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Social effects of oxytocin in humans: context and person matter

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Building on animal research, the past decade has witnessed a surge of interest in the effects of oxytocin on social cognition and prosocial behavior in humans. This work has generated considerable excitement about identifying the neurochemical underpinnings of sociality in humans, and discovering compounds to treat social functioning deficits. Inspection of the literature, however, reveals that the effects of oxytocin in the social domain are often weak and/or inconsistent. We propose that this literature can be informed by an interactionist approach in which the effects of oxytocin are constrained by features of situations and/or individuals. We show how this approach can improve understanding of extant research, suggest novel mechanisms through which oxytocin might operate, and refine predictions about oxytocin pharmacotherapy.

The rise of oxytocin research in humans

The past decade has produced nearly a fourfold increase in published studies on the effects of exogenous oxytocin on social cognition and prosocial behavior in humans [1,2] motivated largely by research showing that oxytocin is involved in regulating such social processes in animals [3]. The excitement about oxytocin has not been confined to the scientific community: dubbed the ‘love hormone’ (e.g. Alleyne, R., *The Telegraph*, 23 September 2010; <http://www.telegraph.co.uk/health/healthnews/8020464/Oxytocin-the-love-hormone-could-cure-shyness.html>), oxytocin is a frequent topic in the popular press and among the general public. Indeed, ‘Google Insights’ reveals that searches for ‘oxytocin nasal spray,’ ‘oxytocin autism’ and ‘oxytocin social anxiety’ have grown by more than 5000% since 2004 (information obtained 14 April 2011).

Although some parallels exist between the social effects of oxytocin across species [4,5], inspection of extant data in humans reveals inconsistencies and small effect sizes that prompt the question: ‘what effect, if any, does oxytocin have on human social cognition and prosocial behavior?’ This observation echoes the doubts that faced personality psychology in the 1960s due to findings that personality traits rarely predicted behavior in a consistent fashion (Box 1) [6–9]. This impasse was resolved by adopting an interactionist approach in which dispositions were viewed as combining with features of a situation to produce

behavior. We argue that a similar interactionist approach can clarify the role of oxytocin in human social cognition and prosocial behavior. Oxytocin is generally thought to exert situation-invariant effects on behavior, being described, for example, as improving social cognition or promoting prosocial behavior. As detailed below, however, empirical support for this view is surprisingly inconsistent, and the effects of oxytocin are often moderated by contextual factors (i.e. features of the situation in which oxytocin is administered) or by stable characteristics of the individuals to whom oxytocin is administered.

This pattern of findings suggests that two key features of an interactionist approach could improve our understanding of the social effects of oxytocin. First, inconsistencies across studies should not be seen as ‘noise,’ but as clues to the context- and person-dependent nature of the effects of oxytocin. Second, characterizing this context- and person-dependency could enable more refined theorizing on the social effects of oxytocin in humans. Viewing the effects of oxytocin in this way casts new light on extant and emerging empirical data, and can inform a more individualized use of oxytocin as a therapeutic agent.

In this article we review the findings published to date documenting the effects of oxytocin on social cognition and prosociality more broadly to illustrate the context- and person-dependent effects of oxytocin. Studies that do not directly assess social cognitive and/or behavioral outcomes (e.g. functional imaging studies without cognitive and/or behavioral measures, and studies investigating the effects of oxytocin on stress reactivity) will not be focused on in our empirical review, but will be considered in our discussion of potential mechanisms underlying the social effects of oxytocin. Moreover, we focus on studies that experimentally manipulate the availability of oxytocin (e.g. via intranasal administration of synthetic oxytocin) rather than studies investigating the correlates of endogenous oxytocin levels because our primary concern is with understanding the social effects of oxytocin in humans (although we do discuss the literature on endogenous oxytocin towards the end of this review because we suspect that such natural variation could crucially moderate the effects of exogenous oxytocin administration). Finally, we note that this article concerns the social effects of oxytocin in humans rather than animals; thus, we reference the animal literature only where it helps to contextualize the human data (there are several comprehensive reviews on this topic, e.g. [3,10–14], for the interested reader).

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Box 1. Roots of interactionism: the trouble with traits

Interactionism in personality and social psychology was put forward to resolve an uncomfortable paradox. On the one hand, researchers and lay conceptions alike posited that individuals have traits (e.g. introversion and aggression) that should reliably predict their behaviors [79]. On the other hand, a cascade of demonstrations indicated that traits, assessed by individuals themselves or by researchers, produced low or nonexistent correlations with behavior assessed across varying situations (e.g. someone judging themselves as conscientious might study hard for exams but be an irresponsible friend or parent) [8,80]. This failure to validate trait models led to a crisis for personality research [8,81] and eventually to a sea change in the interpretation of individual differences that was spearheaded by Mischel and colleagues [82].

