# {Oxytocin & Vasopressin
## HOW SOCIAL TIES ARE FORMED

*By* **Rachel Arens**

Humans are socially bound to one another in complex and fluid ways that are distinct from other mammals. The relationships formed and sustained between two *Homo sapiens* are unique among the animal kingdom and are a large part of why humans have been able to come so far. There is no argument when begged the question, "Which species is most developed?" or perhaps, "Which species is most powerful on Earth?" Humans clearly win out here, as they have the power to build and destroy. In just the past 200 years humans have completely changed the climate and the biological makeup of the Earth. They did this through innovation and elaborate collaboration with each other, in which their ability to form deep and meaningful social bonds was critical. For example, humans have changed the world with their extreme use of fossil fuels. To use these fossil fuels humans first needed to discover how to extract these fuels, and even before that humans needed a purpose for the fuels: machines. To develop a machine, a drug, or a new way of thinking requires a group of people working together towards that common goal. For many hundreds of years, humans have formed families and communities to reach these goals.

So why are humans able to form these social bonds that enable them to change the world? What is different about humans that makes them *special*? Scientists have found that two neuropeptides, oxytocin and vasopressin, may be a part of the answer. While other mammals have these neuropeptides, studies have shown that in humans these play a more significant role in social bonds than in these other animals. As neuropeptides, oxytocin and vasopressin both act as hormones and neurotransmitters. As hormones, they produce physiological effects including uterine contractions or water conservation. As neurotransmitters, their functions are widespread and not completely understood, but revolve around forming social bonds.

### History

Starting in the 1800's, scientists began investigating extracts from the posterior pituitary gland. First, in 1906, Sir Henry Dale found that an extract facilitated uterine contractions in cats[1]. He named the molecule "oxytocin", because it means "quick birth" in Greek. As early as 1911, oxytocin was used to induce labor in women[1]. This practice is still used today, however, rather than giving women oxytocin extracted from other mammals, women are given a synthetic version called pitocin. Pitocin has gained popularity in recent years as many women schedule the birth of their child due to the inflexibility that often comes with being employed[2]. Popularity has also risen due to a shortage of hospital beds in large cities; this shortage pressures providers to get people in and out of the hospital as quickly as possible. Natural labor takes on average 8 hours, but with pitocin this time is cut down to only 6 hours[2]. Thus, women and providers can be aided by this synthetic form of oxytocin, reflected in the doubling of the frequency of labor induction between 1990 and 2012[2]. Oxytocin is often given the abbreviation OT in scientific literature.

In 1913, the antidiuretic component of the extract was discovered by Farini and Vongraven[1]. Because of its properties, it was originally named antidiuretic hormone (ADH). However, as the hormone has gained popularity in neuroscience research and literature, the name vasopressin has also been used, originating from the fact that it is a vasoconstrictor and a pressor agent. In 1954, Vincent du Vigneaud won the Nobel Prize in Chemistry for his organic synthesis of ADH and oxytocin[1]. Following this accomplishment, ADH was frequently used as a medication in the 1960's-1980's to treat diabetes and gastrointestinal hemorrhage.

### Physiology

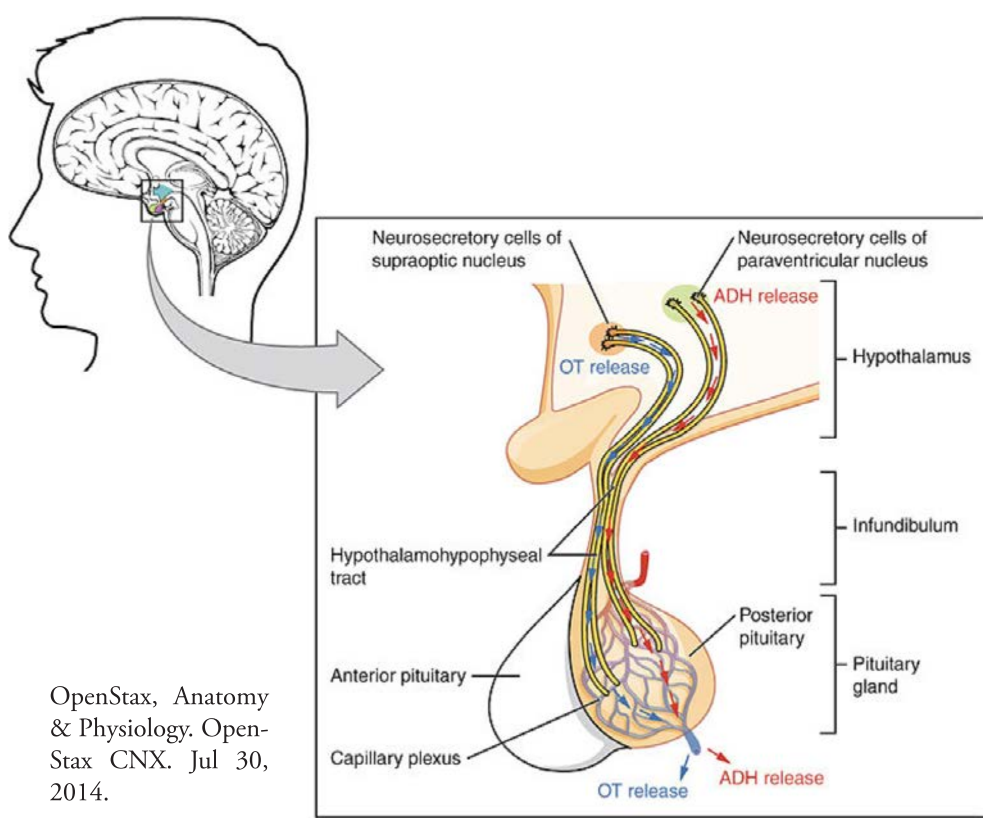
Oxytocin and vasopressin were both originally discovered and known for their roles as posterior pituitary hormones. As hormones, oxytocin and vasopressin are critical for multiple physiological processes. Understanding these processes is important to understanding how these neuropeptides affect the body holistically.

