Love is deeply biological. It pervades every aspect of our lives and has inspired countless works of art. Love also has a profound effect on our mental and physical state. A “broken heart” or a failed relationship can have disastrous effects; bereavement disrupts human physiology and may even precipitate death. Without loving relationships, humans fail to flourish, even if all of their other basic needs are met. As such, love is clearly not “just” an emotion; it is a biological process that is both dynamic and bidirectional in several dimensions. Social interactions between individuals, for example, trigger cognitive and physiological processes that influence emotional and mental states. In turn, these changes influence future social interactions. Similarly, the maintenance of loving relationships requires constant feedback through sensory and cognitive systems; the body seeks love and responds constantly to interactions with loved ones or to the absence of such interactions. The evolutionary principles and ancient hormonal and neural systems that support the beneficial and healing effects of loving relationships are described here.

Learning Objectives

• Understand the role of Oxytocin in social behaviors.
• Articulate the functional differences between Vasopressin and Oxytocin.
• List sex differences in reaction to stress.

Introduction
Although evidence exists for the healing power of love, only recently has science turned its attention to providing a physiological explanation for love. The study of love in this context offers insight into many important topics, including the biological basis of interpersonal relationships and why and how disruptions in social bonds have such pervasive consequences for behavior and physiology. Some of the answers will be found in our growing knowledge of the neurobiological and endocrinological mechanisms of social behavior and interpersonal engagement.

The evolution of social behavior

Nothing in biology makes sense except in the light of evolution. Theodosius Dobzhansky's famous dictum also holds true for explaining the evolution of love. Life on earth is fundamentally social: The ability to dynamically interact with other living organisms to support mutual homeostasis, growth, and reproduction evolved very early. Social interactions are present in primitive invertebrates and even among prokaryotes: Bacteria recognize and approach members of their own species. Bacteria also reproduce more successfully in the presence of their own kind and are able to form communities with physical and chemical characteristics that go far beyond the capabilities of the individual cell (Ingham & Ben-Jacob, 2008).

As another example, various insect species have evolved particularly complex social systems, known as eusociality. Characterized by a division of labor, eusociality appears to have evolved independently at least 11 times in insects. Research on honeybees indicates that a complex set of genes and their interactions regulate eusociality, and that these resulted from an “accelerated form of evolution” (Woodard et al., 2011). In other words, molecular mechanisms favoring high levels of sociality seem to be on an evolutionary fast track.

The evolutionary pathways that led from reptiles to mammals allowed the emergence of the unique anatomical
systems and biochemical mechanisms that enable social engagement and selectively reciprocal sociality. Reptiles show minimal parental investment in offspring and form nonselective relationships between individuals. Pet owners may become emotionally attached to their turtle or snake, but this relationship is not reciprocal. In contrast, most mammals show intense parental investment in offspring and form lasting bonds with their children. Many mammalian species—including humans, wolves, and prairie voles—also develop long-lasting, reciprocal, and selective relationships between adults, with several features of what humans experience as “love.” In turn, these reciprocal interactions trigger dynamic feedback mechanisms that foster growth and health.

What is love? An evolutionary and physiological perspective

Human love is more complex than simple feedback mechanisms. Love may create its own reality. The biology of love originates in the primitive parts of the brain—the emotional core of the human nervous system—which evolved long before the cerebral cortex. The brain “in love” is flooded with vague sensations, often transmitted by the vagus nerve, and creating much of what we experience as emotion. The modern cortex struggles to interpret love's primal messages, and weaves a narrative around incoming visceral experiences, potentially reacting to that narrative rather than to reality. It also is helpful to realize that mammalian social behavior is supported by biological components that were repurposed or co-opted over the course of mammalian evolution, eventually permitting lasting relationships between adults.

Is there a hormone of love and other relationships?