Mischel's reconceptualization of personality made two fundamental points. First, individual differences are best described not as predictors of behavior across all situations but rather as stable predictors of behavior within specific contexts [82]. For example, in several field studies individuals did not differ in their overall display of a given behavior (e.g. verbal aggression) but rather showed stable patterns of individual variability in the situational predictors of the behavior (e.g. one teenager became aggressive when scolded by a teacher but not when teased by a peer, whereas another teenager showed the opposite pattern; see [83,84]). Second, individuals' behavioral profiles across contexts reflect not only the gross features of situations themselves but also the ways individuals interpret those features [82]. Importantly, individuals can differ in the value they assign to certain stimulus types or in the expectancies they have about the meaning of those stimuli, and these 'psychological ingredients' underlie individual differences in behaviors in a given context [82,85]. We argue that both of these points can illuminate our understanding of the effects of oxytocin on human social cognition and behavior.

The effects of oxytocin on social cognition and prosociality in humans*Social cognition*

Research shows that oxytocin plays a central role in social recognition in animals (e.g. [15–18]). This research inspired numerous studies examining whether oxytocin has similar effects on social memory in humans [19–21,23], as well as studies examining other aspects of human social cognition such as emotion detection [24–27], emotion recognition or 'theory of mind' [5,28–30], and empathy, including the vicarious sharing of others' internal states [29,31]. Several of these studies report beneficial effects of oxytocin. For example oxytocin has been shown to improve an individual's ability to produce normative ratings of others' emotions based on pictures of the eye region of the face in healthy adults [5], and in individuals with autism spectrum disorders (ASD) [30].

Such findings are clearly grounds for excitement about the therapeutic use of oxytocin to improve social cognitive abilities. However, a closer look at the data reveals that the effects of oxytocin are often nuanced and inconsistent. For example three of the six studies/outcomes evaluating the effects of oxytocin on emotion recognition or affect sharing/empathy report nonsignificant main effects of oxytocin [28,29,31]. Perhaps more importantly, more than two-thirds of studies on oxytocin and social cognition, both those reporting significant and null main effects, demonstrate effects qualified by interactions with task or stimulus variables [5,19–21,23–25,27,28,30] (Table 1). This suggests that the most appropriate question is not 'does oxytocin improve social cognition?' but rather 'under what

circumstances does oxytocin improve social cognition?' This question is crucial both to understanding the basic mechanisms through which oxytocin works, and for clarifying the circumstances under which it can be expected to serve as a treatment for psychiatric illnesses involving prominent social deficits such as ASD and schizophrenia.

Although the factors moderating the effects of oxytocin on social cognition are varied, we focus on one to illustrate the point that the relationship between oxytocin and social cognition can be constrained by contextual and/or individual difference factors. Of the four studies investigating the effects of oxytocin on emotion recognition [5,28–30], three have been qualified by factors reflecting task difficulty (the fourth study found no effect of oxytocin on emotion recognition). Namely, one study found that, for typically developing individuals, oxytocin improved performance only on more difficult test items (i.e. pictures generating < 70% accuracy at baseline [5]). A second study found that for adolescents with ASD, oxytocin improved performance only on easier test items (specifically, adolescents with ASD performed poorly in all conditions except the easy items plus oxytocin condition [30]). Although seemingly contradictory with the first study, this discrepancy can be resolved by considering the possibility that 'easy' items might actually be difficult for individuals with ASD [30]. Finally, one study employing a naturalistic empathic accuracy task to assess emotion recognition [32,33] found that oxytocin had no main effect on the accuracy of interpersonal judgments [28]. Instead, the effect of oxytocin was moderated by individual differences in social proficiency: oxytocin selectively improved empathic accuracy performance for less socially proficient individuals (who performed worse on the task overall and probably found it more challenging) but it had no effect on performance for more socially proficient individuals (who performed equally well whether they were given intranasal oxytocin or placebo) [28]. Taken together, these studies support the view that oxytocin improves emotion recognition only under certain circumstances, such as when a task is demanding for the individual performing it; they also indicate that there is a point beyond which oxytocin cannot improve social cognitive abilities [28,30].

