# Oxytocin and human social behavior

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## ABSTRACT

Despite a general consensus that oxytocin has prosocial effects, there is no clear agreement on how these effects are achieved. Human research on oxytocin is reviewed under three broad research initiatives; attachment and trust, social memory and fear reduction. A tentative model addressing both causes and effects of alterations in oxytocin level is proposed. The model must remain provisional until conceptual and methodological problems are addressed arising from a failure to distinguish between traits and states, differing research paradigms used in relation to OT as an independent versus dependent variable, and the possibility that OT effects depend upon the initial emotional state of the individual. Social and personality psychologists have important roles to play in developing more rigorous and creative research designs.

Interest in oxytocin (OT) has spread swiftly from endocrinology journals to the popular media (Young, 2009). Its popularity owes much to the attractive and accessible terms used to describe its psychological effects---"love", "trust" and "bonding"---terms which have traditionally been the domain of social, personality and developmental psychology. The majority of OT research is reported in journals targeted specifically at endocrinologists and biological psychologists, understandable in light of the early pioneering research which was performed on rodents. Recently however new techniques have become available which allow experimental research on human participants. It is here that social psychologists, with their extensive history of research in human relationships, have much to offer at a conceptual and methodological level. Currently, studies on humans are relatively few and still inconclusive in their results. Research has been propelled by a wave of enthusiasm that has resulted in a scattergun of studies spanning several psychological domains rather than a systematic program of research. While there is general agreement on OT's prosocial effects, there are various suggestions about how these are mediated although these differences are often implicit rather than clearly delineated. In the present article I examine the evidence behind three proposals about OT's effects with the aim of making explicit the connections among them and with social psychology. These proposals are that (1) OT enhances attachment and trust, (2) OT improves social memory and (3) OT reduces fear. Although I will briefly summarise research on non-human animals, the chief focus of this review is the impact of OT on human emotions and behavior. I begin with a short

description of the peptide together with some important considerations in interpreting the research literature.

**Oxytocin: A primer and some caveats**

Oxytocin is a peptide hormone composed of nine amino acids. It is highly conserved across species in terms of structure and function, although there is inter-species variability in the specific behaviors that it controls. OT has both peripheral and central effects. Peripherally, OT regulates uterine contractions during labour and milk ejection during lactation. It is synthesised in magnocellular neurons of the paraventricular (PVN) and supraoptic (SON) nuclei of the hypothalamus which project to the posterior pituitary where OT is released into peripheral circulation. Centrally, OT acts as a neuromodulator. It is synthesised in the parvocellular neurons of the hypothalamic PVN which projects to limbic sites (hippocampus, amygdala, striatum, hypothalamus, nucleus accumbens) and to the brain stem. Central OT effects include maternal and sexual behavior, pair bonding and social recognition.

In interpreting the results of studies that I review here, it is important to note the source of OT. Because peripheral OT can be assayed from blood samples while central OT requires more invasive measurement of cerebrospinal fluid, most human studies of endogenous OT tell us about peripheral effects. The extent to which peripheral and central release is coordinated is doubtful (Gimpl & Fahrenholz, 2001). In some species a small quantity of peripherally administered OT may cross the blood–brain barrier or influence behavior via afferent feedback to the CNS. Studies of plasma OT also vary in their use of basal versus reactive measures.

Bear in mind also that, although both sexes have OT receptors (Goodson & Bass, 2001), oxytocin is of special relevance to females because OT synthesis and OT receptors are upregulated by estrogen (Lim & Young, 2006; Patisaul, Scordalakes, Young & Rissman, 2003 ). Indeed, McCarthy, McDonald, Brooks and Goldman (1996, p.1209) observe that the OT receptor is "one of the most strongly estrogen-regulated systems in the brain… estrogen-induced increase in oxytocin receptor binding is integral to its behavior-modifying effects". OT's sister nonapeptide argentine vasopressin (AVP), which is very similar in structure, appears to play a more important role in males although OT has been shown to affect some male behaviors including partner preferences, sexual behavior and social recognition (Cushing & Kramer, 2005). Both sexes have receptors for both neuropeptides (Goodson & Bass, 2001) and to complicate matters further, the structural similarity of AVP and OT means that they may be capable of binding to each others' receptors.

The effects of the same peptide can also vary dramatically in males and females. For example, in men intranasally administered AVP stimulates agonistic facial expressions and decreased perception of friendliness in response to images of same-sex strangers. In women administration of the same peptide, results in affiliative facial expressions and increased perception of friendliness (Thompson, George, Walton, Orr & Benson, 2006). Studies which assay plasma OT as a dependent variable are most often performed on women although some studies also include men. However nearly all studies where OT is centrally administered as an independent variable use male participants only because of the small possibility of OT entering the

bloodstream where it might cause uterine contractions. Thus there is a potential confound between participant sex on one hand, and study design (whether OT is an independent or dependent variable) and OT system (central versus peripheral) on the other.

Another note of caution is warranted. Much of our basic knowledge about OT has come from research on rodents and even here there are important differences between taxa. Extrapolations to humans must be made with caution because there is considerable variation in receptor distribution across mammalian species. In humans, we do not yet know the extent to which 'hard-wired' responses, such as maternal behavior, pair bonding and affiliation have been superseded by the learning and cultural transmission afforded by increased cortical size.

There is general consensus that OT has positive effects on human social behavior but there are at least three implicit proposals about the mediators of these prosocial effects.

