# 6

# Effects of Oxytocin Injections

Oxytocin is with us throughout our lives. When you were born, oxytocin helped expel you from your mother's womb and then made it possible for her to nurse you. As a small child, you enjoyed your mother's and father's loving touch because it released oxytocin in your body. As an adult, you experience the effects of oxytocin when you enjoy good food, or a massage, or an intimate interlude with your romantic partner. Oxytocin is active in all these situations, and more.

Many of the effects of oxytocin described in this book have been demonstrated in research with animals. Researchers have observed not only changes in animals' behavior but also various measurable physiological changes in their bodies. Most of these effects have also been confirmed in humans, not as a result of experimental doses of oxytocin but by observation of changes that occur in connection with the natural release of the substance.

## *Less Fearful, More Sociable and Nurturing*

Oxytocin functions as a "turbo-booster" for several types of normal behavior in rats. Greater amounts of the substance cause the effects to be achieved more quickly.

Rats that receive low doses of oxytocin become less fearful and more curious. They are more likely to dare to leave the safety of the nest and explore unfamiliar surroundings. Oxytocin has a clear antianxiety effect.

When given oxytocin, groups of rats of the same sex become more gregarious and less afraid of contact. As aggression in the group decreases noticeably, friendly socializing replaces it. Rather than avoid each other, the rats prefer to sit near each other. This closeness leads in its turn to the release of still more oxytocin. (Later we will see how touch and bodily contact play a big role in the release of oxytocin.)

It is interesting that vasopressin, oxytocin's "sister" substance, which differs by only two amino acids, also makes rats unafraid, but in an entirely different manner. Vasopressin instills courage by making the individual feel aggressive and fearless. The rat, male or female, is prepared to attack, mark territory, and vigorously defend itself. Oxytocin instead fosters courage by diminishing the feeling of danger and conveying the sense that there is less to be afraid of. Animal studies appear to show that oxytocin has a special ability to make animals "nice." Physiologically, therefore, a substance related to strength and readiness (vasopressin) is a close relative to one that produces friendliness



and caring (oxytocin). They function in different ways, and we need them both. As the popular Swedish fictional character Pippi Longstocking says, "The one who is powerfully strong must also be powerfully nice."

Sexual behavior is also stimulated by oxytocin. Oxytocin injections have been shown to accelerate mating, perhaps by reducing fear. Mating in turn leads to the release of oxytocin in both females and males. This release is believed to play a role in, among other things, the transport of the egg and sperm. (Oxytocin and human sexuality are discussed in Chapter 11.)

A striking example of behavior influenced by oxytocin is the interaction between a mother and her young. Rats are timid animals, and normally a female rat is afraid of strangers, including young rats not her own. But when female rats are treated in advance with the female sex hormone estrogen and then given an injection of oxytocin, they begin to exhibit maternal behavior even if they have not produced offspring. In rat terms, this means that they build a nest, carry to it any young in the vicinity, lick and clean them, and defend them against strange rats. Even though these females have no milk, they lie down as though preparing to nurse.

When females actually do have babies, the release of oxytocin is stimulated in the mother during birth and suckling. As we have seen, oxytocin stimulates the uterus to contract and expel the newborn, and it causes the muscles surrounding the milk ducts to contract and expel breast milk. (More about nursing in Chapter 8.) Nursing rats have been observed to lose their natural fear and to keep right on about their maternal business even in the presence of noise and intense light.

### Enhanced Social Memory

Memory and learning are complicated processes that involve many different parts of the brain. When someone makes an indelible impression on us, it may be because we are afraid of that person, but we also may have positive reactions to that person because we met him or her under the influence of oxytocin's nectar, at a time when we felt really good and open to our surroundings.

Oxytocin is thought to have a positive effect on what we call social memory, which, like fear and sociability, is processed to a large extent in the amygdala (discussed in Chapter 4). One example is the ability to recognize someone we have met before, something that animals obviously can also learn. This recognition is speeded up in animals treated with oxytocin. Oxytocin can also hasten the development of "acquaintanceship" in animals, so that they prefer certain individuals over others. A special variant of this ability to recognize acquaintances is bonding or attachment, which happens when, for example, a mother learns to recognize and prefer her own young over others. The mother and her offspring may come to know and bond with each other more quickly because the level of oxytocin is so high in connection with birthing.



