techniques. By doing so, one of the primary mechanisms through which dog ownership potentially benefits human health may be explained. In line with the emergence of One Welfare (Colonius and Earley, 2013), a deepened understanding of human oxytocin responses also has significant potential to optimize the human-dog relationship for improved welfare in both species.

Conclusions

Oxytocin secretion has a substantial influence on social learning and behavior. Its release reduces activation of stress pathways, such as the HPA axis and threat-processing centers, such as the amygdala, implying a beneficial role of oxytocin in maintaining mental and psychosocial well-being. Oxytocin has also been identified as a cardiovascular hormone known to generate a range of protective effects.

Our understanding of the underlying motivations for and mechanisms of human-animal interactions remains limited, with the potential role of oxytocin regularly cited but experimental evidence lacking. Despite this, the literature as a whole displays a generally positive association between human oxytocin concentrations and human-dog interaction. Such work parallels canine oxytocin research findings (Buttner, 2016; Kis et al., 2017), thereby suggesting that the oxytocinergic system mediates interspecies bonding in both species. Some results have suggested that this association may be dependent on gender or previous petexposure, but further evidence is required to support these claims. The oxytocin system exhibits clear potential as a pathway by which companion animals ultimately improve human health.

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Conflict of interest

The authors declare no conflict of interest.

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