**Oxytocin: Attachment and trust.**

The emotional bond between caregiver and offspring, and between adult partners lies at the heart of the psychology of relationships. A secure attachment in infancy is important for normal psychological development and provides a base from which the infant explores the world beyond (Bowlby, 1988). The infant's internal working model of attachment has implications for the nature and quality of later adult relationships (Hazan & Diamond, 2000). The continuities and similarities between these two types of relationship have often been noted by developmental and social psychologists. It has been proposed that successful adult pair-bonding not only depends upon the early

child-parent relationship but that the two share a common psychological mechanism. Although adult relationships incorporate sophisticated cognitive, social and cultural components, they may share a basic emotional infrastructure with our earliest experience of attachment (Hazan & Diamond, 2000). Because mother-infant attachment is ubiquitous in mammals, the possibility of a biological basis attracted research interest.

Early work on OT focused on its role supporting maternal behaviors toward offspring in rodents (see reviews by Broad, Curley & Keverne, 2006; Insel, 2000; Kendrick, 2000). In pregnancy, triggered by rising estrogen levels, OT receptors are upregulated in the uterus and the brain. Vagino-cervical stimulation during parturition activates OT neurons in the hypothalamus, stimulating OT release in many brain areas including the preoptic area, ventral tagmental area and olfactory bulb. These pathways are responsible for coordinating a range of maternal behaviors including nest building, pup retrieval, licking, crouching and maternal aggression. In 1979, Pedersen and Prange first demonstrated that intracerebroventricular (icv) infusion of OT can induce maternal responses in estrogen-primed virgin rats. Reciprocally, the onset of maternal behavior can be inhibited by OT antagonists, lesions of OT cells and antibodies to OT (Insel, 2000). Recent studies using genetic knockout of OT receptors have confirmed significant deficits in mothering (Takayanagi, Yoshida, Bielsky, Ross, Kawamata, Onaka et al., 2005). Even in rodents, the role of OT however is confined to the initiation not the maintenance of maternal behaviour (Kendrick, 2000).

In humans, there is general consensus that prenatal and postpartum OT both enhances the formation of close bonds with the infant and reduces

maternal stress reactivity (Nelson & Panksepp 1998; Neumann 2008). During childbirth there is a rise in OT in the cerebrospinal fluid and post-partum plasma levels are correlated with positive feelings and reduced anxiety (Takagi, Tanizawa, Otsuki, Haruta & Yamaji, 1985). Immediately after birth and prior to their first feeding, infants massage the mother's breast resulting in peripheral OT release which is also elevated during feeding (Matthiesen, Ransio-Arvidson, Nissen & Uvnas-Moberg, 2001). Subjectively, lactation is associated with lowered stress and less negative mood states (Mezzacappa & Katkin, 2002). Biologically, lactation is associated with lowered cortisol (Amico, Johnston & Vagnucci, 1994), attenuated ACTH, cortisol and gluocose responses to exercise stress (Altemus, Deuster, Gallivan, Carter & Gold, 1995) and during suckling there is a negative relationship between plasma OT and ACTH levels (Chiodera, Salvarani, Bacchimodena, Spallanzani, Cigarini, Alboni et al., 1991). Evidence for more wide-ranging behavioural effects of OT has come from studies that assayed plasma OT levels during the first and third trimester, and first postpartum month. A pattern of increasing OT during pregnancy was associated with higher maternal-fetal bonding (Levine, Zagoory-Sharon, Feldman & Weller, 2007). OT levels in early pregnancy and postpartum were significantly correlated with maternal bonding measures including attachment-related thoughts, gaze at the infant, affectionate touch and frequent infant checking (Feldman, Weller, Zagoory-Sharon & Levine, 2007). Although human maternal behavior does not critically depend upon OT as it may do in rodents (in humans high quality infant care is given by adoptive mothers, mothers whose babies have been carried by surrogates,

relatives and other adult caretakers), OT appears to play a supplementary role in enhancing bonding in the early weeks (Kendrick, 2000; Broad et al., 2006).

Rodent studies then explored the possibility that pair-bonding might similarly be associated with OT release, an expectation arising from the proposal that adult attachment may have arisen from or 'exapted' the more primitive mechanism of mother-infant bonding. Two closely related species provided a convenient natural experiment (Insel & Shapiro, 1992). The prairie vole shows a strong partner preference and bi-parental care in contrast to the promiscuous montane vole. In the female prairie vole, OT administration facilitates partner preference while OT antagonists block it, without interfering with mating. OT receptors are found in the nucleus accumbens and prelimbic cortex of the prairie vole---areas rich in dopamine receptors. Administration of OT induces central dopamine release and vica versa and their co-action appears to be critical for partner preference (Edwards & Self, 2006; Liu & Wang, 2003; Young & Wang, 2004). In the promiscuous montane vole, the OT and dopamine systems are uncoupled.

The roles of OT and dopamine in interpersonal attraction have been rather freely extrapolated to humans. Although love is a human universal (Jankowiak & Fischer, 1992), social psychologists have made finer distinctions between companionate, romantic and passionate love (Hatfield, 1988; Sternberg 1986). Fisher, Aron and Brown (2006) similarly proposed a sequential analysis in which the sex drive (chiefly associated with androgens) motivates general sexual interest, while romantic love (associated with dopamine and noradrenaline release) is associated with preference for a specific partner, and partner attachment (associated with OT) enables a long-

term bond to be formed to provide bi-parental care. Others consider the simultaneous activation of dopaminergic reward and OT pathways to be critical to relationship formation (Skuse & Gallagher, 2008). Beyond the mating arena, Depue & Morrone-Strupinsky (2005) argue that OT is implicated in both the motivation and the reward associated with social interactions. They propose that dopaminergic neurons running from the ventral tagmental area to the nucleus accumbens are responsible for the motivation to affiliate. Oxytocin and OT receptors are found in these same areas where they interact with the dopamine system. However experiences of affiliative reward derive from endogeneous opiate release and binding which occurs during many of the same socio-sexual experiences that are associated with OT release. OT can increase central opiate release by up to 300 percent (Csiffary, Ruttner, Toth & Palkowits, 1992).