One element that repeatedly appears in the biochemistry of love is the neuropeptide oxytocin. In large mammals, oxytocin adopts a central role in reproduction by helping to expel the big-brained baby from the uterus, ejecting milk and sealing a selective and lasting bond between mother and offspring (Keverne, 2006). Mammalian offspring crucially depend on their mother’s milk for some time after birth. Human mothers also form a strong and lasting bond with their newborns immediately after birth, in a time period that is essential for the nourishment and survival of the baby. However, women who give birth by cesarean section without going through labor, or who opt not to breastfeed, are still able to form a strong emotional bond with their children. Furthermore, fathers, grandparents, and adoptive parents also form lifelong attachments to children. Preliminary evidence suggests that the simple presence of an infant can release oxytocin in adults as well (Feldman, 2012; Kenkel et al., 2012). The baby virtually forces us to love it.
The case for a major role for oxytocin in love is strong, but until recently was based largely on extrapolation from research on parental behavior (Feldman, 2012) or social behaviors in animals (Carter, 1998; Kenkel et al., 2012). However, recent human experiments have shown that intranasal delivery of oxytocin can facilitate social behaviors, including eye contact and social cognition (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011)—behaviors that are at the heart of love.

Of course, oxytocin is not the molecular equivalent of love. Rather, it is just one important component of a complex neurochemical system that allows the body to adapt to highly emotional situations. The systems necessary for reciprocal social interactions involve extensive neural networks through the brain and autonomic nervous system that are dynamic and constantly changing across the life span of an individual. We also now know that the properties of oxytocin are not predetermined or fixed. Oxytocin’s cellular receptors are regulated by other hormones and epigenetic factors. These receptors change and adapt based on life experiences. Both oxytocin and the experience of love can change over time. In spite of limitations, new knowledge of the properties of oxytocin has proven useful in explaining several enigmatic features of love.

**Stress and love**

Emotional bonds can form during periods of extreme duress, especially when the survival of one individual depends on the presence and support of another. There also is evidence that oxytocin is released in response to acutely stressful experiences, perhaps serving as hormonal “insurance” against overwhelming stress. Oxytocin may help to ensure that parents and others will engage with and care for infants; develop stable, loving relationships; and seek out and receive support from others in times of need.

**Animal models and the biology of social bonds**

To dissect the anatomy and chemistry of love, scientists needed a biological equivalent of the
Rosetta Stone. Just as the actual stone helped linguists decipher an archaic language by comparison to a known one, animal models are helping biologists draw parallels between ancient physiology and contemporary behaviors. Studies of socially monogamous mammals that form long-lasting social bonds, such as prairie voles, have been especially helpful to an understanding the biology of human social behavior.

There is more to love than oxytocin

Research in prairie voles showed that, as in humans, oxytocin plays a major role in social interactions and parental behavior (Carter, 1998; Carter, Boone, Pournajafi-Nazarloo, & Bales, 2009; Kenkel et al., 2012). Of course, oxytocin does not act alone. Its release and actions depend on many other neurochemicals, including endogenous opioids and dopamine (Aragona & Wang, 2009). Particularly important to social bonding are the interactions of oxytocin with a related neuropeptide known as vasopressin. The systems regulated by oxytocin and vasopressin are sometimes redundant. Both peptides are implicated in behaviors that require social engagement by either males or females, such as huddling over an infant (Kenkel et al., 2012). For example, it was necessary in voles to block both oxytocin and vasopressin receptors to induce a significant reduction in social engagement, either among adults or between adults and infants. Blocking only one of these two receptors did not eliminate social approach or contact. However, antagonists for either the oxytocin or vasopressin receptor inhibited the selective sociality, which is essential for the expression of a social bond (Bales, Kim, Lewis-Reese, & Carter, 2004; Cho, DeVries, Williams, & Carter, 1999).

If we accept selective social bonds, parenting, and mate protection as proxies for love in humans, research in animals supports the hypothesis that oxytocin and vasopressin interact to allow the dynamic behavioral states and behaviors necessary for love.

