The Role of Oxytocin in Social Buffering: What Do Primate Studies Add?

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Abstract The ability to maintain close social bonds impacts on reproductive success, longevity, stress and health in social mammals, including humans (Silk et al., Curr Biol 20(15):1359–1361, 2010; Crockford et al., Horm Behav 53 (1):254–265, 2008; Wittig et al., Horm Behav 54(1):170–177, 2008; Archie et al., Proc R Soc B 281(1793):20141261, 2014; Cameron et al., Proc Natl Acad Sci U S A 106:13850–13853, 2009; Schülke et al., Curr Biol 20:2207–2210, 2010; Silk et al., Science 302:1231–1234, 2003; Holt-Lunstad et al., PLoS Med 7(7):e1000316, 2010). Close social bonds provide an important social support system, at least in part by acting as a buffer against the deleterious effects of chronic exposure to stressors (Young et al., Proc Natl Acad Sci U S A 51:18195–18200, 2014; Heinrichs et al., Biol Psychiatry 54:1389–1398, 2003). There is accumulating evidence that individuals that provide predictable affiliation or support to others (bond partners) may moderate the perception of the stressor as well as of the physiological stress response. The neuropeptide, oxytocin, may mediate social buffering by down-regulating HPA activity and thus reducing the stress response. However, much within this process remains unclear, such as whether oxytocin is always released when exposed to a stressor, whether more oxytocin is released if there is social support, what aspect of stress or social support triggers oxytocin release and whether social support in the absence of a stressor also impacts oxytocin release and HPA activity, during everyday life. We review the literature that addresses each of these questions in an attempt to clarify where future research effort will be helpful. A better understanding of these dynamics is likely to have implications for enhancing social and health gains from human social relationships.

Keywords Cortisol • Field primate studies • Social support • Stress

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1 The Social Buffering Phenomenon

Social buffering is a phenomenon where the presence or actions of a bond partner reduces or eliminates the stress response in another individual (Silk et al. 2010; Crockford et al. 2008; Wittig et al. 2008; Holt-Lunstad et al. 2010; Young et al. 2014; Heinrichs et al. 2003; Sanchez et al. 2015; Cohen and Wills 1985). The phenomenon of social buffering occurs not only in the mother–infant relationship but also in adult relationships and may be a mechanism through which close social relationships can exert beneficial effects on an individual's health and indirectly, their reproductive success (Silk et al. 2003; House et al. 1988; Archie et al. 2014; Holt-Lunstad et al. 2010). The purported mechanism underlying the social buffering hypothesis is that the presence of a close social partner moderates the perception of the stressor (Hostinar et al. 2014; Hostinar and Gunnar 2015). This shift in perception moderates the stress response, that is, the reactivity of the hypothalamic–pituitary–adrenal (HPA) axis. This process buffers against potentially adverse effects that are associated with prolonged or repeated HPA axis activation. Socially isolated individuals are more likely to experience chronically elevated HPA activity, which can in turn lead to suppressed immune functioning, reduced fertility and limited longevity (Holt-Lunstad et al. 2010; Young et al. 2014; Romero 2004; Beehner and Bergman 2017).

Up-regulation of HPA activity in response to a stressor is an adaptive reaction to environmental threats, enabling energy release required for fight or flight (Romero et al. 2009). This process is energetically costly, so once a stressor has passed and the availability of extra energy for flight and fight is no longer advantageous, HPA activity should then decrease. Perceptions of what constitutes a stressor, or the magnitude of the stressor, may vary depending on the social context. In rodents, novel environments can act as stressors resulting in raised corticosterone levels, except when accompanied by a bond partner, when corticosterone levels are not raised (Hennessy et al. 2009). Children exposed to a clown, or who received

vaccination injections, did not show cortisol responses if accompanied by a supportive parent (Hostinar et al. 2014; Lupien et al. 2009). This contrasted with children accompanied by an unsupportive parent, who did show raised cortisol levels. It is likely that the presence of another individual that provides reliable support in the face of a stressor may actually lower the threat posed by the stressor, and hence limit activation of the stress response. Mechanisms that limit chronic HPA activity, such as through reliable social support are likely adaptive.

The neuropeptide, oxytocin, key in the formation of mother–offspring bonds, has for some time also been of interest as a potential mediator of HPA activity through social buffering (e.g., Hostinar et al. 2014; Romero et al. 2009; Lupien et al. 2009; Kikusui et al. 2006). More recent work shows direct implications for oxytocin mediation of HPA activity. Studies indicate that oxytocin down-regulates HPA activity (Heinrichs et al. 2002; Burkett et al. 2016; Neumann 2008), both in direct response to a stressor and in the context of a supportive conspecific. There is also evidence indicating that the prevalence of these effects may differ across mammals and differ in the contexts in which they are expressed.