Human studies have examined plasma OT levels both as a correlate of long-term attachments and as a short -term response to experimental manipulations of relationship variables. Studies which have examined OT's association with ongoing relationship quality have produced counter-intuitive results. Women with high OT levels did not report better emotional relationships with their partners, although they did report more frequent hugs and massages from them (Light, Grewen & Amico, 2005). Indeed basal plasma OT level was positively associated with interpersonal distress, and negatively related to being in a current relationship, marriage quality, degree of partner's understanding and women's ability to open up to them and (Light et al., 2005; Taylor, Gonzago, Klein, Hu, Greendale & Seeman, 2006; Turner, Altemus, Enos, Cooper & McGuinness, 1999). These findings have prompted

some to suggest that increased OT may act as motivator for social contact as well as a response to it (Taylor et al., 2006). Other studies have examined short-term changes in OT levels as a function of recalling positive and negative experiences of romance (Turner et al., 1999; Gonzago, Turner, Keltner, Campos & Altemus, 2006). Again, counter to hypothesis, OT actually decreased over time in response to recalling positive emotion while negative emotion had no effect on OT (Turner, Altemus, Yip, Kupferman, Fletcher, Bostrom et al., 2002).

In the short term, viewing pictures of a romantic partner activates dopaminergic pathways that are also rich in OT receptors (Bartels & Zeki, 2004; Fisher et al., 2006). More directly, OT level have been reported to rise during genital stimulation, copulation and orgasm (Carmichael, Humbert, Dixen, Palmisano, Greenleaf & Davidson, 1987; Uvnäs-Moberg, 1998) though rises in response to massage (typically given by a masseur unacquainted with the participant) are usually non-significant (Wilkstrom, Gunnarsson & Nordin, 2003; Turner et al., 1999). Tactile contact from a partner does not have immediate effects on plasma OT levels. No significant change was found in OT before, during or after a 10-minute period of warm contact with their partner that ended with a hug although, contrary to the above results, those with more supportive partners showed higher levels of OT throughout the period (Grewen, Girdler, Amico & Light, 2005).

Does OT have effects on social relationships beyond the mother-infant and pair bond? Animal studies suggest that it may be implicated in sociability more generally. Bonnet monkeys, a naturally affiliative species, show higher OT levels in cerebrospinal fluid than the less sociable pigtail macaque

(Rosenblum, Smith, Altemus, Scharf, Owens, Nemeroff et al., 2002). In rats, gerbils and squirrel monkeys, intracranial or subcutaneous injection of OT increases social contact time (Razzoli, Cushing, Carter & Valsecchi, 2003; Winslow & Insel, 1991; Witt, Winslow & Insel, 1992). Within species, individual differences in affiliation may reflect early nurturing experiences and their effects on the OT system (Cushing & Kramer, 2005). Rhesus monkeys deprived of maternal care display asocial behavior including avoidance of physical contact and gaze, stereotypic and self-directed behaviours, and attachment to inanimate objects. These monkeys also have decreased cerebrospinal OT measured between 18 and 36 months. Levels of cerebrospinal OT (but not plasma OT) are positively correlated with affiliative behavior (Winslow, 2005).

In humans, the experience of being trusted and reciprocating trust is associated with raised OT levels. Zak, Kurzban and Matzner (2005) employed a Trust Game in which an investor awarded a sum of money (between $1 and $10) to a trustee which was tripled in value by the experimenter. The trustee then had the option of returning some portion of the money to the investor. In a control condition, the amount awarded to the trustee was decided by a random computer draw. Subsequently plasma OT levels in the trustee were significantly higher in the experimental condition. This suggests that the trustees' OT levels were responsive to the intention of trust rather than to the receipt of money per se. The amount returned to the investor (a measure of trustworthiness) was significantly correlated with subsequent OT levels for experimental but not control participants.

Drawing together the research on tactile contact and interpersonal trust, Morhenn, Park, Piper and Zak (2008) examined their joint effects on changes in plasma OT. Participants received a 15-minute massage or rested before playing the Trust Game (a third group received the massage only). Blood draws for OT assays took place on arrival and at the end of the experiment. For the investors, there was no association between the sum of money they transferred ('trust') and change in OT levels either with or without prior massage. But for those trustees who had received the massage, there was a significant positive association between the sum received (their 'trustworthiness') and an increase in their OT level. The amount returned by the trustee to the investor was also correlated with OT change both with and without massage. Because massage alone did not alter OT levels, this study suggests that it is touch associated with being trusted that induces OT elevation. More broadly, one might speculate that it is the positive emotional connotation of touch rather than tactile stimulation per se that raises OT levels.