Oxytocin and vasopressin have shared functions, but they are not identical in their actions. The specific behavioral roles of oxytocin and vasopressin are especially difficult to untangle because they are components of an integrated neural network with many points of intersection. Moreover, the genes that regulate the production of oxytocin and vasopressin...
are located on the same chromosome, possibly allowing coordinated synthesis or release of these peptides. Both peptides can bind to and have antagonist or agonist effects on each other’s receptors. Furthermore, the pathways necessary for reciprocal social behavior are constantly adapting: These peptides and the systems that they regulate are always in flux. In spite of these difficulties, some of the different functions of oxytocin and vasopressin have been identified.

**Functional differences between vasopressin and oxytocin**

Vasopressin is associated with physical and emotional mobilization, and can help support vigilance and behaviors needed for guarding a partner or territory (Carter, 1998), as well as other forms of adaptive self-defense (Ferris, 2008). Vasopressin also may protect against physiologically “shutting down” in the face of danger. In many mammalian species, mothers exhibit agonistic behaviors in defense of their young, possibly through the interactive actions of vasopressin and oxytocin (Bosch & Neumann, 2012). Prior to mating, prairie voles are generally social, even toward strangers. However, within a day or so of mating, they begin to show high levels of aggression toward intruders (Carter, DeVries, & Getz, 1995), possibly serving to protect or guard a mate, family, or territory. This mating-induced aggression is especially obvious in males.

Oxytocin, in contrast, is associated with immobility without fear. This includes relaxed physiological states and postures that permit birth, lactation, and consensual sexual behavior. Although not essential for parenting, the increase of oxytocin associated with birth and lactation may make it easier for a woman to be less anxious around her newborn and to experience and express loving feelings for her child (Carter & Altemus, 1997). In highly social species such as prairie voles (Kenkel et al., 2013), and presumably in humans, the intricate molecular dances of oxytocin and vasopressin fine-tune the coexistence of caretaking and protective aggression.

**Fatherhood also has a biological basis**

The biology of fatherhood is less well-studied than motherhood is. However, male care of offspring also appears to rely on both oxytocin and vasopressin (Kenkel et al., 2012), probably acting in part through effects on the autonomic nervous system (Kenkel et al., 2013). Even sexually naïve male prairie voles show spontaneous parental behavior in the presence of an infant (Carter et al., 1995). However, the stimuli from infants or the nature of the social interactions that release oxytocin and vasopressin may differ between the sexes (Feldman,
At the heart of the benefits of love is a sense of safety

Parental care and support in a safe environment are particularly important for mental health in social mammals, including humans and prairie voles. Studies of rodents and of lactating women suggest that oxytocin has the important capacity to modulate the behavioral and autonomic distress that typically follows separation from a mother, child, or partner, reducing defensive behaviors and thereby supporting growth and health (Carter, 1998).

The absence of love in early life can be detrimental to mental and physical health

During early life in particular, trauma or neglect may produce behaviors and emotional states in humans that are socially pathological. Because the processes involved in creating social behaviors and social emotions are delicately balanced, these be may be triggered in inappropriate contexts, leading to aggression toward friends or family. Alternatively, bonds may be formed with prospective partners who fail to provide social support or protection.

Sex differences exist in the consequences of early life experiences

Males seem to be especially vulnerable to the negative effects of early experiences, possibly helping to explain the increased sensitivity of males to various developmental disorders. The implications of sex differences in the nervous system and in the response to stressful experiences for social behavior are only slowly becoming apparent (Carter et al., 2009). Both males and females produce vasopressin and oxytocin and are capable of responding to both hormones. However, in brain regions that are involved in defensive aggression, such as the extended amygdala and lateral septum, the production of vasopressin is androgen-dependent. Thus, in the face of a threat, males may be experiencing higher central levels of...
vasopressin.