In primates, oxytocin may buffer the HPA access in at least three ways. First, stress itself may trigger central oxytocin release (Torner et al. 2017). While there is good evidence for this in rodents, evidence is contradictory in humans (Brown et al. 2016) and barely addressed in other primates. Second, oxytocin may be released during social buffering (Smith and Wang 2014). It seems plausible that social buffering might operate through the perception that one is safer with a predictable supporter at hand. Whether feeling safer – and oxytocin release – can be achieved through the mere presence of a predictable supporter (bond partner) or whether affiliation is required, such as huddling, grooming, vocal contact ('vocal buffering': Rukstalis and French 2005; Seltzer et al. 2010) or consolation (Burkett et al. 2016) remains to be determined. Third, Cohen and Wills (1985) posited that in addition to social buffering occurring in response to a stressor, social support might also provide health benefits during everyday life, even in the absence of stressors. An example could be that social support occurs by predictably receiving supportive, reassuring behaviour from a bond partner, providing in a sense a prophylactic approach to the perception of stressors. We examine the literature that relates to each of these possibilities.

Both human and non-human primates live in complex social groups, often expressing a diversity of highly differentiated relationships. They not only have protracted mother–offspring bonds that endure for years beyond lactation, some species also show paternal–offspring relationships, pair bonds, adult kin bonds or adult non-kin platonic bonds (Ziegler and Crockford 2017). Thus, in primates, the potential for social buffering through different social relationships and different types of social interaction is substantial. Studying questions related to stressors and social buffering in primates thus may give pertinent insights into these processes in humans that are beyond the reach of rodent models. Thus, whilst we try to draw from all relevant studies, we place a particular emphasis on the role that primate studies might have to offer on this topic.

In this review, we have limited discussion to studies that used oxytocin extraction procedures in plasma or urine. The rationale here is an attempt to clarify sometimes confusing tapestry of results, which may be exacerbated by studies

using unextracted samples, where oxytocin concentrations can inexplicably be magnitudes higher than oxytocin levels from extracted samples (Brown et al. 2016; Horvat-Gordon et al. 2005; Leng and Sabatier 2016).

2 Evidence of Oxytocin Involvement in the Stress Response (See Fig. 1)

Central and peripheral oxytocin can be released in response to a stressor. In rodents, physical (electric shock or forced swimming) as well as social stress (separation) can trigger oxytocin as well as cortisol or corticosterone release (Torner et al. 2017;