However plasma concentrations of nonapetides may not necessarily reflect CNS levels (Landgraf & Neumann, 2004) and recent studies have used intranasal delivery to directly manipulate central OT levels. A quantity of the peptide (usually about 24 I.U.) is inhaled and it is thought that the molecules take an extra-cellular route through the olfactory epithelium where they diffuse into subarachnoid space (Born, Lange, Kern, McGregor, Bickel & Fehm, 2002). Cerebrospinal concentrations of the peptide begin to rise within ten minutes of administration and remain elevated for 80-120 minutes. Intranasal delivery means that levels of central OT can be incorporated into an

experimental design as an independent variable rather than peripheral levels being used as a dependent variable or correlate. Increasingly psychologists are taking advantage of this powerful, non-invasive technique.

Administration of OT increased the positivity of verbal and nonverbal behaviors in couples during a discussion of conflict, suggesting greater positivity even when engaged in a task likely to provoke animosity (Ditzen, Schaer, Gabriel, Bodenmann, Ehlert & Heinrichs, 2009).

Emotional recognition has been examined under the hypothesis that OT administration may selectively enhance identification of positive facial expressions. OT does not appear to increase the identification accuracy, reaction time, gaze duration or fixation count in response to positive or negative facial expressions (Di Simplicio Massey-Chase, Cowen & Harmer, 2009; Guastella, Carson, Dadds, Mitchell & Cox, 2009). Guastella et al (2009) examined recognition of emotional words. No effect of OT was found for reaction time or accuracy in classifying emotional words as likeable or dislikeable, nor was any effect found for either vigilance or accuracy on a visual probe task of positive or negative emotional words. However a semantic task oriented to interpersonal relationships produced more encouraging results. Unkelbach, Guastella & Forgas (2008) presented participants with stimulus words that appeared over 8 seconds from a gradually dissolving black mask. The words were selected from five categories (relationship, sex, safety and threat, happiness and sadness, and other) and participants were asked to rate them as negative or positive in meaning. Although accuracy was not affected by OT, reaction times were

significantly shorter for the sex-related and relationship-related word categories.

Eye gaze toward different facial features in photographs was used as an assay of social interest by Guastella, Mitchell and Dadds (2008). Compared to placebo, OT increased the duration and frequency of men's gaze toward the eyes. The eyes can convey information about a target's emotional state and this has formed the basis for a measure of empathy called the Reading the Mind in the Eyes test (Baron-Cohen, Wheelwright, Hill, Raste & Plumb, 2001). OT increased the correct identification of emotions with the effect being more marked on the most difficult items (Domes, Heinrichs, Michel, Berger & Herpetz, 2007).

Pursuing the empathy hypothesis, Zak, Stanton and Ahmadi (2007) compared the effect of OT on two economic games. In the Ultimatum Game one player is assigned a sum of money to be split with another participant. If the offer is accepted, the money is paid to both participants as agreed but if the offer is rejected, both parties receive nothing. This game is taken as a measure of perspective taking (since the donor must consider what offer the other party is likely to accept). In the Dictator Game, one player makes a decision as to how much of the assigned sum to award to the second party which they have no option but to accept. OT administration significantly increased the money awarded in the Ultimatum Game but not in the Dictator Game suggesting that the effect of OT is on empathy-mediated generosity rather than generous behavior per se. This conclusion reinforces that of Kosfeld, Heinrichs, Zak, Fischbacher and Fehr (2005) in which, following OT or placebo administration, participants played the Trust Game described

earlier. OT increased the value of money transferred by the investor supporting its role in enhancing trusting behavior, although it did not affect subjective ratings of interpersonal trust. However OT had no effect on the back-transfer of money by the trustee suggesting that OT does not have a generalised effect on reciprocity or generosity in the absence of a requirement to empathise with another's perspective.

In summary, the evidence for social bonding effects is equivocal. The hypothesis that plasma OT levels are higher among those in satisfactory emotional relationships has received only weak support and indeed produced some counter-intuitive results suggesting that raised OT may signal emotional distress and stimulate social contact. Even less support has been found for OT changes in response to the recall of bonding emotions. But OT increases trusting behavior and rises in response to it, where this depends upon mind reading or empathy.

**Oxytocin: Social memory.**

The ability to recognise conspecifics (kin, mates, offspring, allies and enemies) forms a crucial basis for our social behavior. Stored information about another's identity and past behaviour informs our interactions with them. In humans, faces provide important information about identity and a specific brain area, the right fusiform gyrus, is critical for face recognition (Kanwisher, McDermott & Chun, 1997). Functional MRI results show that OT administration is associated with activation in the fusiform gyrus (Petrovic, Kalisch, Singer & Dolan, 2008). This area works in concert with the amygdala and the superior temporal sulcus which are implicated in the processing of

facial expressions. OT receptors are present in the amygdala and hippocampus.

OT is critically involved in social memory in the mouse. OT knockout mice (OTKO) completely fail to recognise a conspecific even after repeated encounters although there are no deficits in non-social learning or sensory processing (Ferguson, Aldag, Insel & Young 2001: Fergsuon, Young & Insel, 2002). Social recognition can be restored by icv injection of OT prior to the initial encounter indicating that OT is involved in memory acquisition, rather than consolidation. It appears that olfactory cues are relayed to the amygdala where OT enhances encoding of the encounter. The medial amygdala connects to the bed nucleus of the stria terminalis and to the hippocampus, an area that is critical for memory storage and retrieval. By contrast, OT effects in the rat are much less clear. Central injection of OT can either facilitate or attenuate social recognition depending on the dose (Benelli, Bertolini, Poggioli, Menozzi, Basaglia & Arletti, 1995) and OT antagonists inhibit recognition in females but not in males (Engelmann, Ebner, Wotjak & Landgraf, 1999). Such species differences suggest caution about premature extrapolation to humans.