In one experiment, the oxytocin effect led a female vole to prefer a particular male of her species. If she was given an injection of oxytocin when she had a certain male in front of her, she not only recognized that animal from then on but also chose him in preference to others. Oxytocin is physiology's "forget-me-not" that makes recognition and bonding reverberate in the nerves' pathways. We see this in humans as well. We can also become unforgettable for each other if oxytocin is released when we come together. Someone we have been very close to, in a love relationship, for example, will always be special to us.

### Increased Calm and Less Pain

We have seen that small amounts of oxytocin reduce anxiety and increase curiosity, but larger amounts produce an entirely different effect. A cow will stand still, look drowsy, and sometimes start to ruminate. Rats become calmer, move around less, and may even draw aside to rest or sleep. These effects—in particular reduced curiosity—become more apparent after several oxytocin injections, and they persist long after the last dose has been given.

Another effect in oxytocin's wide sphere of influence is its ability to alleviate pain. Oxytocin sends signals along nerve fibers from their site of origin in the hypothalamus to several areas in the nervous system that relate to the sensation of pain. After oxytocin injections, a rat takes longer to pull its paw away from a hot surface or to flick its tail out of water that is too hot. This behavior can be interpreted as evidence of oxytocin's ability to reduce the sensation of pain. It is probably not that the pain impulse from the paw is registered as weaker, but instead that the reaction to the message of pain diminishes.

Just as the antianxiety effect becomes stronger and longer-lasting after repeated injections, the threshold for reaction to pain increases after multiple oxytocin treatments. The rats' reaction to the heat stimuli described above can remain diminished even a week after the last oxytocin injection.

## Improved Learning Ability

Have you ever tried to learn something new or understand something complicated when you are under stress and pressed for time? Anyone who has been in that situation has known frustration. Your concentration works better if you have had a chance to calm down, either by being left in peace for a while or by having enough time for what you are doing. Since oxytocin reduces stress, it can improve opportunities for learning.

Oxytocin has had an undeservedly bad reputation with regard to memory. For example, some people have claimed that women forget the pangs of childbirth because their oxytocin level is so high at that time. In some animal studies, oxytocin injections have led to worse memory. In tests of rat learning, such as navigating a maze, oxytocin has had a short-term negative effect on memory functions. Vasopressin has had the opposite effect, facilitating learning. It is possible that this effect is caused by the vasopressin, which makes the animals more alert, and that this increased wakefulness lies behind the improvement in memory.



I've observed, however, that the effect of oxytocin is most often precisely the opposite; it improves learning ability, especially if injections of the substance are repeated several times. By chance, my colleagues and I discovered that a special type of laboratory rat has a difficult time learning to avoid an unpleasant situation, for example, a weak electric shock. Ordinary rats learned very quickly to avoid this negative stimulus. But after five oxytocin injections, the animals that at first had difficulty learning became as clever as the normal rats at avoiding the shock. Even several days after the end of the oxytocin injections, the usually "dumb" rats retained their improved memory. This effect appears to have little direct connection with the rats' intelligence or memory functions, but is a result of the calming effect of oxytocin described above.

We all know it's difficult to learn something if one is extremely drowsy. But it is equally difficult if we try to learn something new while anxious and stressed. It's best to be just alert and just relaxed enough. When a friend advises you to calm down and take it easy when everything is piling up around you, difficult as that may seem, it is good advice for several reasons. When you achieve a better balance internally between stress hormones and calm and connection hormones, you will not only feel better but also probably comprehend the situation better and find more adaptive solutions.

In fact, the rats that were considered "dumb" but later showed improvements in learning after oxytocin treatment were also (before the oxytocin injections) easier to disturb and had higher levels of the stress hormone cortisol than rats with ordinary learning abilities; after the injections, however, the symptoms of stress in the "dumb" rats normalized. This is a provocative finding, since we can observe that people who are stressed and depressed also generally have difficulties with learning.

The long-term effects of oxytocin cannot depend on the direct influence of the substance, since it disappears very quickly from the blood. The reason why the effects can last for many days after the last injection probably has to do with oxytocin's ability to influence the operation of other signaling substances in a long-lasting way. (More about that in the next chapter.)

### *Effects on Blood Pressure*

Just as we can measure indications of oxytocin's mildly activating and calming effects on behavior, we can also observe other ways that it produces activity and relaxation. Oxytocin can, for example, raise and lower the pulse rate and blood pressure. Which effect is produced depends on the situation, the animal's hormone levels, and the type of animal used in the research.