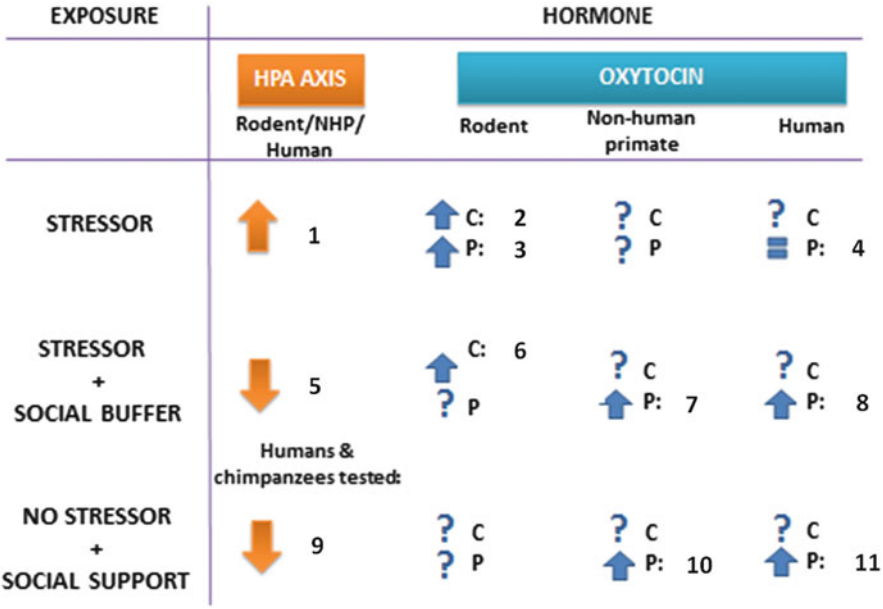

Fig. 1 Established effects of exposure to stressors or to social contact on the HPA axis and oxytocin system in two classes of mammalian taxa. Legend: *Arrows* indicate direction of effect: *Orange*: HPA axis; *Blue*: Oxytocin; *C* central oxytocin, *P* peripheral oxytocin, *NHP* non-human primate, ? not yet tested, = no change. Numbers reference studies. (*1*) Holt-Lunstad et al. (2010), Young et al. (2014), Heinrichs et al. (2003), Sanchez et al. (2015), Hostinar et al. (2014), Hennessy et al. (2009), Torner et al. (2017), and Wittig et al. (2015, 2016). (*2*) Olff et al. (2013), Torner et al. (2017), Jezová et al. (1993), and Babygirija et al. (2012). (*3*) Torner et al. (2017). (*4*) Seltzer et al. (2010). (*5*) Holt-Lunstad et al. (2010), Young et al. (2014), Heinrichs et al. (2003), Sanchez et al. (2015), Hostinar et al. (2014), Hennessy et al. (2009), Smith and Wang (2014), Seltzer et al. (2010), Kiyokawa et al. (2004), and Wittig et al. (2016). (*6*) Hostinar et al. (2014), Hennessy et al. (2009), Burkett et al. (2016), and Smith and Wang (2014). (*7*) Samuni et al. (2017). (*8*) Seltzer et al. (2010). (*9*) Cohen and Wills (1985), Wittig et al. (2016), Field et al. (2013), Ponzi et al. (2016), and Kornienko et al. (2013). (*10*) Crockford et al. (2013). (*11*) Grewen et al. (2005) and Holt-Lunstad et al. (2008). Due to space constraints, in cases of many studies, only a few are represented here

Smith and Wang 2014; Olff et al. 2013; Engelmann et al. 1999). In vole and rat brains, increases in oxytocin concentrations occur in the paraventricular nucleus (PVN) following a stressor (Smith and Wang 2014; Jezová et al. 1993; Babygirija et al. 2012), but not in other parts of the brain (Torner et al. 2017). Torner et al. (2017) have further detailed this pathway in rats, showing that forced swimming triggers rapid HPA activation, with increased levels of ACTH released from the anterior pituitary followed by corticosterone release from the adrenal glands. Oxytocin was simultaneously released peripherally from the posterior pituitary into the blood and then centrally within the paraventricular nucleus. Although oxytocin was released both peripherally and centrally in response to the physical stressor, it seems oxytocin was released by a different trigger in each case. Peripheral release occurred first, possibly through vagal nerve stimulation, whereas central release was likely triggered by the increase in corticosterone levels.

This study indicates that stress leads to both central and peripheral oxytocin release, albeit by different pathways. However, not all studies show this pattern, whether due to species, context or methodological differences (Engelmann et al. 1999; Jezová et al. 1993; Babygirija et al. 2012). The Torner et al. (2017) study suggests that, at least in some cases, peripheral oxytocin release may reflect central oxytocin release, but under what conditions this occurs requires further investigation. In terms of function, centrally released oxytocin seems to down-regulate HPA axis activity. Smith and Wang (2014) showed that female voles experiencing oxytocin microinjections into the PVN during an immobilization stressor had lower resulting corticosterone levels than those receiving a vehicle.

In human studies, the evidence is less clear as to whether a stressor alone, in the absence of social buffering, triggers oxytocin release, with studies being mainly reliant on methods that examine non-invasive peripheral oxytocin release. Some studies suggest that physical endurance is associated with high plasma oxytocin levels, but this is mainly after extreme physical exhaustion. Hew-Butler et al. (2008), for example, conducted a study designed to examine the impact of sodium balance on neuropeptide release. They found raised levels of plasma oxytocin and arginine vasopressin following ultramarathon running and with reduced plasma fluid levels. The high levels are likely a response to restore body fluid balance after extreme physical exhaustion.

A recent meta-analysis of 21 plasma oxytocin and cortisol studies examined the impact of the anticipation of laboratory procedures on human participants' plasma oxytocin and cortisol levels (Brown et al. 2016). Samples were compared after subjects arrived in the laboratory but before anticipated procedures had been carried out. Procedures varied from drug administration to psychological stress tests or simply blood withdrawal. The results showed an overall positive correlation between plasma oxytocin and cortisol levels. There was also substantial variation across studies. Positive oxytocin and cortisol correlations were more likely from those anticipating a procedure compared with those experiencing no further procedure after blood withdrawal. The authors concluded that stressors (the novel environment and procedure anticipation) caused increases in both cortisol and oxytocin levels. However, only 4 of 21 plasma studies showed significant positive correlations between oxytocin and cortisol levels: one was the ultramarathon study

already mentioned designed to test body fluid balance (Hew-Butler et al. 2008), the other three were in anticipation of MDMA (ecstasy), LSD and anti-depressant administration. Thus, whether participants in these three studies would feel anticipatory stress is perhaps hard to predict. This again leaves us without conclusive results as to whether a stressor alone triggers oxytocin release in humans.

The Brown et al. (2016) study does point out the importance of controlling for context to minimize the potential of confounding factors to precipitate hormonal changes, such as novel environments and anticipatory stress responses. Given that social context is also known to impact on endogenous oxytocin (Olff et al. 2013; Crockford et al. 2014), controlling for social context in laboratory studies might also help limit unanticipated variance, such as controlling for social and physical contact provided by experimenters when greeting participants, explaining procedures or drawing blood explicitly. Given that drawing blood can itself be a stressor, standard practice for medical and nursing staff is to offer reassurance during the blood drawing procedure (see p. 13 in WHO 2010). We are not aware of experiments explicitly designed to test whether such 'procedural-related' human contact during potential stressors is sufficient to evoke social buffering mechanisms, hence altering hormone levels although we suggest that such potential outcomes should be controlled for.