The role of oxytocin in general physiology is centered around reproduction. In relation to this fact, the highest concentration of oxytocin receptors is found in the magnocellular neurons of the hypothalamic paraventricular and supraoptic nuclei[3]. These nuclei are key in processes associated with reproduction, stress, growth, and metabolic rate. When a mammal encounters a stressful stimulus or a stimulus associated with reproduction (like suckling) oxytocin is released from the posterior pituitary into the bloodstream. In addition to these nuclei, oxytocin is secreted by multiple other tissues, including the uterus and testes, the placenta, and the heart[3]. As mentioned earlier, oxytocin is critical in the induction of labor through stimulation of the smooth uterine muscles. On a molecular basis, this happens through an up-regulation of oxytocin receptors in the myometrium and decidua, resulting in an increase in a steroid called PGF(2 alpha), which increases the body's sensitivity to oxytocin[3]. In males, oxytocin is important in the generation of spontaneous erections and ejaculation.

Based on the physiological processes in which oxytocin is involved, it is easy to imagine that oxytocin may also play a role in social bonding. Vasopressin's role is a little more elusive. Vasopressin is involved in many physiological processes, most of which have to do with the maintenance of body homeostasis, not reproduction. The two main sites of action for vasopressin are the kidneys and the blood vessels, where its primary function is to regulate the kidney's management of water[4]. This regulation happens when vasopressin binds to V2 receptors located in renal collecting ducts, increasing water permeability via a cAMP mechanism[4]. This process decreases the formation of urine while increasing blood volume. There are also V1 receptors, which are involved in vasoconstriction, the secondary physiological function of vasopressin. This process increases arterial pressure through a complicated combination of the IP3 signal transduction pathway and Rho-kinase pathway[4]. Release of vasopressin occurs through stimulation of stretch receptors within arterial walls and large veins, alerting the body to a decrease in arterial pressure often due to dehydration or hemorrhage[4]. These stretch receptors communicate with the medulla, which sends the message to the hypothalamus, which then relays to the posterior pituitary that vasopressin should be released.

### Neural Anatomy

While oxytocin and vasopressin

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have many roles within the body, they also have roles in the brain. As stated above, the highest amount of oxytocin receptors is found in the magnocellular neurons of the hypothalamic paraventricular and supraoptic nuclei, which are heavily related to reproduction. However, there are also high concentrations of oxytocin receptors in the central amygdala[5]. Similarly, there are high concentrations of vasopressin receptors in the medial amygdala, another section of this brain structure[5].

The amygdala is a brain structure heavily associated with the processing of fear, anger, and emotion in general. Among the neuroscience community the amygdala is jokingly called "the teenager center" of the brain. Specifically, the central amygdala is the area that communicates with the hypothalamus, alerting the brain to stimuli that induce fear, anxiety, or other strong emotions. The hypothalamus then tells the posterior pituitary to release oxytocin and vasopressin.

How does the placement of oxytocin and vasopressin receptors in the amygdala affect behavior? Because the amygdala is associated with emotion and anxiety, the fact that there are so many receptors here is good evidence for these neuropeptides relating to these feelings. Interestingly, these two neuropeptides can have seemingly opposite effects, with oxytocin producing maternal care and positive social interactions while vasopressin produces aggression and anxiety. Although these neuropeptides may have different effects, on a cellular basis they both excite the brain regions with which they are associated. This circuit places the role of oxytocin and vasopressin in the realm of emotion, but exactly what type of emotion and what purpose does that serve?