Early human studies examined verbal memory with some finding that OT impaired memory and others reporting no effect (see Heinrichs, Meinlschmidt, Wippich, Ehlert & Hellhammer, 2004). More recently, researchers have focused explicitly on social memory. They have investigated selective memory for facial identity, and for emotional and relationship-relevant stimuli. Following administration of OT or placebo, Rimmele, Hediger, Heinrichs and Klaver (2009) presented faces and non-

social stimuli. Twenty-four hours later a surprise recognition test was given. No effect was found for non-social stimuli but, although OT did not affect facial recall ('remember') performance, it increased the accuracy of facial familiarity ('know') ratings independent of the valence of the facial expression. However De Simplicio et al. (2009) found no effect of OT (administered before encoding and still active during recognition) on either accuracy or speed using the Cambridge Face Memory Test.

With regard to emotional expressions, it has been hypothesised that, by increasing interpersonal positivity, OT selectively enhances memory for positive emotions. Again, the results are mixed. Following OT or placebo administration, participants viewed neutral, happy or angry faces (Guastella, Mitchell & Matthews, 2008). A surprise recognition test conducted the following day revealed that, compared to placebo, OT enhanced the accuracy of 'remember' judgements for happy faces only and increased the accuracy of 'familiarity' judgements for happy as compared to angry and neutral faces. A second study examined OT effects on memory consolidation with opposite results (Savaskan, Ehrhardt, Schulz, Walter & Schachinger, 2008). OT was administered after exposure to happy, angry and neutral faces and recognition memory was tested after 30 minutes and 24 hours. OT enhanced recognition of neutral and angry but not happy faces.

Other experiments have used semantic rather photographic stimuli. Following OT or placebo administration, participants were shown sixty personality terms (Di Simplicio et al., 2009). Twenty minutes later, OT had no significant effect on the recall or recognition of personality terms (although there was a non-significant trend toward more accurate recognition of positive

then negative words by the OT group). Heinrichs et al. (2004) examined the effects of OT on three memory tests following exposure to reproductively relevant (e.g. sex, baby) and neutral words (e.g. car, sweets). In two implicit memory tests, participants were instructed to respond to prompts with whatever word came to mind. OT had no effect on implicit perceptual memory (participants were cued with word stems from the encoding phase) but impaired implicit conceptual memory for reproduction-relevant words (participants were cued with category terms relevant to the encoding phase). OT also impaired explicit memory irrespective of semantic category (participants were cued with word stems and explicitly asked to recall the presented words).

Given the hypothesis that OT should enhance social memory, the pattern of results is inconclusive to say the least. For facial identity memory, two studies report opposite effects and the positive effect of OT is confined to familiarity judgements only. For emotional expressions, OT appears to selectively enhance the encoding of happy faces and the consolidation of neutral and angry faces. OT has no impact on the semantic encoding of either positive or negative personality terms, but it impairs explicit recall regardless of word type and implicit recall specifically of reproductively relevant words. Before memory research can be integrated into the full picture of OT effects, clearer hypotheses drawing on the extensive cognitive literature are needed (Mitte, 2008) that specify the anticipated effects of OT on various forms of memory as a function of their emotional content.

**Oxytocin: Fear reduction.**

The anxiolytic effects of OT are the most unanimously recognised in non-human animal research. Administering OT reduces amygdala activation, increases parasympathetic functioning, inhibits corticotropin releasing factor neurons, decreases corticosteroid release, and results in lower levels of fearful behavior (Engelmann, Landgraf & Wotjak, 2004; Neumann, 2007; Viviani & Stoop, 2008). OT activates neurons in the lateral and capsular portion of the central amygdala which inhibit, via GABA projections, the fear-inducing effects of AVP in the medial central amygdala (Huber, Veinante & Stoop, 2005).

In humans, OT administration in conjunction with fMRI imaging has produced interesting and positive findings. In response to fear-provoking visual stimuli, OT reduced amygdala activation and the connectivity between the amygdala and the upper brainstem implicated in autonomic nervous system reactions to threat (Kirsch, Esslinger, Chen, Mier, Lis, Siddhanti, et al., 2005). Petrovic et al. (2008) conditioned a set of faces to electric shock. After OT treatment, participants showed reduced activity in the anterior medial temporal cortex (anterior to and extending into the amygdala) and in the anterior cingulate cortex. For fear-conditioned faces displaying direct gaze (taken to be the most threatening) activity in the right amygdala was significantly higher in the placebo group. The OT group also showed a significant attenuation in their affective ratings of the fear-conditioned faces. Another study (Domes, Heinrichs, Glascher, Buchel, Braus & Herpetz, 2007) found that OT eliminated the heightened right amygdala activation seen in the placebo group to emotional versus neutral faces. However this effect was

seen for happy as well as sad and fearful faces, suggesting that OT effects may not be specific to fear reduction.

However studies which have examined correlations between psychometric measures of trait anxiety and plasma OT levels have produced mixed results with reports of negative (Uvnäs-Moberg, Widström, Nissen & Björvell, 1990), positive associations (Uvnas-Moberg, Arn, Theorell and Jonsson, 1991) and null relationships (Uvnäs-Moberg, Arn, Jonsson, Ek & Nilsonne, 1993).