In contrast to most of the above studies with human subjects, a study in humans specifically designed to examine the impact of a standard psychological stressor on endogenous oxytocin and cortisol levels showed no rise in urinary oxytocin levels in response to the psychological stressor alone (Seltzer et al. 2010). In two further conditions, after exposure to the Trier Social Stress Test (TSST), child participants were allowed to seek comfort from their mother. The results showed that raised urinary oxytocin levels were only observed after a stressor in the two conditions where comfort from the mother was provided. Salivary cortisol increased during exposure to the stressor in all three conditions but reduced more rapidly in the two conditions with post-stressor mother comfort. Torner et al. (2017) indicate that plasma oxytocin increases following forced swimming show only moderate increases. It is thus possible that in Seltzer et al. (2010), the psychological stressor did trigger small amounts of oxytocin release, too small to be measured in the cumulative sampling method offered by urine. Nonetheless, the results clearly show that in humans, relevant contact from a bond partner following a stressor releases considerably more oxytocin than a stressor alone. Together with the cortisol measures, oxytocin patterns indicate that if small quantities of oxytocin were released during exposure to the stressor, they did not facilitate cortisol decline. In contrast, the oxytocin release and subsequent cortisol decline observed in the two mother comfort conditions is consistent with oxytocin facilitating HPA axis down-regulation, after subjects experienced social support.

If neuropeptide functioning operates differently in rodents compared to humans during exposure to stressors, the question arises whether non-human primate oxytocinergic and HPA axis interactions are more similar to those of rodents or of humans. Modelling the Seltzer et al. (2010) design of contrasting a stressor followed or not followed by bond partner affiliation could be a way to tackle this question.

3 Evidence Supporting the Involvement of Oxytocin in Social Buffering (See Fig. 1)

3.1 Rodent Studies

Kiyokawa et al. (2004) showed that rats exposed to a shock box had decreased c-fos immunoreactivity in the paraventricular nucleus (PVN) when accompanied by a partner rather than experiencing the stressor alone, where c-fos is an amino acid used as an indirect marker of neural activity. Smith and Wang (2014) showed that after experiencing a stressor (1 h of restraint), female monogamous prairie voles allowed to recover with their male partner, rather than alone, showed oxytocin release from the paraventricular nucleus as well as a blunting of the corticosterone response and a reduction in anxiety-associated behaviours. Administration of an oxytocin antagonist blocked social buffering effects. The results show that social buffering is mediated by oxytocin released from the PVN.

3.2 Laboratory Primate and Human Studies

Cavanaugh et al. (2016) showed that female marmoset monkeys had lower urinary cortisol levels when exposed to a novel-housing stressor, when with their pair-bond partner compared to without their pair-bond partner. Male marmosets exhibited higher urinary cortisol levels during the stressor when given a prior oxytocin antagonist compared to those given saline, suggesting that the oxytocin system may inhibit the stress-induced rise in cortisol levels. Rukstalis and French (2005) showed, in marmosets, that separation of bonded pairs resulted in increased urinary cortisol levels. In addition, marmosets hearing vocalizations of their partner during separation, rather than those of a stranger or no vocalizations, had an attenuated cortisol response, indicating that hearing one's partner was sufficient to precipitate social buffering effects.

In humans, Heinrichs et al. (2003) showed that the presence of a friend together with intranasal oxytocin administration was associated with the lowest salivary cortisol levels following a standard psychological stress test (TSST), compared with conditions with no social support or no administered oxytocin. Seltzer et al. (2010) showed that, for children experiencing the TSST, post-test comfort from a mother decreased salivary cortisol earlier and raised urinary oxytocin more than in the no comfort control condition. However, McQuaid et al. (2016) found no support for oxytocin involvement during social buffering in humans. Although participants, with a friend present rather than no friend present during a psychological stressor (TSST), showed lower plasma cortisol levels and reported fewer negative emotions, there were no changes to plasma oxytocin levels.

3.3 Field Primate Studies

To date, primate field studies have examined naturally occurring events either in association with the HPA axis, measuring glucocorticoid levels, or in association with oxytocin levels but not yet measuring both hormones simultaneously. These studies nonetheless give indicators for future research effort. In terms of the HPA axis, they have shown that having bond partners seems to buffer baseline faecal or urinary GC levels following stressors, such as the threat of infanticide (Beehner et al. 2005), sudden social isolation (Engh et al. 2006), hostile inter-group encounters (Wittig et al. 2016), or high rates of conspecific aggression or temperature changes (Young et al. 2014). Thus, changes in GC levels followed the predictions of the social buffering hypothesis (Cohen and Wills 1985). All studies examined social bonds in same-sex platonic adult relationships, some between kin and some between non-kin adults. These studies indicate that in wild adult primates, social bonds provide social buffering effects. Particularly Young et al. (2014) and Wittig et al. (2016) also indicate that platonic adult relationships, or friendships, can work like mother–offspring, kin or pair bonds in buffering against adversity.