Prosociality

In addition to social cognition, oxytocin has been shown to play a role regulating a suite of behaviors that support the formation and maintenance of attachment bonds in animals (for review see [10]). Building on this research, there are now several published studies investigating the prosocial effects of oxytocin in humans: behaviors that facilitate interpersonal relations, including trusting behavior, generosity and cooperation [4,34–40]; perceiving others in ways that facilitate affiliation/bonding (e.g. perceptions of trustworthiness [34–36,41,42], attractiveness [41], approachability [20], infrahumanization [43], attachment [44,45]), and social-emotional responses such as envy [46] and social aversion [47,48]; as well as various other variables that facilitate interpersonal connection (e.g. ethnocentrism [43], social motivation [49] and social awareness/attentional bias [22,42,50], eye gaze [42,51,52] and communication style [53]). Again, many promising findings

Table 1. Summary of the social effects of acute oxytocin (OT) administration in humans

SOCIAL COGNITION						
Ref. ¹	Phenomenon	Procedure/Task	OT Effect ²	OT Moderated ³	Moderator	Sample ⁴
[19]	Social memory	Memory for faces	Null	Yes	Expression valence	M
[20]	Social memory	Memory for faces	Sig	Yes	Mnemonic task	M
[21]	Social memory	Memory for facial identity and expression	Sig	Yes	Mnemonic task and expression valence	M & F
[23]	Social memory	Memory for words	Sig	Yes	Mnemonic task and word type	M
[29]	Emotion recognition	Identify emotion in photos	Null	No		M
[5]	Emotion recognition	RMET	Sig	Yes	Item difficulty	M
[28]	Emotion recognition	Empathic accuracy	Null	Yes	Baseline social competence	M
[30]	Emotion recognition	RMET	Sig	Yes	Item difficulty	M; ASD
[24]	Emotion detection	Recognition of emotion / morphed faces task	Sig	Yes	Expression valence	M & F
[26]	Emotion detection (early stage)	Detection of emotional faces	Null	No		M & F
[25]	Emotion detection	Morphed emotional faces: emotion classification + RT	Sig	Yes	Expression valence	M
[27]	Emotion detection (early stage)	Detection of angry and happy faces	Sig	Yes	Expression valence	M
[31]	Affect sharing	Neural and behavioral empathy for pain	Null	No		M
[29]	Affect sharing	Self-reported emotion sharing	Sig	No		M
PROSOCIALITY						
Ref.	Phenomenon	Procedure/Task	OT Effect	OT Moderated	Moderator	Sample
[4]	Trust behavior	Trust Game; \$ transfer	Sig	No		M
[40]	Trust behavior (following trust violation)	Trust Game; \$ transfer	Sig	No		M
[38]	Trust behavior	Trust game; \$ transfer	Sig	Yes	Opponent reliability	M
[39]	Trust behavior	Confidential information	Sig	No		M
[35]	Trust behavior/cooperation	AG; decisions with \$ consequences	Null	Yes*	BPD/anxious attachment	M & F; BPD*
[34]	Trust behavior/cooperation	CG (AG) and PD; decisions with \$ consequences	Null	Yes*	Opponent familiarity	M & F
[36] (Study 1)	Trust behavior/cooperation/altruism	IPD-MD; \$ decisions	N.A.	Yes	Opponent: in- vs. out-group	M
[36] (Study 2)	Trust behavior/cooperation/altruism	IPD-MD; decisions with \$ consequences	N.A.	Yes	Opponent: in- vs. out-group	M
[36] (Study 3)	Trust behavior/cooperation/altruism	BG-PD; cooperation	N.A.	Yes*	Opponent: in- vs. out-group	M
[37]	Generosity	UG; \$ decisions	Sig	No		M
[37]	Altruism	DG; \$ decisions	Null	No		M
[46]	Social-emotional responses	Competitive game of chance; envy	Sig	Yes*	Losing (vs. winning)	M & F
[46]	Social-emotional responses	Competitive game of chance; gloating	Sig	Yes*	Winning (vs. losing)	M & F
[47]	Social-emotional responses	Aversive conditioning task	Sig	No		M
[48]	Social-emotional responses	Associative learning task; reduced aversion to faces	Null	Yes	Facial expression (angry)	M
[35]	Social perception	AG; partner strategy expectations/trust	Null	Yes*	BPD/anxious attachment	M & F; BPD*
[34]	Social perception	CG (AG) and PD; partner strategy expectations	Null	Yes	Opponent familiarity	M & F
[36] (Study 1)	Social perception	IPD-MD; partner strategy expectations	N.A.	Yes	Opponent: in- vs. out-group	M
[36] (Study 2)	Social perception	IPD-MD; partner strategy expectations	N.A.	Yes	Opponent: in- vs. out-group	M
[42]	Social perception	Cyberball (modified); trust, preference	N.A.	Yes	Partner: 'good' vs. 'bad'	M & F; ASD
[41]	Social perception	Faces (strangers); trustworthiness	Sig	No		M & F

Table 1 (Continued)