Experimental studies have manipulated participants' stress to observe situational or 'state' effects on OT levels. In a study of older women's response to the Trier Social Stress Test, cortisol levels (an index of stress) were measured at eight points over the course of the task showing the expected elevation followed by decline. However basal OT levels were not associated with these changes in cortisol (Taylor et al., 2006). The authors conclude that heightened basal OT levels are not protective against cortisol responses to stress. Experimental administration of OT prior to the same stress test does not significantly reduce cortisol levels (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). However two studies suggest the possibility of a trait-state interaction. In response to an uncontrollable auditory stressor, plasma OT rose but only among women high in trait anxiety as measured by the N scale of the Eysenck Personality Questionnaire (Sanders, Freilicher & Lightman, 1990). In another study, response to administration of cortisol (normally released by the HPA in response to stress), OT levels rose but only for women who scored high on a questionnaire assessing a tendency express emotion outwardly (Tops, van Peer & Korf, 2007). An individual's

basal level of anxiety or emotional expressiveness may augment the 'dose' of experimentally manipulated stress revealing increases in OT levels.

Other studies have administered OT prior to stress manipulation to examine possible anxiolytic effects. When asked to discuss an area of conflict in their relationship (designed to induce stress), post-discussion cortisol levels were significantly lower in those couples who had previously received OT (Ditzen et al., 2008). Taylor (2006) proposed a link between OT and social affiliation as coordinated responses to stress. The tendency to seek the company of others as a source of joint protection and support under stress is well documented (and is particularly marked in women). Taylor suggests that bursts of OT, released under stress, prompt this desire for affiliation. The separate and joint effects of OT and social support on stress reactivity were examined by Heinrichs et al. (2003). The experimental design compared four groups resulting from pharmacological condition (OT or placebo administration) and presence or absence of social support (participants brought a friend who accompanied them during the 10 minute preparation period prior to a public speech). Although OT alone was insignificant in reducing cortisol levels during the Trier Social Stress Test, participants receiving social support and OT showed the lowest cortisol response to the stressor. A comparison of pre- and post-stress anxiety levels showed that OT significantly reduced self-reported anxiety.

A number of researchers have proposed that the prosocial effects of OT (described earlier) derive from its anxiolytic properties. OT, by reducing interpersonal fear or anxiety, allows for the formation of positive bonds. In the Trust paradigm described earlier (Kosfeld et al., 2005), the authors concluded

that the higher level of trust after OT administration was caused by a decrease in betrayal aversion and social avoidance. Interacting with a stranger, whose reputation and past behaviour are unknown to us, is normally associated with a degree of apprehension which is decreased by OT thereby permitting trust. But what happens when a stranger's behaviour generates a realistic fear of betrayal? Does OT diminish the normal mistrust that would be triggered by their action? A subsequent study (Baumgartner, Heinrichs, Volanthen, Fischbacher & Fehr, 2008) examined the impact of a breach of trust on trusting behavior by the investor. After being informed that the trustee had only repaid them on 50 per cent of occasions, the placebo group showed a decrease in trusting behavior (reduced money transfer) accompanied by increased activation in bilateral amygdala and brainstem effector sites. These changes in response to feedback were not seen in the OT group. These results are taken to support the view that OT reduces fear and enhances trust even in situations of betrayal.

**Toward integration**

With respect to these three broad areas of human research, a range of causal pathways have been suggested that together accommodate almost every possible permutation of relationship. However a broad consensus has begun to emerge forged upon the most robust empirical finding; That OT depresses amygdala activity and HPA stress responses and this reduction is linked to stronger social approach behavior. As Carter (1998, p.782) summarises it "oxytocin…may serve to inhibit defensive behaviors associated with stress, anxiety or fear, and allow positive social interactions and the development of bonds".

My elaboration of this proposal is represented in Figure 1. The initiation of OT release and uptake is triggered by interpersonal challenges to bodily or psychological integrity. While we tend to ascribe a positive hedonic valence to sexual relations, childbirth and lactation, if we take a more biological view these events can also be seen as invasions of the usual bodily boundaries that define the individual as a discrete organism. Such somatic intrusions carry the possibility of trauma (rape, injury, death of mother or baby, pain) as well as satisfaction. Nonetheless in evolutionary terms such encounters are vital to the continuation of the germ line and, to reduce the stress occasioned by such encounters, OT is released to depress HPA axis reactivity. This stress reduction is able, under appropriate interpersonal circumstances, to enable positive exchanges by increasing trust, enhancing mind reading and promoting affiliation. Note that this proposal addresses an apparent anomaly in the OT literature: the inverse association between relationship quality and OT levels. The initial expectation of a positive relationship was founded on the notion of OT as a 'bonding' hormone. The data better support the notion of OT as a response to psychological threat or stress.

*Traits, states and research paradigms.*

While such a proposal is satisfying it is necessarily an over-simplified schematisation of our current knowledge. Complications arise as we consider the problems posed by an empirical failure to distinguish between traits and states, differing research paradigms used in relation to OT as an independent versus dependent variable, and the possibility that OT effects depend upon the initial emotional state of the individual.

Before proceeding, we should note that terms such as ‘stress’, ‘anxiety’, and ‘fear’ have been used rather loosely in the OT literature. An often unrecognised distinction, though one that is very familiar to personality researchers, is between traits and states. Traits are stable and enduring characteristics of persons: hence anxiety may be conceived of as a trait or a state. By extension we can think of relationships in similar terms so that a marriage is an enduring connection parallel to a trait while briefer interpersonal exchanges are parallel to states. When we ask about the status of a relationship we effectively ask the respondent to aggregate and summarise specific events and experiences into a numerical rating, in the same way that self-report personality items implicitly ask the respondent to compute an ‘average’ of their responses over many different settings. In contrast, states represent short-term modulations of mood and biological functioning in response to specific events. By analogy this trait-state distinction holds also for hormones. Basal levels of OT (taken at rest without experimental manipulation) are thought to reflect a stable aspect of neurohormonal functioning characterising an individual. Reactive levels of OT measure an individuals’ hormonal response to a specific stimulus. As with psychological traits, these traits and states likely interact to determine hormone levels.