Studies have examined wild chimpanzees when exposed to a natural and potentially life-threatening stressor, inter-group encounters. One study (Wittig et al. 2016) compared urinary GC levels after inter-group encounters with urinary GC levels during resting control periods, using a within-subjects design event-sampling approach. Urinary GCs were sampled following each event noting whether chimpanzees engaged in the event with or without a friend. Urinary GCs were significantly higher than resting controls, only when engaging in inter-group encounters without a friend. When engaging in inter-group encounters with a friend, urinary GCs were not higher than resting controls. The results suggested that engaging in a stressor together with a friend offers social buffering effects. Another study showed that urinary oxytocin levels during inter-group encounters are higher than during control samples (Samuni et al. 2017). Together these studies suggest that social buffering or social support effects observed during a stressor may be mediated by oxytocin regulating-effects on the HPA axis.

4 The Involvement of Neural Circuitry in Social Buffering

Hostinar et al. (Hostinar et al. 2014; Hostinar and Gunnar 2015) have written two excellent reviews making the case that, in addition to the oxytocin system, social buffering may be mediated by cortical control of negative emotions, through neural circuits known to moderate fear and pain, such as right anterior insula and superior frontal gyrus, but more specifically in the pre-frontal cortex (PFC). Assessment of stressors occurs in the pre-frontal cortex, which then sends information to limbic regions, such as the amygdala, which are in turn strongly connected to the PVN. Individuals who experience a sense of safety from their attachment figures also

show PFC activity. In threat regulation tests, women with higher psychosocial resources and lower cortisol levels showed greater ventro-medial PFC activation and a decrease in amygdala activation (Taylor et al. 2008). Oxytocin is known to stimulate and inhibit neural activation in at least some of the same brain regions. This suggests that the extent or limit of oxytocin's role in neural activation in social buffering contexts needs to be assessed. Other possible sources of neural regulation of the perception of exposure to stressors include the hippocampus, which has inhibitory projections to the HPA axis and plays an important role in reducing cortisol excretion (Ulrich-Lai and Herman 2009).

5 The Potential Roles of Oxytocin Involvement During Stress Exposure

In rodents, oxytocin microinjections into the PVN can limit stress-induced increases in corticosterone levels during exposure to a stressor, as well as limiting associated anxiety behaviours (Smith and Wang 2012). This is similar to the impact of social buffering after a stressor, in terms of both hormone and behaviour patterns (Smith and Wang 2014). One role of oxytocin release during a stressor in a social support context is to provide buffering of the stress response, as seen in monogamous voles (Smith and Wang 2014).

In marmosets, Cavanaugh et al. (2016) found that male and female marmoset pairs spent less time together after receiving an oxytocin antagonist, rather than saline, prior to exposure to a novel-housing stressor. This indicates that the oxytocin system may be important for social support-seeking behaviour during a stressor.

Whilst it might be that a function of oxytocin release during exposure to a stressor may be HPA axis down-regulation, oxytocin may have other possible roles in this context, specifically related to perceptual priming and stress-coping strategies. In support of perceptual priming, Eckstein et al. (2014) found that human participants exposed to a stressor expressed enhanced sensations of stress after intranasal oxytocin was administered, prior to exposure to the stressor, compared to those administered a placebo. One could speculate that enhanced sensation of stress may facilitate social-support seeking behaviour. Finding social support may then precipitate further oxytocin release. The social support may alter the perception of the stressor, or assist in eliminating the source of the stressor, mediated through oxytocin. Oxytocin may also facilitate HPA axis down-regulation.

With regard to stress-coping strategies, in humans severe stressors, such as death of a bond partner precipitating bereavement, can trigger depressive-like symptoms or passive stress-coping styles (Eckstein et al. 2014). A recent study in voles showed that oxytocin involvement may differ in acute versus chronic HPA activation. Voles experiencing partner loss showed a compromised oxytocin system in multiple ways, possibly through chronic activation of corticotropin releasing hormone (Bosch et al. 2016). Bosch et al. (2016) showed that administered oxytocin

may inhibit the potential to respond to a severe social stressor with passive stress-coping styles. They proposed that the suppression of oxytocin signaling may be adaptive during short separations, encouraging reunion with the partner, and may have evolved to maintain long-term partnerships. They also proposed that therapeutic strategies targeting these systems could be considered for treatment of depression precipitated by social loss.