**Neurobiological Purpose**

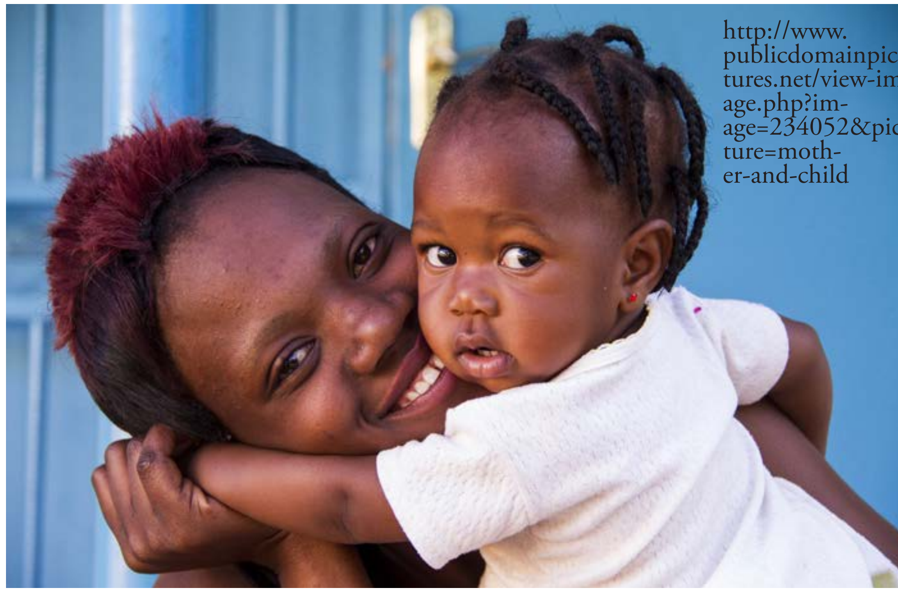
Through years of research, oxytocin and vasopressin have been found to be critical in pair bonding. The most obvious example of this is the bonding that occurs between a mother and her infant; during birth and breastfeeding there is an up-regulation of oxytocin receptors, thus an overall increase in sensitivity to the neuropeptide[3]. It has been found that while oxytocin is critical to the physiology of these processes, there is also a strong psychological component due to the upregulation of the receptors in the central amygdala and other brain regions. When women give birth, breastfeed, or even just hold their child, they receive a burst of oxytocin which bonds them to their infant.

The psychological side effects of this increase in sensitivity to oxytocin include an increase in maternal behavior, an increase in feeling close to someone, and a decrease in anxiety. A study found that when virgin rats were given an exogenous dose of oxytocin, they behaved maternally to pups that were not theirs and had no relation to them[6]. This is interesting because the rats did not go through any natural processes that elevate oxytocin levels (e.g., labor, milk production and let down), yet exogenous oxytocin was sufficient to induce maternal behavior including carrying the pups away from a dangerous stimulus. This same study looked at the effect exogenous vasopressin had on the maternal behavior of the virgin rats. Interestingly, the exogenous vasopressin did elicit maternal behavior towards the pups, but not as "complete" as the maternal behavior triggered by oxytocin[6].

Interestingly, these maternal bonds go both ways; the increase in oxytocin in females who give birth and who breastfeed is mirrored in their offspring. One study found that when young men were given an intranasal dose of oxytocin, they looked upon their childhood memories of their mother more fondly[7]. With exogenous oxytocin, these men were more likely to say that their mother was "exceptionally caring" than men without exogenous oxytocin. This was especially true for men that already felt close to their mothers; the oxytocin amplified the positive feelings that were already present[7]. This provides evidence that oxytocin is critical for the bonding between a mother and their child.

The ways in which oxytocin and vasopressin produce social bonds goes beyond the formation of mother-child relationships. Curiously, these neuropeptides facilitate the induction of many different human relationships. One study found that oxytocin increased participants' propensity to blindly trust others; for example, there was one participant that was more or less at the mercy of another participant[8]. Individuals who were given a nasal dose of oxytocin were much more likely to trust the person who held all the power in the situation. There was no discussion between the two participants and they were complete strangers, so there was no reason for one participant to trust the other, but with oxytocin the participant trusted against logic. Thus, oxytocin helps build friendships and professional relationships in addition to familial ties, critical for the formation of the communities humans rely on.

With respect to familial ties, we've previously only talked about mother-child bonds. However, oxytocin, and to some extent vasopressin, have also been shown to be important in the formation and strength of relationships between spouses. In a study where they administered small blister wounds to spouses, they measured levels of oxytocin, vasopressin, and the rate of wound healing in relation to the relationship between the spouses[9]. Amazingly it was found that spouses that reported feeling closer to one another and had very positive relationships had the highest levels of oxytocin and vasopressin as well as the fastest rate of wound healing[9]. This demonstrates how complex and widespread the effects of oxytocin and vasopressin are in the relationships that humans form as well as how these neuropeptides are involved in a human's stress response.'