### EFFECTS OF OXYTOCIN INJECTIONS ON BEHAVIOR

The following changes in behavior have been observed in animals (especially rats) after oxytocin injections:

- a rapid development of maternal behavior (even in females who have never had babies);
- stimulated and facilitated mating;
- more social contact between individuals;
- less anxiety, increased boldness and curiosity (with low doses of oxytocin);
- a calming, even sleep-inducing effect (with high doses of oxytocin);
- a diminished sensation of pain (more powerful and long-lasting alleviation with repeated injections); and
- facilitated learning, even in individuals with learning difficulties.

In apes and humans, oxytocin appears to lower only pulse and blood pressure. The effects are produced by influencing the sympathetic and parasympathetic nerves, either directly or through connections higher up in the brain. As we saw, the paraventricular cell group in the hypothalamus is one of the locations in the brain where oxytocin is produced. When this part of the brain was electrically stimulated, the animals' blood pressure went down. This effect probably occurs because the electrical current causes the release of oxytocin into the areas of the brain where blood pressure is controlled.

Oxytocin's effect is gradual. When single injections are given, pulse rate and blood pressure increase temporarily, then sink slowly to a level lower than they were before the injection. If we administer oxytocin several times, blood pressure is significantly lowered, an effect that lasts longer than the result produced by a single injection.

Even though oxytocin is not solely a female hormone, its effects in females are more pronounced. If oxytocin is given to female animals five days in a row, the lowered blood pressure lasts for three weeks. In male animals, the effect on blood pressure is the same, but lasts only half as long. The reason for this difference is the female sex hormone estrogen, which, as we saw, reinforces the influence of oxytocin and produces the longer-lasting effect in females. Female rats without ovaries, like males, lack this reinforcement, and accordingly the lowered blood pressure does not last as long with them. However, in both these females and the males, the effect lasts for three weeks if they receive twice as many injections. Females without ovaries and males must therefore have twice the amount of oxytocin to achieve the same effect produced in females with normal estrogen levels.

### Balancing Body Temperature

Each individual, human or nonhuman, must be able to control body temperature. In humans, this is done through sweating and shivering. In rats, the tail is the most important way to regulate temperature. A red tail means that the blood vessels are dilated, and energy in the form of body heat is escaping. But when the blood vessels in the tail contract, less heat escapes and the rat conserves energy.



Oxytocin can influence body temperature in part by lowering the temperature of the tail in rats and allowing the rat to conserve energy. The heat is redistributed so that the tail becomes cold, but other parts of the body become warmer. Other research supports this view of oxytocin as a sort of thermostat that does not keep the temperature constant but instead shifts the warmth from one part of the body to another.

In a suckling mother rat, the blood vessels on the frontal side are dilated by oxytocin. This means that the female can warm her small offspring while they nurse. The same phenomenon appears also in nursing women, as well as with fathers who are holding their babies. These blood vessels also dilate in both men and women during sexual activity. In all these situations we see warm chests and rosy cheeks. Oxytocin is the reason.

### Regulating Digestion

Oxytocin plays yet another important role in the process of converting food and drink in the body. An interesting aspect of oxytocin's role in digestion is that it differs according to whether an animal is full or hungry. A sort of intelligence applies to oxytocin's way of working, because its effects vary to promote the optimal outcome in each situation.

Animals receiving oxytocin lose their appetites for several hours. But over a longer period, oxytocin injections produce increased appetite, especially in females and in connection with nursing. Over time, the digestive process works more effectively, in part because oxytocin stimulates the secretion of gastric juices and the release of digestive hormones such as gastrin, cholecystokinin, somatostatin, and insulin. The last three also help promote the storage of nourishment in the body.

Oxytocin can cause two entirely different response patterns, depending on the situation. Animals with food in their stomachs react with increased digestive activity and storage of nutrition. But if they are hungry—their stomachs empty—they have a reaction that inhibits the digestive process. Oxytocin produces both these effects by influencing the activity in the part of the parasympathetic nervous system (the vagus nerve) that controls the functioning of the intestines. (Chapter 14 will show other examples of nature's ingenious method for optimal adaptation to each situation.)

### *Regulating Fluid Levels*

Another balancing act accomplished by oxytocin is its effect on fluid levels in the body. Oxytocin works with its partner hormone, vasopressin, to maintain the body's fluid balance by either expelling water, especially in the form of urine, or promoting the storage of bodily fluids. Oxytocin and vasopressin have entirely opposite effects on fluid levels.



Oxytocin, not surprisingly, is responsible for the first function. It stimulates the extraction of sodium by the kidneys and promotes urination. Animals receiving oxytocin become less enthusiastic about eating salt; the result is a lowering of the body's sodium content and a reduction in the retention of water.