PROSOCIALITY						
Ref.	Phenomenon	Procedure/Task	OT Effect	OT Moderated	Moderator	Sample
[41]	Social perception	Faces (strangers); attractiveness	Sig	No		M & F
[20]	Social perception	Faces (strangers); approachability	Null	No		M
[45]	Social perception	Subjective feelings of attachment (AAP) security	Sig	Yes	Preoccupied attachment	M
[44]	Social perception	Memories of maternal care (PBI) and closeness (IOS)	Null	Yes*	Anxious attachment	M
[43] (Study 1)	Social perception/ in-group favoritism	IAT	Null	Yes*	Target: in- vs. out-group	M
[43] (Study 2)	Social perception/ in-group favoritism	IAT	Null	Yes	Target: in- vs. out-group	M
[43] (Study 3)	Social perception/ in-group favoritism	Infrahumanization task	Null	Yes	Target: in- vs. out-group	M
[43] (Study 4)	In-group favoritism	MCDT	Null	Yes	Target: in- vs. out-group	M
[43] (Study 5)	In-group favoritism	MCDT	Null	Yes	Target: in- vs. out-group	M
[50]	Social perception/ attention	Biological motion	Sig	No		M & F
[22]	Social perception/ attention	Constructive-recognition task; recognition and categorization of sex and relationship words	Sig	Yes	Word type and valence	M
[42]	Social awareness	Cyberball (modified); ball tosses to 'good' player	Sig	No		M & F; ASD
[42]	Face processing/ attention	Gaze to eye region	Sig	No		M & F; ASD
[51]	Face processing/ attention	Gaze to eye region	Sig	No		M
[49]	Response to rejection	Cyberball	Null	No		M & F
[49]	Social motivation	Cyberball; desire for future engagement	Null	Yes	Being included (vs. ostracized)	M & F
[53]	Positive communication behavior	Couple conflict discussion	Sig	No		M & F

Abbreviations (in alphabetical order): AAP, Adult Attachment Projective Picture System; AG, assurance game; BG-PD, between group prisoners' dilemma; BPD, Borderline Personality Disorder; CG, coordination game; DG, dictator game; IAT, implicit association test; IOS, Inclusion of Other in Self scale; IPD-MD, intergroup prisoners' dilemma maximizing differences game; MCDT, moral choice dilemma task; PBI, Parental Bonding Instrument; PD, prisoners' dilemma game; RMET, Reading the Mind in the Eyes Test; RT, reaction time and UG, ultimatum game.

¹ In general each row reflects one publication, however, if more than one study is conducted in a single publication or more than one primary outcome is reported in a study (e.g. trust perceptions and cooperative behavior), then each study/outcome is listed on a separate row because it is sometimes the case that one outcome in a study will be positive but another will be null, or one outcome will be moderated and another will not.

² The 'OT Effect' column lists whether oxytocin (OT) exerts a significant main effect (Sig) versus no significant main effect (Null) on the outcome reported irrespective of any moderating factors. 'N.A.' is used for studies where the main effect of OT is not reported.

³ The 'OT Moderated' column indicates whether the effect of OT is significantly moderated by situational or individual difference factors. In this column we also indicate (with an asterisk) whether OT produces a negative (i.e. antisocial or not-prosocial) effect overall or for any group of participants in the study.

⁴ This column indicates the sample population characteristics, both in terms of gender and whether the sample involves a clinical population; an asterisk is used to indicate whether gender or population moderated the effects of OT.

have been reported (for recent reviews see [2,54]), generating considerable excitement about the potential of oxytocin to ameliorate social functioning deficits in various psychiatric populations.

As with the social cognition data, however, a closer look reveals the variable nature of the effects of oxytocin on prosociality. As detailed (Table 1), almost half of the studies/outcomes reported in the prosociality domain found no significant main effect of oxytocin (not including those where the main effect of oxytocin is not reported). Moreover, situational or individual difference factors moderated 60% of the outcomes reported. Finally, although many of the reported effects of oxytocin were positive/beneficial, a sizeable minority (21%) of the published studies on oxytocin and prosociality report negative – that is, antisocial (i.e.

not prosocial) – effects, such as increasing feelings of envy [46], mistrust [34,35], attachment insecurity [44] or out-group derogation [43].

These inconsistencies suggest that situational and/or individual difference moderators might play a role in determining what type of effect oxytocin will have on prosocial cognition and behavior. As an example, consider the effects of oxytocin on trust and/or cooperation. In their seminal study, Kosfeld *et al.* [4] demonstrated that oxytocin increased trusting behavior in a well-known economic game. However, since this report, other studies have shown that the positive effects of oxytocin on trust-related behaviors and/or cognitions disappear if the potentially trusted other is portrayed as untrustworthy [38], is unknown [34] or is a member of a social out-group (and

out-group threat is high) [36]. In the latter two examples, oxytocin actually *decreased* cooperation. Similarly, oxytocin was recently shown to decrease trust perceptions and the likelihood of cooperation in those who are highly rejection sensitive (i.e. those with borderline personality disorder) [35].