For at least some species, oxytocin is released as an early response to a stressor. Oxytocin may in addition be released, and possibly in greater quantities, in response to *social support* offered before, during or after the stress, as suggested by human and non-human primate studies (Heinrichs et al. 2003; Seltzer et al. 2010; Wittig et al. 2016; Samuni et al. 2017).

What might the differing roles of OT release be when triggered by these two different stimuli: exposure to a stressor or social buffering? If OT is priming the perceptual awareness parts of the brain, heightening the sensation of threat imposed by the stressor, this may facilitate activation of the stress response. It may also activate social-support seeking behaviour. Finding active social support may, in some cases, effectively lower the threat for the individual, such as when facing a predator or an aggressive conspecific. Two or more individuals may be more likely to deter the predator or aggressive conspecific rather than one, or when huddling to protect against cold temperatures. Given that the function of the stress response is to prime the body for fight or flight against a threat, when social support is available, individuals may actually face a lower threat from any given stressor. Whether or not this process during social support requires greater oxytocin release than when experiencing a stressor without social support, or whether this is moderated, for example, by cortical control in the PFC, remains to be confirmed.

6 Social Mechanisms That May Be Associated with Social Buffering Effects

6.1 Can Social Buffering Help Explain In-Group/Out-Group Effects?

Humans are highly territorial and from a young age show robust tendencies to classify others into in-group/out-group dichotomies, showing more cooperative behaviour towards ‘in-group’ members (De Dreu 2012; Over 2016). Examining the physiological mechanisms underlying this often divisive aspect of human nature may be useful in moderating it (Ziegler and Crockford 2017; De Dreu 2012). In chimpanzees, we recently examined HPA activity and oxytocin release during a stressor that individuals of a group face simultaneously, the threat of hostility from an out-group. Like humans, chimpanzees are highly territorial. Encounters with out-groups precipitate coordinated hostile attacks from group members towards out-group chimpanzees. If a chimpanzee faces an out-group alone, there is greater

chance of injury and death. Winning territory disputes is a numbers game, such that the group that out-numbers the other is most likely to win (Wrangham and Glowacki 2012). Both of these facts indicate that the threat of injury or loss of territory is reduced when individuals face an out-group together rather than alone, but only when agonistic support can be counted on. If an individual defects rather than remains, then the imposed threat is not reduced.

In chimpanzees, facing an out-group results in higher urinary glucocorticoid excretion (Wittig et al. 2016; Sobolewski 2012). Facing the threat of an out-group with a friend, from whom support can be counted on, likely reduces the risk incurred and moderates the stress response, resulting in lower urinary glucocorticoid levels (Wittig et al. 2016). In both humans and chimpanzees, perception of an out-group is positively associated with oxytocin (Samuni et al. 2017; De Dreu 2012). In humans, intranasal oxytocin administration enhances in-group cooperation against an out-group (De Dreu 2012), suggesting that in-group cooperation in the face of an out-group is mediated by the oxytocin system. In chimpanzees, the threat of an out-group precipitates oxytocin release with individuals showing higher urinary oxytocin levels before and during out-group contexts than in control contexts (Samuni et al. 2017). This is associated with highly cohesive, coordinated behaviour that likely reduces the risk of injury from rivals during the inter-group conflict.

Stressor and social buffering contexts have been examined from the perspective of an individual facing a threat. In-group/out-group contexts differ only in that a stressor context is examined from the perspective of several individuals facing a threat simultaneously. During single-individual stressor contexts with social support, individuals experience oxytocin release and HPA axis up-regulation. At least in human and non-human primates, this likely facilitates partner-seeking behaviour. Extrapolating from single-individual stressor contexts to multi-individual stressor contexts, if individuals are all simultaneously engaging in partner-seeking behaviour, this will likely facilitate group cohesion and may be a mechanism that has been co-opted for the kind of group-level agonistic support and cooperation observed in chimpanzee and human territorial contexts. Cooperative breeders, like some bird species, such as green woodhoopoes and babblers (Radford 2008), also engage in forms of coordinated territorial defence. In green woodhoopoes, territorial encounters are followed by increased rates of affiliation (Radford 2011) and may be mediated by the co-evolution of similar mechanisms.

6.2 Social Support in the Absence of a Stressor (See Fig. 1)

The impact and benefits of social support have been discussed in the medical and psychological literature for the last 30 years (Cohen and Wills 1985; Thoits 2011), with repeated calls for explicit testing of the impact of social support during everyday life, even in the absence of stressors (Lakey and Orehek 2011). Mainly using self-report techniques, such as answering questionnaires, some studies have

examined the impact of social integration or social support on quality of life, or have examined how the perception of social support impacts on the perception of general 'stress' levels. Few studies have examined the impact of social parameters directly on cortisol measures (Lakey and Orehek 2011). A study on chimpanzees (Wittig et al. 2016) suggests that down-regulation of the HPA axis due to social support from a bond partner may not be limited to stressor contexts. Decreases in urinary glucocorticoid levels were found following social interactions with bond partners but not with other individuals, whether during stressors (inter-group encounters) or during everyday contexts such as grooming. Again in the absence of explicit exposure to stressors, a study on women with pre-natal depression found that those who engaged in-group support activities reported less depression-associated symptoms and lower cortisol levels, directly following support sessions (Field et al. 2013). Likewise, one study each on children and on students showed that those self-reporting more rather than less connected social networks had lower salivary cortisol levels (Ponzi et al. 2016; Kornienko et al. 2013).