Oxytocin and vasopressin pathways, including the peptides and their receptors, are regulated by coordinated genetic, hormonal, and epigenetic factors that influence the adaptive and behavioral functions of these peptides across the animal's life span. As a result, the endocrine and behavioral consequences of a stress or challenge may be different for males and females (DeVries, DeVries, Taymans, & Carter, 1996). For example, when unpaired prairie voles were exposed to an intense but brief stressor, such as a few minutes of swimming, or injection of the adrenal hormone corticosterone, the males (but not females) quickly formed new pair bonds. These and other experiments suggest that males and females have different coping strategies, and possibly may experience both stressful experiences, and even love, in ways that are gender-specific.

In the context of nature and evolution, sex differences in the nervous system are important. However, sex differences in brain and behavior also may help to explain gender differences in the vulnerability to mental and physical disorders (Taylor, et al., 2000). Better understanding these differences will provide clues to the physiology of human mental health in both sexes.

**Loving relationships in early life can have epigenetic consequences**

Love is “epigenetic.” That is, positive experiences in early life can act upon and alter the expression of specific genes. These changes in gene expression may have behavioral consequences through simple biochemical changes, such as adding a methyl group to a particular site within the genome (Zhang & Meaney, 2010). It is possible that these changes in the genome may even be passed to the next generation.

Social behaviors, emotional attachment to others, and long-lasting reciprocal relationships also are both plastic and adaptive, and so is the biology upon which they are based. For example, infants of traumatized or highly stressed parents...
might be chronically exposed to vasopressin, either through their own increased production of the peptide, or through higher levels of vasopressin in maternal milk. Such increased exposure could sensitize the infant to defensive behaviors or create a lifelong tendency to overreact to threat. Based on research in rats, it seems that in response to adverse early experiences of chronic isolation, the genes for vasopressin receptors can become upregulated (Zhang et al., 2012), leading to an increased sensitivity to acute stressors or anxiety that may persist throughout life.

Epigenetic programming triggered by early life experiences is adaptive in allowing neuroendocrine systems to project and plan for future behavioral demands. But epigenetic changes that are long-lasting also can create atypical social or emotional behaviors (Zhang & Meaney, 2010) that may be especially likely to surface in later life, and in the face of social or emotional challenges.

Exposure to exogenous hormones in early life also may be epigenetic. For example, prairie voles treated postnatally with vasopressin (especially males) were later more aggressive, whereas those exposed to a vasopressin antagonist showed less aggression in adulthood. Conversely, in voles the exposure of infants to slightly increased levels of oxytocin during development increased the tendency to show a pair bond. However, these studies also showed that a single exposure to a higher level of oxytocin in early life could disrupt the later capacity to pair bond (Carter et al., 2009).

There is little doubt that either early social experiences or the effects of developmental exposure to these neuropeptides holds the potential to have long-lasting effects on behavior. Both parental care and exposure to oxytocin in early life can permanently modify hormonal systems, altering the capacity to form relationships and influence the expression of love across the life span. Our preliminary findings in voles further suggest that early life experiences affect the methylation of the oxytocin receptor gene and its expression (Connelly, Kenkel, Erickson, & Carter, 2011). Thus, we can plausibly argue that love is epigenetic.

The absence of social behavior or isolation also has consequences for the oxytocin system

Given the power of positive social experiences, it is not surprising that a lack of social relationships also may lead to alterations in behavior as well as changes in oxytocin and vasopressin pathways. We have found that social isolation reduced the expression of the gene for the oxytocin receptor, and at the same time increased the expression of genes for the vasopressin peptide. In female prairie voles, isolation also was accompanied by an increase
in blood levels of oxytocin, possibly as a coping mechanism. However, over time, isolated prairie voles of both sexes showed increases in measures of depression, anxiety, and physiological arousal, and these changes were observed even when endogenous oxytocin was elevated. Thus, even the hormonal insurance provided by endogenous oxytocin in face of the chronic stress of isolation was not sufficient to dampen the consequences of living alone. Predictably, when isolated voles were given additional exogenous oxytocin, this treatment did restore many of these functions to normal (Grippo, Trahanas, Zimmerman, Porges, & Carter, 2009).