Together, this work motivates the idea that far from being uniformly positive the effects of oxytocin on trust could crucially depend on situational factors that make trust-related or trust-inconsistent cognitions salient, including cooperation versus competition [36], trustworthiness/familiarity of other player [34,38] or stable individual differences in interpersonal uncertainty [35].

Context as a clue to mechanism

Our review of the human oxytocin literature indicates that the effects of exogenous oxytocin on social cognition and prosociality are more nuanced than previously thought. Of the studies/outcomes tested, 43% indicate no main effect of oxytocin, and 63% report situational and/or individual difference moderators (Table 1). Finally, a sizeable minority show that oxytocin can produce antisocial (i.e. not prosocial) effects under certain conditions. Although differences in the procedure or task can introduce variance across studies, we propose that much of the variance observed is in fact systematic and a function of the context- and person-dependent nature of the social effects of oxytocin in humans because even studies that employ the same

procedure or task show situational and/or individual difference moderators (e.g. [4] and [38], or [34] and [35]). Moreover, we believe this context- and person-dependency can provide clues about more basic psychological and/or biological processes at play. Below we discuss three mechanisms by which exogenous oxytocin could affect social cognition and prosocial behavior in humans: anxiety reduction, affiliative motivation and perceptual selectivity/social salience. At the outset we emphasize that these mechanisms are not mutually exclusive and indeed might even combine to produce the effects of oxytocin in some contexts (Figure 1).

Anxiety reduction

One mechanism to explain the social effects of oxytocin in humans is that oxytocin reduces anxiety, especially social anxiety (e.g. [1,55–57]). The anxiety reduction hypothesis is grounded in literature showing that oxytocin modulates anxiety and fear in animals [57], and is consistent with research showing that oxytocin can modulate stress reactivity in humans (e.g. [53], but again these effects are often qualified by features of the situation [58] and/or person [59]). This hypothesis also is consistent with functional magnetic resonance imaging (fMRI) studies showing that oxytocin decreases amygdala reactivity to fearful [60,61] and other social stimuli [31,40,62] (but see [63]). Indeed, the anxiety reduction hypothesis has been put forward to explain some of the prosocial effects of oxytocin (e.g. increased trust/social