Some human studies have also examined the impact of perceived social support on *oxytocin* levels outside of stress-exposure contexts. Grewen et al. (2005) found that both men and women had higher plasma oxytocin levels, following 10 min of resting, when they reported that they had supportive rather than unsupportive partners. Holt-Lunstad et al. (2008) found that couples engaged in a program of affiliative touch over a 4-week period resulted in higher post-treatment salivary oxytocin levels than couples in the non-intervention group. No effects were found, however, on salivary cortisol.

In chimpanzees, the impact of bond partners in a non-stressor context, grooming, was examined. Urinary oxytocin levels after grooming mirrored urinary GC levels, with urinary oxytocin levels being higher than resting control periods after grooming with bond partners, but not different to resting control periods after grooming with non-bond partners (Wittig et al. 2016; Crockford et al. 2013). These studies suggest that social buffering or social support effects observed in non-stressful contexts may be mediated by oxytocin regulating-effects on the HPA axis.

In the absence of specific exposure to stressors, initial human studies generally show positive correlations between self-report measures of social support and oxytocin levels, and negative correlations with cortisol levels. Potential advantages of non-human primate studies are being able to objectively measure social support through direct behavioural observations, and to non-invasively measure associated hormone levels, after the occurrence of natural events, either stressors or non-stressors. Considerable scope for further research is open here to determine how everyday social interactions may alter the perception of an individual's exposure to stressors and, hence, facilitate HPA axis regulation.

7 Potential Triggers for Oxytocin Involvement in Social Buffering

Hostinar et al. (2014) suggest that behavioural triggers of social buffering effects – and potentially oxytocin release – change during ontogeny. Across mammals, infants require physical affiliative contact, whereas in adults proximity may be sufficient.

A number of captive studies have examined the impact of separation and reunion on primates' GC levels, depending on the relationship between individuals separated or reunited (e.g., Kikusui et al. 2006; Rukstalis and French 2005; Kiyokawa et al. 2004). Few studies, captive or wild, however, have actually tested social buffering effects of specific social interactions on cortisol levels. A rare exception is Rukstalis and French (2005), who showed that marmosets hearing vocalizations of their partner during separation, rather than those of a stranger or no vocalizations, had an attenuated cortisol response, indicating that hearing one's partner was sufficient to precipitate social buffering effects.

In some studies on wild primates, rates of behavioural exchange over time within certain dyads correlated with GC levels. In chacma baboons, for example, focused rather than diffuse grooming networks influenced faecal GC levels, but rates of aggression did not (Crockford et al. 2008). Also, during a period of male immigration that corresponded with raised female faecal GC levels, females who had strong social bonds showed more focused grooming on bond partners after than before the rank change began. These females also showed faster return of faecal GC levels to baseline levels in the following weeks than females with weak social bonds (Wittig et al. 2008). Thus, it seems that, in female baboons, partner-specific grooming may impact on HPA activity.

This is further supported by two chimpanzee studies which showed that grooming with bond partners is associated with higher urinary oxytocin and lower urinary glucocorticoids than grooming with other individuals or than resting controls (Wittig et al. 2016; Crockford et al. 2013). Both of these studies also showed that the effects were not as strong when bond partners were merely present but not grooming. Whilst it seems that the act of grooming with bond partners more than the mere presence of bond partners decreases urinary GC levels, further details on what exactly triggers social buffering effects remain unclear. It cannot be the act of affiliative touch per se, given that grooming with non-bond partners did not show elevated urinary oxytocin or decreased urinary glucocorticoid levels. This suggests that there is a perceptual change for the groomers. Individuals may, for example, feel safer when grooming with individuals that provide predictable support, compared with grooming with individuals that do not. In these studies, bond partners are operationally defined as dyads within a population that provide each other with affiliation and support at higher rates than other dyads, and hence their affiliation and support is relatively predictable (Wittig et al. 2016; Crockford et al. 2013; Silk 2007).

In chimpanzees, engaging in cooperative behaviours such as food sharing, hunting and territorial defence is also associated with high urinary oxytocin levels (Wittig et al. 2016; Samuni et al. 2017). The latter two are group-level coordinated events, where working in coordination with other group members is more likely to result in catching a monkey or in winning a risky inter-group encounter, respectively. These results, together with those in grooming contexts, suggest that there is a psychological dimension that facilitates both the social buffering effects and events requiring group coordination. In both cases, perceptual change may be related to the perception of support, the feeling of being supported or being safer, the feeling of being in something together or a sense of togetherness. Studies on humans are needed to examine whether such a perceptual change would be a cause or a consequence of oxytocin release.