As for conserving bodily fluids, an increase in the stress hormones vasopressin and corticotropin releasing factor (CRF) produces an increased desire for salt. Vasopressin leads also to decreased urine production and the retention of salt and fluid. At the same time, it contracts the blood vessels, producing higher blood pressure. We need to conserve fluids if our situation appears dangerous and we are at risk of wounds that would cause the loss of blood and other body fluids. Vasopressin and CRF accomplish this.

### *Growth and Healing of Wounds*

Oxytocin stimulates growth, not only by promoting the development of the animal as a whole but also by accelerating the healing of wounds. Oxytocin injections make sores on a rat's back heal more quickly than they would otherwise. They also heal and rejuvenate mucous membranes, and produce anti-inflammatory reactions.

### *Effects on Other Hormones*

As we saw, both oxytocin and vasopressin are produced in the hypothalamus and transported to the pituitary gland's

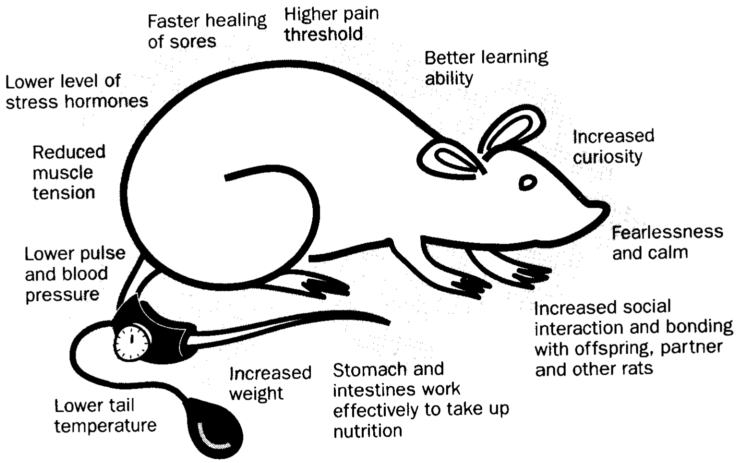


FIGURE 6.1 Effects of oxytocin injections in rats.

dorsal lobe, from which they are released into the bloodstream. The pituitary's frontal lobe secretes several other hormones, but these are regulated in a manner different from that of the dorsal lobe hormones. Special control substances created in the hypothalamus are conducted through a localized circulation system to the pituitary's frontal lobe, where they cause the release of the other hormones into the bloodstream.

Certain nerves release oxytocin into the blood vessels that connect with the pituitary's frontal lobe. In this way, oxytocin stimulates the pituitary's release of, for example, prolactin, growth hormone (GH), and adrenocorticotropic hormone (ACTH). The increased levels of these hormones produce various effects. Prolactin, for example, stimulates the production of milk in suckling females and nursing



## PHYSIOLOGICAL EFFECTS OF OXYTOCIN INJECTIONS

1. Short-term activating effect in the form of higher blood pressure, pulse, and levels of stress hormones (with single injection)
2. Lower blood pressure, pulse, and levels of stress hormones (with repeated injections) over a longer period
3. Longer-lasting effects in females with estrogen
4. Raised body temperature in rats (and other animals, including humans), especially on the frontal side, but lower temperature in the tail
5. Reduced muscle tension
6. Temporarily reduced appetite; but with repeated injections, increased appetite over the longer term
7. Stimulated digestion when the stomach is full, inhibited when empty
8. Increased urination, in part by causing the body to excrete more salt and in part by reducing the desire for salt, which causes the body to retain less water
9. Faster-healing wounds, reduced inflammation

mothers. Growth hormone stimulates the body's growth, and ACTH directs the production of the stress hormone cortisol by the adrenal gland.

The effect of oxytocin on ACTH and corticosterone is, however, much more complicated. As we saw with respect to blood pressure, oxytocin can initially give rise to a short-term increase in ACTH and thereby in the level of corticosterone, at least in rats. But as before, this stimulating effect of oxytocin is short-lived. After a brief time, this increase switches over to its opposite, and the level drops. With repeated treatments, a long-term lowering of corticosterone is achieved. This effect occurs because the entire control system is influenced. Production of the control substance ACTH in the hypothalamus drops, as does the production of corticosterone in the adrenal gland. As a result, the regulating system that attempts to keep the level constant becomes less sensitive. Low cortisol levels, in turn, contribute to a state of calm, quiet, and well-being. The body's innate system of checks and balances is complex; oxytocin is constantly present and working in many different ways. The effects of this coordinated system are connected like the threads in a marvelous web.