The first part of Figure 1 considers OT level as a dependent variable effectively posing the question: What factors are associated with heightened OT? Some researchers have addressed this question by computing the correlation between a trait and OT level. Individual traits (e.g. anxiety) as well as relationship traits (marriage quality) have been used. Personality traits are

inconsistently and weakly associated with OT while relationship traits show a more consistent negative relationship. This suggests that while basal OT may be elevated as a function of ongoing discrete emotional 'skirmishes', it is not a reliable index of characteristic temperament. But such studies present the familiar problem that correlation cannot separate cause and effect. Hence we cannot be sure whether OT is a cause of anxiety or a response to it. The former seems unlikely given that administration of OT tends to have anxiolytic effects but these results are based on studies of state not trait anxiety and the manipulation of central OT levels.

A more stringent experimental approach to the causes of OT release manipulates participants' mood (for example by imposing stress, administering cortisol or providing physical or social contact) and measures alterations in OT. This is a 'state' manipulation but firm conclusions remain compromised by the fact that the dependent variable (OT) is taken from plasma (as it is in correlational studies). The relationship between central and peripheral OT circulation remains uncertain and it is conceivable that they are differentially responsive to environmental stimuli. Although central OT can be measured in cerebrospinal fluid, this procedure is highly invasive. Blood draws are also uncomfortable and typically only one or two samples are taken. This raises measurement issues of assay sensitivity and reliability because random error diminishes the magnitude of association that can be shown with any other variable. In correlational studies a single plasma assay is presumed to reflect a stable basal OT level (analogous to a 'trait') but research is needed to establish the temporal stability of these measures. Even assuming error-free measurement, we rarely investigate (let alone take into

account) OT level fluctuations as a function of circadian rhythms, menstrual cycle, interactions with other hormones, or uncontrolled events beyond the laboratory.

The second part of the figure addresses OT as an independent variable. In these studies OT is typically delivered intranasally and its impact upon performance on a given task is evaluated. Although peripheral OT can be manipulated by intravenous delivery this is rarely done. Because central OT manipulation is relatively straightforward, there has been a recent explosion of such studies. It is likely that we will be much better informed about the effects of central OT perhaps to the detriment of or understanding of the factors associated with OT release.

*Emotional valence and intensity: Variable OT effects.*

Studies using OT administration are informative about 'state' effects of the hormone. In addition to the above distinction between trait and state, I now consider finer distinctions with short-term 'states' and how these may be differentially affected by OT administration.

On a continuum of interpersonal perception, trust and fear reside at opposite extremes. Trust indicates a belief in the reliability and goodwill of another person and can range from provisional favourability to complete confidence. Fear signals threat, hostility and possible attack, and can range from mild apprehension to outright panic. These are not merely semantic distinctions. The behavioral manifestation of OT's anxiolytic action may depend on where an individual is located on this interpersonal continuum between trust and fear. It may downgrade terror to fear, or shift mild apprehension to unconditional trust.

Animal research is instructive at the very high end of the fear continuum. OT enhances maternal aggression (Debiec, 2005; Pedersen, 2004). Maternal aggression is associated with low levels of fear (Neumann, 2008; but see Lonstein & Gammie, 2002). Following parturition there is down-regulation of corticotropin releasing factor which controls activity in the hypothalamic pituitary axis (Lonstein 2005; Neumann, 2002, 2003). Intracerebroventricular infusion of CRF significantly inhibits maternal aggression while leaving other maternal behaviors unaffected (Gammie, Negron, Newman & Rhodes, 2004). At very high fear levels, with no escape route, both humans and rodents respond with freezing or tonic immobility (Blanchard, Hynd, Minke, Minemoto & Blanchard, 2001; Moskowitz, 2006). The expression 'scared stiff' captures this behavioral effect which appears to be reduced by OT thus permitting maternal attack.

This line of argument contrasts with that of Taylor, Klein, Lewis, Gruenewald, Gurung & Updegraff (2000). They propose that, for females, OT released under stress reduces the probability of aggressive attack and enhances 'befriending' (seeking protection by affiliating with other females). This is suggested to have evolved because of the centrality of the mother to her infant's survival (Campbell, 1999) which might be jeopardised by direct attack against a conspecific. Yet this leaves maternal aggression, ubiquitous in mammals, unexplained. The key issue distinguishing between the two positions is the behavioural impact of fear reduction on aggression. I and others (Campbell, 2006; Neumann, 2008) have argued that extreme fear is antithetical to aggression so that, by reducing it, the likelihood of attack is increased. Taylor et al. propose that fear reduction should diminish the

likelihood of attack. Here again, it may be a matter of intensity---the behavioural manifestation of the anxioytic effects of OT on paralysing fear may be different from those on mild fear.