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**Evolutionary Significance of these Social Bonds**

Let us return to the original question of why these neuropeptides are so important to humans. For the entirety of our existence, Homo sapiens have been very social creatures. The social nature of humans has evolved over time to increase the survival rates of humans.

Humans are known as "high K organisms" meaning that they only have a few offspring and they spend significant time and energy on these few offspring to ensure their success and survival. In humans, there is a long gestation period and a long period of dependence on the parents after birth. When humans are infants, they cannot even lift up their head without the help of a parent. This makes infants extremely vulnerable, why it has become so important for parents to be bonded with their children and to have an intrinsic desire to take care of their young.

During labor and then afterwards through breastfeeding, the infant and the mother spend a significant amount of time together, with the survival of the infant being completely dependent on how the mother cares for it. Additionally, it has been argued that humans are born prematurely so they can fit through the birth canal. This early birth makes human offspring especially vulnerable and the parental care of the offspring even more important. The chances of an offspring surviving to adulthood were much higher for humans if a parent was around to protect the offspring and teach it how to hunt, find shelter, etc. This dependence is one of the ways which oxytocin, and to some extent vasopressin, had the potential to evolve into a neuropeptide that has the power to form social bonds in addition to impacting physiological processes.

Beyond the mother-infant relationship, humans are incredibly social creatures. On a daily basis, neurotypical people work closely with others to complete projects, come up with new ideas, cook dinner, and raise families. Humans have consistently formed communities and chosen to gather and work together rather than be on their own for thousands of years. Many other mammals also form cohorts or packs as this increases survival rates; if there are many animals, there is a high probability that many will escape a predator. There is strength in numbers. So then why have humans done this to a much greater extent than other mammals? Why is simply having a large cohort not sufficient, why do humans have these intense, deep social bonds?

Humans first started to stand out from the rest of the mammals when they started forming communities with gendered roles, hunting and gathering. Theoretically, each human could hunt or gather food on its own. However, humans developed a complex system where they depended on one another; the women gathered fruits and vegetables while the men hunted meat. All of this food was critical for survival at the time. From this original setup developed towns, cities, and countries.

**Medical Uses of Oxytocin and Vasopressin**

Because oxytocin and vasopressin are so important to the development of social bonds, many have hypothesized that an exogenous dose of these neuropeptides may be useful to those who have disorders that affect one's social interactions with others. Autism spectrum disorder (ASD) has gained the most attention in the field. Many researchers have investigated whether additional oxytocin or vasopressin can help people with ASD be less anxious in social situations and if it can help these individuals better interpret and understand others' emotions.

One of the greatest struggles individuals with ASD face in social interactions is the deficiency or lack in ability to recognize the emotion of others' faces. This poses a problem because someone may look sad or angry, but a person with ASD, unable to recognize that emotion, could say or do something that may make the other person feel worse. Luckily, the intuitions that scientists have had regarding these neuropeptides has been supported by research. Many studies have shown that children, adolescents, and adults with ASD have much more success and ease with understanding how other people feel and what their facial expression means when they have an exogenous dose of oxytocin[10,11]. Unfortunately, although a great deal of literature has supported the potentiality of oxytocin as a treatment for social deficiencies in people with ASD, it has not become a widespread medication. This may be due to insufficient research, the extremely short half-life of the drug, or potential side effects not discussed in these studies.

Another mental illness that has received attention from this field is Generalized Anxiety Disorder (GAD), especially people with social phobia. In this disorder, the amygdala, the brain structure discussed earlier, is hyperactive. This hyperactivity makes people feel fearful or anxious when there is no real danger. Because oxytocin helps decrease anxiety and facilitate the formation and maintenance of social bonds, researchers expected individuals given oxytocin to have a less hyperactive amygdala. As hypothesized, researchers have found that individuals suffering from GAD have lowered amounts of amygdala hyperactivity, and thus less anxiety, when administered oxytocin[12]. This makes oxytocin an interesting target for further research on potential clinical applications for these neuropeptides.

Oxytocin and vasopressin are two neuropeptides with a myriad of physiological and psychological purposes. They regulate many biological processes in humans, including the process of relationship formation. The ways in which humans interact with one another and form friendships, fall in love, and connect with their children are the central interests of many academic fields, including neuroscience. Further, understanding of the ways in which humans bond could help us form humans bonds where they are most needed: in the face of hate, discrimination, and war. These are terrible and common parts of the human narrative that occur because people are divided, but if we understand the neurobiological basis of the interactions that bond us, we may be able to form bridges between groups currently in opposition of one another. What will we learn about these neuropeptides next?

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