Lost connections: Oxytocin and the neural, physiological and behavioural consequences of disrupted relationships

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Int. J. Psychophysiology 2017, DOI: 10.1016/j.ijpsycho.2017.12.011

Oxytocin, a chemical produced in the brain of humans and other mammals, has been called the 'cuddle hormone' because of its role in the formation of social bonds. It is implicated in bonding between parents and their infants, bonding between partners and even the formation of friendships. There is a down side to this, however. Dysfunctional relationships and disruption to established ones causes a breakdown in oxytocin function that in turn will affect an individual's physical and mental health. Many researchers have explored the way that oxytocin and its activity mediates both the positive effects of close relationships and the negative effects of disruptive ones in humans and in animal models. In this extensive review, Tobias Pohl and Oliver Bosch from the University of Regensburg in Germany and Larry Young from Emory University, Atlanta, Georgia, USA examine studies of the link between parent-infant and partner bonding, oxytocin and health outcomes in humans and in a rodent, the prairie vole. Prairie voles, which are found throughout North American grasslands, are unlike most other rodents in that they are monogamous and gregarious, and both parents are involved in caring for the young. They are therefore considered to be a useful animal model for studies of human social, sexual and parent-infant relationships.

Human beings are naturally social animals, and the strong relationships between positive social relationships and human flourishing, and conversely between negative ones and physical and psychological problems, have been well studied on many levels. Rewarding personal relationships both within and outside the family unit correlate with a lower susceptibility to depression and other illnesses and even with a decreased risk of death. Unsurprisingly, however, it is the quality of family relationships that have the greatest effect on human wellbeing. Positive family relationships provide a 'buffering' effect against stress through damping down biochemical stress responses. This has been associated with increases in oxytocin levels, and administration of oxytocin through the nose seems to potentiate such calming and pro-social effects. These results, however, have been difficult to confirm.

The relationships that have the strongest effect on well-being are those between parents and children and between marriage partners. Individuals who receive close, sensitive and stable care in infancy and early childhood are better able to respond to stress in adulthood, and children brought up in a stable, emotionally warm, two-parent family are, on average, less susceptible to a range of psychiatric disorders in later life. Partners in successful marriages and similar stable unions have been found, statistically, to live longer in better health than the divorced, the unhappily married and the single. And the physiological basis for this link seems likely to involve oxytocin: administering it through the nose can increase brain activity linked to building pair-

bonds, for example by increasing a man's physical attraction to his partner compared to other women.

There is a negative side to all this, however. A troubled close relationship or one that is broken by divorce or death is known to be associated with an increased risk of physical and psychiatric problems. Interestingly, an increase in the level of oxytocin in blood plasma has been associated with both high and low levels of conflict in close relationships. The role of oxytocin in mediating the link between healthy childhood relationships and the development of the stress response seems to be clearer. Both men and women who were maltreated in childhood have lower oxytocin levels than their peers, and the effect of oxytocin on their stress response is less sensitive.

The loss of a partner, whether through separation or death, is often regarded as the most traumatic of all life experiences. In most individuals, bereavement or divorce causes severe short-term grief but has little effect on long-term health. However, in about 10-20% of cases, grief following the loss of a partner is complicated and long-lasting, increasing the risk of a variety of physical illnesses and psychiatric problems. Individuals experiencing complex grief have also been shown to have disturbances in the oxytocin-related signalling pathways in their brains.

In summary, experiments have shown a link between the quality of human parent-child and other close family relationships, the activity of oxytocin in the brain, and the development of the stress response, but the nature of this relationship is not yet clear. Such studies are understandably complicated by ethical considerations, and some types of experiment are simply impossible to carry out on human subjects. Much work has gone into developing suitable animal models for studies of social relationships and stress. The prairie vole is considered to be a particularly appropriate model because it forms strong, monogamous pair bonds and both parents are involved in rearing the pups. Experiments with prairie voles are shedding light on the mechanisms through which oxytocin can mediate the effects of bonding on stress responses and thus on overall health.

Many experiments with prairie voles have implicated oxytocin and another hormone, vasopressin, in the development of monogamous pair bonds and mother-infant bonds and in the onset of maternal behaviour. Prairie voles have higher concentrations of the protein that responds to oxytocin – known simply as the oxytocin receptor – in some brain regions than members of a similar, non-monogamous vole species. Blocking the interaction between oxytocin and this receptor impairs pair bonding in male prairie voles; pair bonding in females is accelerated if larger numbers of receptors are produced. The biochemical signalling pathways that this interaction triggers are thought to increase active communication between certain regions of the brain.

Mother prairie voles nurture their pups principally through licking and grooming. Stimulating this response artificially by separating a mother and pups for a very short period, minutes rather than hours, has been found to increase brain oxytocin in pups when they reach maturity, and, interestingly, if these pups are female they will lick and groom more when they themselves become mothers. Pups also seem to thrive more if

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their fathers are involved in their care, either directly or indirectly through defending the nest.

In contrast, voles that experience poor care as pups show an increased response to fearful stimuli and poor ability to form pair bonds. Poor care can be replicated under experimental conditions by removing pups from their mothers and rearing them in isolation. Prairie vole pups reared in this way show anxiety-related behaviour and females lick and groom their pups less when they become mothers. Interestingly, removing the father from a nest of prairie voles reduces the mother's licking and grooming behaviour, leading to similar changes in pup behaviour. There is, however, considerable variation between individual voles, as well as between the sexes: in females this has been found to be associated with the natural density of oxytocin receptors in the brain. Female voles with a higher density of receptors appear more resilient to the negative effects of poor early care.

Prairie voles can also be also good models of the physical and psychological effects of adult social relationships, particularly between partners. Female voles that are stressed (e.g. with a mild shock to the foot) recover more quickly if they are placed with their partners, and the partners respond by grooming. This decrease in stress symptoms in response to what can be interpreted as 'consoling' behaviour has been shown to correlate with an increase in oxytocin signalling and blocking this signalling in the male reduces the grooming behaviour. Sudden separation of a pair of voles increases physiological stress responses in both partners, leading to a behaviour pattern that mimics depression. This, also, has been linked to disruptions in oxytocin signalling, particularly in a brain region known as the nucleus accumbens. Infusing oxytocin directly into this region can dampen down the stress response. Taken together, these results suggest that a 'normal' pattern of oxytocin signalling is necessary for maintaining strong pair bonds.

Pohl and his co-authors conclude that in humans and prairie voles strong, healthy relationships between partners and between parents and offspring protect against stressful circumstances, and that this is mediated by signalling pathways involving oxytocin and its receptors in the brain. Conversely, at least some of the harmful physiological and psychological effects of broken or difficult parent-child or partner relationships are mediated by disruptions in oxytocin signalling. Experiments with voles have shown that artificially stimulating the oxytocin system can reverse some of these, and if these results, also, are replicated in humans this hormone may provide a pharmacological treatment for some of the problems caused by relationship breakdown and child neglect.

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