Although human studies of the effect of OT on high fear levels present ethical issues, the idea of fear down-regulation may shed light on a crucial and unresolved anomaly in the aggression literature: The well-established sex difference in aggression found where the target is same-sex or unspecified, disappears and even reverses where the target is an intimate partner (Archer, 2000). The usual fear experienced by women contemplating an attack on a stronger, larger male opponent is reduced in the context of partner-directed aggression (Fiebert & Gonzalez, 1997), an effect that may be mediated by the increase in trust associated with physical intimacy and OT release. The trust (reduced fear) necessary for intimate sexual contact may diminish the threshold for female-to-male aggression.

We know that in rodents oestrous females are typically wary of a strange male and the release of OT inhibits defensive aggression and facilitates lordosis (Debiec 2007; Pedersen & Boccia, 2006). At the risk of anthropomorphism, we might conceive of OT as shifting the female from apprehension to the trust necessary to permit mating. In human relationships, male aggression and date rape represent a real danger to women (Surbey & Conohan, 2000) and typically women require some period of social interaction in order to establish a degree of trust in a potential sexual partner. OT may enhance social affiliation and non-sexual physical contact and reduce wariness to allow sexual relations.

Most of our social interactions are with acquaintances or kin where prior knowledge and experience increase the predictability of the exchange. Strangers represent an unknown quantity with correspondingly higher levels of subjective uncertainty about their motives and behaviour. In interactions between strangers, terms such as 'fear reduction' have been used to describe increased trust after OT administration, yet the effect of OT might be more accurately and modestly described as a reduction in the normal apprehension associated with stranger interaction. Baumgartner et al's (2008) follow-up study found that, while the placebo group showed a decrease in trust following betrayal, OT was associated with no change in trusting behavior. Betrayal shifted the placebo group from trust toward hostility, while the effect of OT was to maintain (but not increase) trusting behavior.

OT facilitates empathy and the effect of OT on prosocial behavior is most evident when an individual must take into account another's viewpoint. Romantic relationships, associated with OT release, involve continual monitoring of another's viewpoint (Fisher et al., 2006; but see Zeki, 2007) and human mothering involves maternal 'mind-mindedness' with regard to the infant (Meins, Fernyhough, Fradley & Tuckey, 2001). By lowering threat and increasing trust, OT appears to facilitate empathic identification. Individuals in less satisfactory relationships displayed heightened OT levels. This may be a hormonal response which reduces interpersonal apprehension and facilitates a more positive empathic engagement. In summary, the effects of OT may crucially depend on where the individual currently stands on the spectrum of interpersonal perception from terror through apprehension and wariness to trust.

The future research agenda is likely to become increasingly complex as we discover more about OT's interactions with its sister nanopeptide argentine vasopressin as well as with steroid, stress and classical neurotransmitter systems (Depue & Morrone-Strupinsky, 2005; Jorgensen, Kjaer, Knigge, Moller & Warberg, 2003). But OT, recently called "the great facilitator of life" (Lee, Macbeth, Feldman & Weller, 2009), is too important to be studied only by endocrinologists. It is relevant to psychologists understanding of aggression, affiliation, cooperation, empathy, love, mate choice and mother-infant attachment. In the clinical area, research has already begun on the application of OT to ADHD, autism spectrum and conduct disorders (e.g. Bartz & Hollander, 2006; Hollander, Novotny, Hanratty, Yaffe, DeCarial, Aronowitz et al., 2003). Social psychology's expertise and ingenuity in operationalizing and measuring complex social constructs has an important role to play in exploring the promise of oxytocin.

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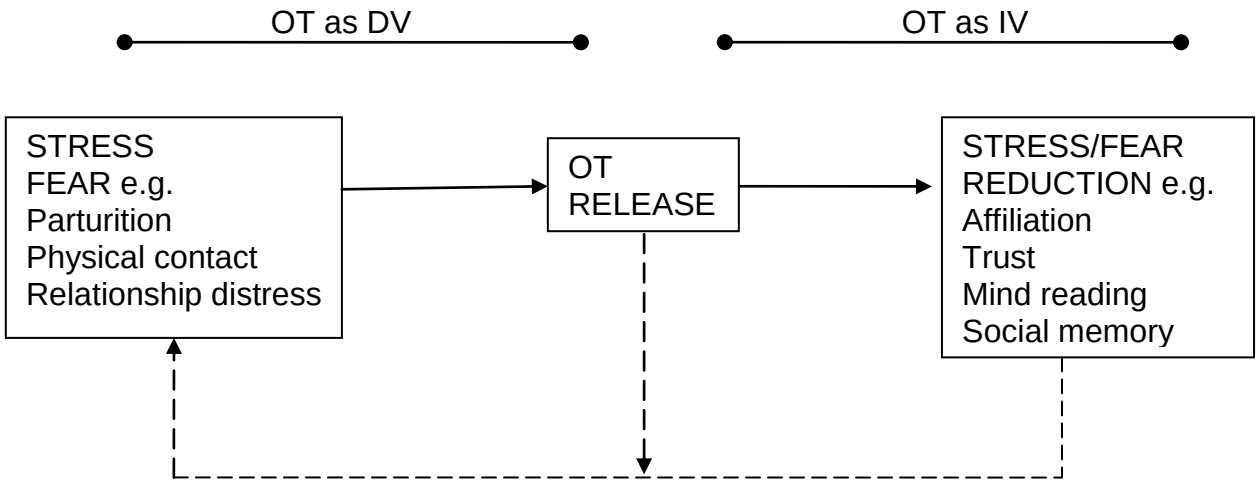


Figure 1. A simplified proposal of OT action.

Unbroken lines represent positive causal pathways. Dotted lines represent negative feedback pathways.