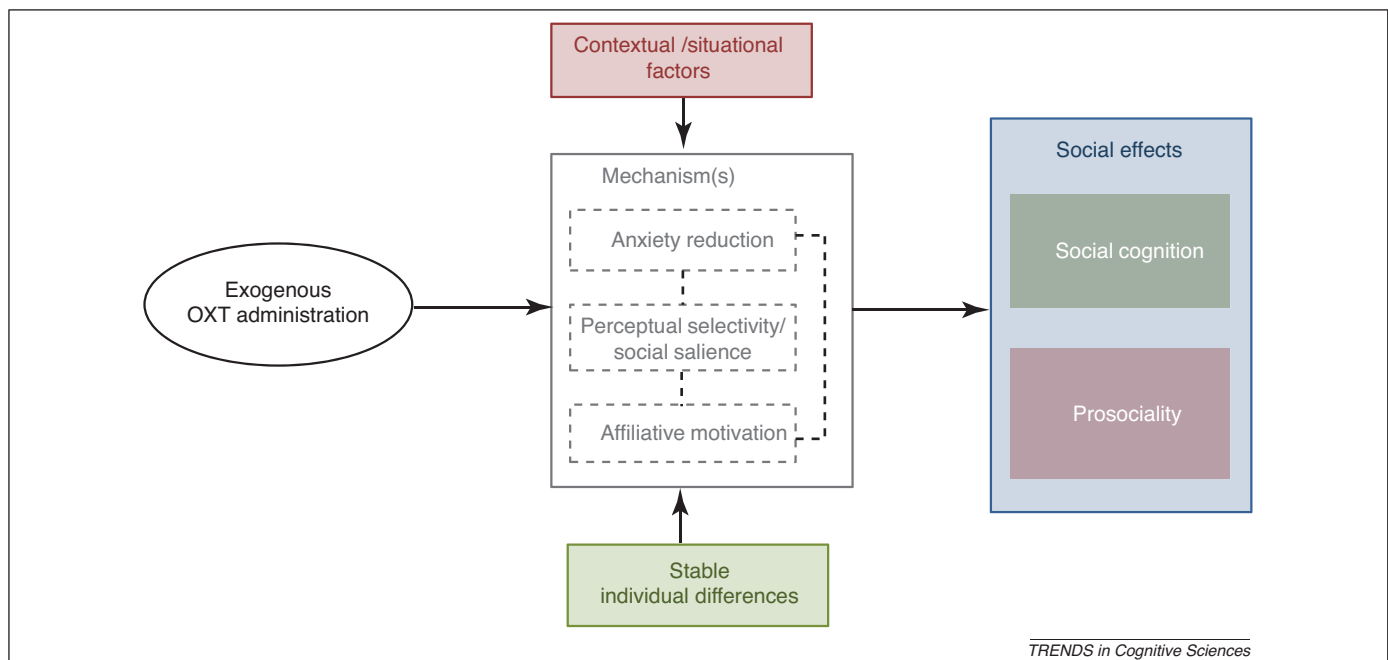


Figure 1. Interactionist model of the social effects of oxytocin in humans. Exogenously administered (e.g. intranasal) oxytocin influences a range of outcomes related to social cognition (e.g. emotion recognition and empathy) and prosociality more broadly (e.g. trust perceptions and trust behavior) but these effects of oxytocin are often moderated by features of the social situation in which oxytocin is administered and/or the individual to whom oxytocin is administered. Situational moderators can include task set difficulty, stimuli valence, as well as opponent familiarity, reliability and in- versus out-group status. Individual difference moderators can include behavioral characteristics such as social cognitive proficiency, trait-level individual differences such as attachment anxiety, or population-specific effects such as borderline personality disorder; such individual differences might also reflect natural variation in the endogenous oxytocin system (e.g. plasma oxytocin levels and/or polymorphisms of the oxytocin receptor gene). In addition to these moderator variables, the effects of oxytocin on social cognition and prosociality are likely to be mediated by one, or more, more basic mechanistic processes; specifically by: reducing anxiety and especially social anxiety, increasing social motivation/affiliative drive and/or increasing the salience of social cues. As indicated by the dashed-line linking these hypothetical mechanisms, these mechanisms could work independently or together to mediate the effects of oxytocin on social cognition and prosociality. For example oxytocin could increase the salience of social cues by reducing social anxiety and allowing socially anxious people to attend to the social cues they might otherwise avoid. Oxytocin could also increase the salience of social cues by activating affiliative motives that should increase people's attention to the social information in the environment that work to promote or hinder such goals. Finally, oxytocin could increase affiliative drive/social approach by decreasing social anxiety.

approach [56]). This hypothesis also could account for the selectively beneficial effects of oxytocin for individuals who report features of autism [28] because social anxiety is a commonly associated symptom of autism [64], and has been proposed as a primary factor in undermining social cognition and functioning in this population [65]. That being said, it is less clear how the anxiety reduction hypothesis explains other reported effects of oxytocin, for instance why reducing anxiety would promote other aspects of social cognition such as memory for faces [20], or such negative social emotions as ‘envy’ [46] and distrust [34,35].

Affiliative motivation

A second possible mechanism to explain the social effects of oxytocin in humans is that oxytocin affects motivational states related to affiliation (e.g. [1,2,55,66,67]). This hypothesis is consistent with research in animals on oxytocin and attachment bonding [10], and with human studies showing that oxytocin increases trust behavior [4] and perceptions [41]. This hypothesis also is compatible with reports showing selective effects of oxytocin on memory for and/or recognition of positively valenced social cues [19,24,25] (although it should be noted that not all studies find evidence for such a positive bias [e.g. 5,20,28]). Perhaps the most compelling support for this hypothesis comes from a recent imaging study [52] that found that oxytocin differentially affected activity in specific amygdala subregions depending on the valence of the social stimuli. Oxytocin attenuated activity in the lateral and dorsal regions of the anterior amygdala following exposure to negative social cues but increased activity in these regions for positive social cues. These differential effects of oxytocin on amygdala activity strongly support the view that the social effects of oxytocin go beyond simple anxiety reduction.

With respect to other reported effects of oxytocin, one could see how activating affiliative motives might improve social memory and emotion recognition if the underlying reason for deficits in these skills is diminished interest in the social world [68]. It is less obvious, however, how increasing affiliative goals might increase negative social emotions and behavior. One possibility is that activating affiliative goals increases people’s attention to and processing of socially relevant information in their environment, including the contextual factors that promote or work against the goal [34,38] and, by the same token, stable individual differences in people’s expectancies about achieving affiliative goals [35].