Studies show social buffering effects in adult pair–bond relationships (Hennessy et al. 2009; Kikusui et al. 2006) as well as in adult same-sex friendships, whether with kin or with non-kin (Wittig et al. 2016). Current thinking suggests that the most likely path for the evolution of adult friendships and the resulting social buffering effects is through the co-opting of oxytocin-neural circuitry that supports mother–offspring bonds (Hostinar et al. 2014; Ziegler and Crockford 2017). A central role of nurturing mothering behaviour, required to assist offspring survival, is protecting offspring from exposure to stressors, such as predators, extreme temperatures, conspecific aggression and so on. Social buffering is likely to be associated with this protective behaviour (Hostinar et al. 2014). Examining both within and between species, it may be that, where social bonds have evolved, social buffering is also likely. A productive approach to determine what might trigger social buffering and its beneficial effects (positive perceptual change and down-regulation of the HPA axis) may be to examine what aspects of mother behaviour towards offspring precipitates social buffering effects in offspring.

8 Conclusions and Future Directions

Across mammals, evidence suggests that social buffering is likely an effective social strategy to limit both the exposure to stressors and any negative physiological impact from over-exposure to stressors. Social mechanisms that minimize exposure to stressors are likely to assist in maintaining HPA axis regulation. At a hormonal level, the HPA axis provides an appropriate ‘flight or fight’ response to stressors. Social mechanisms, such as receiving social support that reduce the risk posed by a current stressor (such as receiving coalitionary support during an attack by a predator or conspecifics or huddling during exposure to cold temperatures), may reduce the need for a ‘flight or fight’ response, and hence reduce the frequency and degree of HPA axis up-regulation. In addition to reducing exposure to stressors and reducing the risk posed by a current stressor, it seems that bond partner support triggers oxytocin release, which may be an important regulator of the HPA axis, at least in mammals. It may be that the perception of receiving predictable support

(either in terms of affiliation or cooperation) is critical for triggering oxytocin release.

It seems likely that hormonal and neural circuits precipitating social buffering effects, especially those involving oxytocin, have been co-opted from mother relationships to offspring, where social buffering can totally eliminate up-regulation of HPA activity to stimuli, that when offspring are alone, are perceived as a stressor (see Hostinar et al. 2014). This is likely to be the case if the stressor no longer poses any real threat to the offspring, because the mother provides a protective presence.

It is possible that other affiliative or cohesive social behaviours are underpinned by neuro-endocrine pathways co-opted from mother–offspring relationships. For example, a group of animals facing a stressor together, such as a hostile out-group, show anticipatory oxytocin release and coordinated in-group behaviour against the out-group. Other, not yet examined candidates include reconciliation, a common affiliative behaviour in primates, where previous opponents affiliate after a fight (a social stressor (Wittig et al. 2015)). Reconciliation functions to re-establish relationships within group-living animals. Studies have found that reconciliation post-aggression is more likely when the aggression occurred between individuals that share a valuable relationship, such as bond partners (Wittig and Boesch 2005) or bonded pairs (ravens: Fraser and Bugnyar 2011). Reconciliation, which functionally enables individuals to cooperate again, may also provide an enhanced feeling of safety, triggering oxytocin release and down-regulating GC production.

Studies to date suggest that HPA axis activity is relatively consistent across mammals during exposure to stressors and stress-buffers. However, there may be variation across mammals in *oxytocin* activation, particularly to stressors. Studies with rodents show oxytocin release during exposure to stressors. To our knowledge, this has not been shown to be the case in humans, although this could be due to differences in sampling substrates. If substantiated, it may be that primates, with their phylogenetic proximity to humans, will provide a helpful model species for addressing oxytocin and stress-related questions, particularly now that non-invasive sampling methods have improved.

Other reasons that primate studies will be valuable include the opportunities offered from studying their diverse and multi-dimensional social systems. Like humans, primates express a variety of social behaviours and social relationships throughout their lives. Methods for objectively assessing the strength, number and duration of social bonds, as well as how integrated individuals are into a social network, are well established, measures that can be problematic to assess objectively in humans. Also, methods for non-invasive sampling of hormones are well established in primates, bypassing potential confounds related to laboratory testing situations in humans (see Brown et al. 2016). To date, the vast majority of studies into social buffering have been conducted on a few species. Examining cooperative or affiliative social behaviours before and during stressors across a wider range of species and social systems may be productive in further mapping the social-buffering system and how to maximize social and health gains for humans from this system. Primate studies have the potential to play an important role in this research.

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