In modern societies, humans can survive, at least after childhood, with little or no human contact. Communication technology, social media, electronic parenting, and many other recent technological advances may reduce social behaviors, placing both children and adults at risk for social isolation and disorders of the autonomic nervous system, including deficits in their capacity for social engagement and love (Porges, 2011).

Social engagement actually helps us to cope with stress. The same hormones and areas of the brain that increase the capacity of the body to survive stress also enable us to better adapt to an ever-changing social and physical environment. Individuals with strong emotional support and relationships are more resilient in the face of stressors than those who feel isolated or lonely. Lesions in various bodily tissues, including the brain, heal more quickly in animals that are living socially versus in isolation (Karelina & DeVries, 2011). The protective effects of positive sociality seem to rely on the same cocktail of hormones that carries a biological message of “love” throughout the body.

**Can love—or perhaps oxytocin—be a medicine?**

Although research has only begun to examine the physiological effects of these peptides beyond social behavior, there is a wealth of new evidence showing that oxytocin can influence physiological responses to stress and injury. As only one example, the molecules associated with love have restorative properties, including the ability to literally heal a “broken heart.” Oxytocin receptors are expressed in the heart, and precursors for oxytocin appear to be critical for the development of the fetal heart (Danalache, Gutkowska, Sluszar, Berezowska, & Jankowski, 2010). Oxytocin exerts protective and restorative effects in part through its capacity to convert undifferentiated stem cells into cardiomyocytes. Oxytocin can facilitate adult neurogenesis and tissue repair, especially after a stressful experience. We now know that oxytocin has direct anti-inflammatory and antioxidant properties in *in vitro* models of atherosclerosis (Szeto et al., 2008). The heart seems to rely on oxytocin as part of a normal process of protection and self-healing.
Thus, oxytocin exposure early in life not only regulates our ability to love and form social bonds, it also affects our health and well-being. Oxytocin modulates the hypothalamic–pituitary adrenal (HPA) axis, especially in response to disruptions in homeostasis (Carter, 1998), and coordinates demands on the immune system and energy balance. Long-term, secure relationships provide emotional support and down-regulate reactivity of the HPA axis, whereas intense stressors, including birth, trigger activation of the HPA axis and sympathetic nervous system. The ability of oxytocin to regulate these systems probably explains the exceptional capacity of most women to cope with the challenges of childbirth and childrearing.

Dozens of ongoing clinical trials are currently attempting to examine the therapeutic potential of oxytocin in disorders ranging from autism to heart disease. Of course, as in hormonal studies in voles, the effects are likely to depend on the history of the individual and the context, and to be dose-dependent. As this research is emerging, a variety of individual differences and apparent discrepancies in the effects of exogenous oxytocin are being reported. Most of these studies do not include any information on the endogenous hormones, or on the oxytocin or vasopressin receptors, which are likely to affect the outcome of such treatments.

Conclusion

Research in this field is new and there is much left to understand. However, it is already clear that both love and oxytocin are powerful. Of course, with power comes responsibility. Although research into mechanisms through which love—or hormones such as oxytocin—may protect us against stress and disease is in its infancy, this knowledge will ultimately increase our understanding of the way that our emotions impact upon health and disease. The same molecules that allow us to give and receive love also link our need for others with health and well-being.

Acknowledgments
C. Sue Carter and Stephen W. Porges are both Professors of Psychiatry at the University of North Carolina, Chapel Hill, and also are Research Professors of Psychology at Northeastern University, Boston.

Discussions of “love and forgiveness” with members of the Fetzer Institute's Advisory Committee on Natural Sciences led to this essay and are gratefully acknowledged here. We are especially appreciative of thoughtful editorial input from Dr. James Harris. Studies from the authors’ laboratories were sponsored by the National Institutes of Health. We also express our gratitude for this support and to our colleagues, whose input and hard work informed the ideas expressed in this article. A version of this paper was previously published in *EMBO Reports* in the series on “Sex and Society”; this paper is reproduced with the permission of the publishers of that journal.
Outside Resources


Web: Database of publicly and privately supported clinical studies of human participants conducted around the world.
http://www.clinicaltrials.gov

Web: PubMed comprises over 22 million citations for biomedical literature from MEDLINE, life science journals, and online books. PubMed citations and abstracts include the fields of biomedicine and health, covering portions of the life sciences, behavioral sciences, chemical sciences, and bioengineering. PubMed also provides access to additional relevant web sites and links to the other NCBI molecular biology resources.