Perceptual selectivity/social salience

A third hypothesis about the mechanism underlying the social effects of oxytocin is that oxytocin alters the perceptual salience and/or processing of social cues. This hypothesis has been put forward to explain the effects of oxytocin on social recognition in animals (e.g. [3,15,69,70]) (Box 2) and could apply to humans as well (e.g. [35,46,71]). Supporting the perceptual selectivity/social salience hypothesis is data showing that intranasal oxytocin increases gaze to the eye region [42,51] (perhaps the most socially communicative aspect of the face) [72]. Moreover, the fMRI study noted above [52] found that such gaze shifts to the eye region of faces were related to enhanced functional

Box 2. Social recognition in sheep and the social salience hypothesis

Although there is little human data that speak directly to the social salience hypothesis, research on the neural control of maternal behavior in sheep illustrates how oxytocin can modulate perceptual selectivity/social salience. Sheep are highly selective and bond only with their own offspring; research shows that oxytocin supports attachment bonding in sheep by modulating perceptual states that promote the selective recognition of offspring [18,70]. Specifically, Keverne and colleagues [70] exposed prepartum and postpartum ewes to various olfactory cues and observed in the olfactory bulb an increase in the response rate of mitral cells and an increased release of certain neurotransmitters when postpartum (vs. prepartum) ewes were exposed to lamb odors in general and to offspring odors in particular. By contrast, lamb odor had negligible effects on neural activity or neurotransmitter release in prepartum ewes [18,70]. Crucially, this ‘reorganization’ of the olfactory bulb was thought to be due largely to the actions of oxytocin there following birth [86].

In the same way that oxytocin biases a ewe’s neural network to preferentially respond to specific social stimuli, oxytocin could bias neural systems in humans to preferentially respond to and/or enhance the processing of social information (also see [3]). Of course, in contrast to sheep, humans do not primarily rely on the olfactory system to process social information. If oxytocin modulates perceptual selectivity/social salience in humans, then it is probable that such effects would be mediated by other systems, such as the visual system, which is highly developed in humans, and the supporting brain regions including the fusiform gyrus, and superior temporal sulcus. More generally, one could imagine that oxytocin might similarly bias neuronal activity to preferentially respond to social information across species, albeit in a species-specific manner [87].

coupling of the posterior amygdala and the superior colliculi, further supporting the idea that oxytocin increases the salience of social visual information. Finally, other support for the notion that oxytocin is involved in allocating attentional resources to social stimuli comes from data showing that oxytocin enhanced the differential response of electroencephalographic rhythms in the mu/alpha and beta ranges during tasks involving perception of biological versus nonbiological motion [73].

More generally, of the three mechanisms discussed here, we propose that the salience hypothesis is best positioned to account for the existing data. First, the social salience hypothesis can explain why the social context is so crucial in shaping the effects of oxytocin on social cognition and prosociality. Increasing the salience of social cues should have widely varying effects on ‘downstream’ cognition and behavior that depend on the specific social information that is attended to (e.g. positive or negative facial expressions) and the situation in which social salience is increased (e.g. cooperative or competitive interactions). Second, the social salience hypothesis can simultaneously account for both the socially desirable and socially undesirable effects of oxytocin. Specifically, increasing people’s attention to social cues can be expected to magnify prosociality when dealing with familiar, close or reliable others but diminish prosociality under situations of competition [46], uncertainty [34] or when interacting with out-group members [36]. Third, the social salience hypothesis sheds light on the individual- and population-specific effects of oxytocin. If oxytocin increases people’s attention to social cues, then it should be especially helpful for those who are less attuned to such cues at baseline, such as the less socially proficient individuals in the study of empathic

Box 3. Endogenous oxytocin might moderate response to exogenous oxytocin

Individuals differ in endogenous oxytocin levels and such variance seems to be behaviorally relevant. For example, lower plasma oxytocin levels are associated with autism [88] and, in patients with schizophrenia, symptom severity [89] and poorer social cognitive performance [90]. Higher plasma oxytocin levels, by contrast, paint a more complicated picture. On the one hand, higher plasma oxytocin levels have been associated with trust [91], supportive communication [92] and positive parenting styles [93–96]. On the other hand, higher plasma oxytocin levels have also been associated with perceptions of interpersonal distress [97–99] and major depression, both when measured at baseline [100] (but see [101]), and during an affiliation imagery task [102].

To date, the meaning of such variability in plasma levels is not known. One hypothesis we propose is that endogenous oxytocin could be a biomarker of sensitivity to social cues and/or social motivation. Not only would this explain findings related to low plasma levels (e.g. at least some forms of autism are characterized by diminished social sensitivity and motivation) but also the complex picture associated with high plasma levels. If higher plasma oxytocin levels reflect increased social sensitivity and/or social motivation one would expect that such individuals would display more prosocial

behavior and interpersonal sensitivity in general but that they would also be especially aware of and distressed in situations where their social needs are not met (also see [66]). Finally, as noted in the main text, the notion that endogenous oxytocin reflects individual differences in social sensitivity and/or social motivation is compatible with findings that individuals can differ in response to exogenous oxytocin; indeed, baseline social sensitivity/social motivation would be an obvious individual difference moderator if exogenous oxytocin functioned to increase the salience of social cues and/or increase affiliative motivation. Future work is needed to look at whether endogenous oxytocin (or vasopressin) levels moderate response to exogenously administered oxytocin.