Web: Website of author Stephen Porges
http://www.stephenporges.com/

Discussion Questions

1. If love is so important in human behavior, why is it so hard to describe and understand?
2. Discuss the role of evolution in understanding what humans call “love” or other forms of prosociality.
3. What are the common biological and neuroendocrine elements that appear in maternal love and adult-adult relationships?
4. Oxytocin and vasopressin are biochemically similar. What are some of the differences between the actions of oxytocin and vasopressin?
5. How may the properties of oxytocin and vasopressin help us understand the biological bases of love?
6. What are common features of the biochemistry of “love” and “safety,” and why are these important to human health?
Vocabulary

Epigenetics
Heritable changes in gene activity that are not caused by changes in the DNA sequence. http://en.wikipedia.org/wiki/Epigenetics

Oxytocin
A nine amino acid mammalian neuropeptide. Oxytocin is synthesized primarily in the brain, but also in other tissues such as uterus, heart and thymus, with local effects. Oxytocin is best known as a hormone of female reproduction due to its capacity to cause uterine contractions and eject milk. Oxytocin has effects on brain tissue, but also acts throughout the body in some cases as an antioxidant or anti-inflammatory.

Vagus nerve
The 10th cranial nerve. The mammalian vagus has an older unmyelinated branch which originates in the dorsal motor complex and a more recently evolved, myelinated branch, with origins in the ventral vagal complex including the nucleus ambiguous. The vagus is the primary source of autonomic-parasympathetic regulation for various internal organs, including the heart, lungs and other parts of the viscera. The vagus nerve is primarily sensory (afferent), transmitting abundant visceral input to the central nervous system.

Vasopressin
A nine amino acid mammalian neuropeptide. Vasopressin is synthesized primarily in the brain, but also may be made in other tissues. Vasopressin is best known for its effects on the cardiovascular system (increasing blood pressure) and also the kidneys (causing water retention). Vasopressin has effects on brain tissue, but also acts throughout the body.
References


protects against negative behavioral and autonomic consequences of long-term social isolation. *Psychoneuroendocrinology*, 34, 1542–1553.


About Noba

The Diener Education Fund (DEF) is a non-profit organization founded with the mission of re-inventing higher education to serve the changing needs of students and professors. The initial focus of the DEF is on making information, especially of the type found in textbooks, widely available to people of all backgrounds. This mission is embodied in the Noba project.

Noba is an open and free online platform that provides high-quality, flexibly structured textbooks and educational materials. The goals of Noba are three-fold:

- To reduce financial burden on students by providing access to free educational content
- To provide instructors with a platform to customize educational content to better suit their curriculum
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The Diener Education Fund is co-founded by Drs. Ed and Carol Diener. Ed is the Joseph Smiley Distinguished Professor of Psychology (Emeritus) at the University of Illinois. Carol Diener is the former director of the Mental Health Worker and the Juvenile Justice Programs at the University of Illinois. Both Ed and Carol are award-winning university teachers.

Acknowledgements

The Diener Education Fund would like to acknowledge the following individuals and companies for their contribution to the Noba Project: The staff of Positive Acorn, including Robert Biswas-Diener as managing editor and Peter Lindberg as Project Manager; The Other Firm for user experience design and web development; Sockeye Creative for their work on brand and identity development; Arthur Mount for illustrations; Chad Hurst for photography; EEI Communications for manuscript proofreading; Marissa Diener, Shigehiro Oishi, Daniel Simons, Robert Levine, Lorin Lachs and Thomas Sander for their feedback and suggestions in the early stages of the project.
How to cite a Noba chapter using APA Style