In addition to variation in endogenous oxytocin levels, research has shown that polymorphisms of the oxytocin receptor (OXTR) gene are also related to social cognition and social behavior. Variations of the OXTR have been associated with sensitive parenting [103], behavioral and dispositional empathy [104], prosocial behavior [105], positive affect [106], prosocial temperament [107] and seeking support under distress [108]. In line with the discussion above, future work should investigate whether allelic variation in the OXTR gene moderates response to exogenously administered oxytocin. _ENREF_16

accuracy [28]. By the same token, increasing people's attention to social cues could be detrimental to individuals who are generally hypersensitive to social cues and have a bias towards interpreting them negatively [35]. Indeed, these individual- and population-specific effects of exogenous oxytocin might reflect differences in the endogenous oxytocin system (Box 3).

In sum, we have reviewed three mechanisms to explain how oxytocin could influence sociality in humans. As noted at the outset of this section, although we describe the anxiety reduction, affiliative motivation and perceptual selectivity/social salience hypotheses as independent, they could work together to mediate the effects of oxytocin on human social cognition and prosocial behavior. For example, reducing social anxiety could allow socially anxious people to attend to the social cues they normally avoid thereby increasing the salience of social cues. Similarly, activating affiliative goals should increase people's attention to and processing of socially relevant information in their environment because activation of a goal affects attention to goal-relevant information [74–76]. Future research is needed to systematically, and simultaneously, test each mechanistic hypothesis to determine whether, and in what contexts, any or all operate.

Implications for oxytocin pharmacotherapy

Preliminary evidence concerning the effects of oxytocin have produced optimism about its potential to improve social cognition in autistic individuals [5,30,77], and to facilitate trust and reduce social anxiety in conditions such as social phobia and borderline personality disorder [1,4,56,78]. We share this enthusiasm but believe that all such work should be mindful of the variance in extant findings and the idea that oxytocin, although helpful in some contexts, might not be helpful in others. Intervention designs should consider whether increasing the salience of social cues would be expected to improve, leave unaltered, or worsen social cognition and behavior depending on the context and/or person to whom oxytocin is administered.

In fact, the context- and person-dependent nature of oxytocin indicates that a more strategic therapeutic approach might be warranted. One fruitful strategy might be to combine oxytocin pharmacotherapy with a psychosocial intervention to target specific cognitive or behavioral outcomes. For example one could administer oxytocin in conjunction with face processing or emotion recognition training to target social cognitive deficits in autism.

Concluding remarks

The research reviewed in preceding sections indicates that the view of exogenous oxytocin as broadly and invariantly

Box 4. Questions for future research

- Does oxytocin modulate social cognition and social behavior by reducing anxiety, increasing affiliative drive, increasing the salience of social cues or some combination of these three mechanisms? Are there contextual and/or individual difference factors that influence the relative importance of any of these mechanisms in shaping the effects of exogenous oxytocin?
- What contextual and individual difference factors moderate the effects of exogenous oxytocin? Are these moderators stable or do they depend on the outcome being tested? Are individual difference moderators associated with biological indicators of the endogenous oxytocin (or vasopressin) system, for example plasma levels and/or polymorphisms of the oxytocin (or vasopressin) gene? What are the effects of gender and do such effects depend on the outcome being tested? Similarly, are there population-specific effects of oxytocin?
- How do contextual and individual differences factors modulate the effects of oxytocin on neural responses to social stimuli? How do the neural effects of oxytocin parallel its nuanced behavioral effects?
- What is the relation between endogenous and exogenous oxytocin? Does exogenous oxytocin administration mimic the effects of endogenous oxytocin? If the effects of exogenous and endogenous oxytocin are similar, then are the effect sizes also similar? If the effects of exogenous and endogenous oxytocin are different, then in what ways do they differ? Is there an effect of dose? If so, is the effect of dose linear or more complicated (e.g. inverted-U-shaped)?
- Does oxytocin interact with other neurotransmitter systems to influence social cognition and prosociality and, if so, what other neurotransmitter systems are involved?

improving social cognition or prosocial behavior is incorrect, and could impede progress in understanding the function and potential utility of it in treatment. We propose that exogenous oxytocin can be viewed as altering the basic processing of social stimuli, for example the salience of interpersonal cues that in turn could produce a wide variety of behavioral effects depending on situational and/or dispositional factors. Finally, we believe our interactionist perspective not only refines our understanding of existing studies published to date on the social effects of oxytocin in humans but also raises several questions to be tested in future research (Box 4).

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