Oxytocin (Greek, “quick birth”) is a mammalian hormone that also acts as a neurotransmitter in the brain.

In humans, oxytocin is thought to be released during hugging, touching, and orgasm in both sexes. In the brain, oxytocin is involved in social recognition and bonding, and may be involved in the formation of trust between people and generosity. [1][2][3]

In women, it is released in large amounts after distension of the cervix and vagina during labor, and after stimulation of the nipples, facilitating birth and breastfeeding, respectively. Synthetic oxytocin is sold as medication under the trade names Pitocin and Syntocinon as well as generic oxytocin.

Actions of oxytocin within the brain

Oxytocin secreted from the pituitary gland cannot re-enter the brain because of the blood-brain barrier. Instead, the behavioral effects of oxytocin are thought to reflect release from centrally projecting oxytocin neurons, different from those that project to the pituitary gland. Oxytocin receptors are expressed by neurons in many parts of the brain and spinal cord, including the amygdala, ventromedial hypothalamus, septum and brainstem.

- Sexual arousal. Oxytocin injected into the cerebrospinal fluid causes spontaneous erections in rats,[12] reflecting actions in the hypothalamus and spinal cord.
- Bonding. In the Prairie Vole, oxytocin released into the brain of the female during sexual activity is important for forming a monogamous pair bond with her sexual partner. Vasopressin appears to have a similar effect in males.[13] In people, plasma concentrations of oxytocin have been reported to be higher amongst people who claim to be falling in love.[citation needed] Oxytocin has a role in social behaviors in many species, and so it seems likely that it has similar roles in humans.
- Autism. A 1998 study found significantly lower levels of oxytocin in blood plasma of autistic children.[14] A 2003 study found a decrease in autism spectrum repetitive behaviors when oxytocin was administered intravenously.[15] A 2007 study reported that oxytocin helped autistic adults retain the ability to evaluate the emotional significance of speech intonation.[16]
- Maternal behavior. Sheep and rat females given oxytocin antagonists after giving birth do not exhibit typical maternal behavior. By contrast, virgin female sheep show maternal behavior towards foreign lambs upon cerebrospinal fluid infusion of oxytocin, which they would not do otherwise. [17]
- Increasing trust and reducing fear. In a risky investment game, experimental subjects given nasally administered oxytocin displayed “the highest level of trust” twice as often as the control group. Subjects who were told that they were interacting with a computer showed no such reaction, leading to the conclusion that oxytocin was not merely affecting risk-aversion.[18] Nasally administered oxytocin has also been reported to reduce fear, possibly by inhibiting the amygdala (which is
thought to be responsible for fear responses). There is no conclusive evidence for access of oxytocin to the brain through intranasal administration, however.

- Affecting generosity by increasing empathy during perspective taking. In a neuroeconomics experiment, intranasal oxytocin increased generosity in the Ultimatum Game by 80% but has no effect in the Dictator Game that measures altruism. Perspective-taking is not required in the Dictator Game, but the researchers in this experimental explicitly induced perspective-taking in the Ultimatum Game by not identifying to participants which role they would be in.

- According to some studies in animals, oxytocin inhibits the development of tolerance to various addictive drugs (opiates, cocaine, alcohol) and reduces withdrawal symptoms.

- Preparing fetal neurons for delivery. Crossing the placenta, maternal oxytocin reaches the fetal brain and induces a switch in the action of neurotransmitter GABA from excitatory to inhibitory on fetal cortical neurons. This silences the fetal brain for the period of delivery and reduces its vulnerability to hypoxic damage.

- Certain learning and memory functions are impaired by centrally administered oxytocin. Also, systemic oxytocin administration can impair memory retrieval in certain aversive memory tasks.

- MDMA (ecstasy) may increase feelings of love, empathy and connection to others by stimulating oxytocin activity via activation of serotonin 5-HT1A receptors, if initial studies in animals apply to humans.

Peripheral (hormonal) actions of oxytocin

The actions of oxytocin are mediated by specific, high affinity oxytocin receptors. The peripheral actions of oxytocin mainly reflect secretion from the pituitary gland.

- Letdown reflex – in lactating (breastfeeding) mothers, oxytocin acts at the mammary glands, causing milk to be ‘let down’ into a collecting chamber, from where it can be extracted by compressing the areola and sucking at the nipple. Sucking by the infant at the nipple is relayed by spinal nerves to the hypothalamus. The stimulation causes neurons that make oxytocin to fire action potentials in intermittent bursts; these bursts result in the secretion of pulses of oxytocin from the neurosecretory nerve terminals of the pituitary gland.

- Uterine contraction – important for cervical dilation before birth and causes contractions during the second and third stages of labor. Oxytocin release during breastfeeding causes mild but often painful uterine contractions during the first few weeks of lactation. This also serves to assist the uterus in clotting the placental attachment point postpartum. However, in knockout mice lacking the oxytocin receptor, reproductive behavior and parturition is normal.

- The relationship between oxytocin and human sexual response is unclear. At least two non-controlled studies have found increases in plasma oxytocin at orgasm – in both men and women. The authors of one of these studies speculated that oxytocin’s effects on muscle contractibility may facilitate sperm and egg transport. Murphy et al. (1987), studying men, found that oxytocin levels were raised throughout sexual arousal and there was no acute increase at orgasm. A more recent study of men found an increase in plasma oxytocin immediately after orgasm, but only in a portion of their sample that did not reach statistical significance. The authors noted that these changes “may simply reflect contractile properties on reproductive tissue.”

- Due to its similarity to vasopressin, it can reduce the excretion of urine slightly. More important, in several species, oxytocin can stimulate sodium excretion from the
kidneys (natriuresis), and in humans, high doses of oxytocin can result in hyponatremia.

- Oxytocin and oxytocin receptors are also found in the heart in some rodents, and the hormone may play a role in the embryonal development of the heart by promoting cardiomyocyte differentiation. [9][10] However, the absence of either oxytocin or its receptor in knockout mice has not been reported to produce cardiac insufficiencies.[4]

- Modulation of hypothalamic-pituitary-adrenal axis activity. Oxytocin, under certain circumstances, indirectly inhibits release of adrenocorticotropic hormone and cortisol and, in those situations, may be considered an antagonist of vasopressin. [11]

Drug forms of oxytocin

Synthetic oxytocin is sold as medication under the trade names Pitocin and Syntocinon and also as generic oxytocin. Oxytocin is destroyed in the gastrointestinal tract, and therefore must be administered by injection or as nasal spray. Oxytocin has a half-life of typically about three minutes in the blood. Oxytocin given intravenously does not enter the brain in significant quantities - it is excluded from the brain by the blood-brain barrier. There is no evidence for significant CNS entry of oxytocin by nasal spray. Oxytocin nasal sprays have been used to stimulate breastfeeding but the efficacy of this approach is doubtful[25].

Injected oxytocin analogues are used to induce labor and support labor in case of non-progression of parturition. It has largely replaced ergotamine as the principal agent to increase uterine tone in acute postpartum haemorrhage. Oxytocin is also used in veterinary medicine to facilitate birth and to increase milk production. The tocolytic agent atosiban (Tractocile) acts as an antagonist of oxytocin receptors; this drug is registered in many countries to suppress premature labour between 24 and 33 weeks of gestation. It has fewer side-effects than drugs previously used for this purpose (ritodrine, salbutamol and terbutaline).

Some have suggested that the trust-inducing property of oxytocin might help those who suffer from social anxieties, while others have noted the potential for abuse with confidence tricks. [26]

Synthesis, storage and release of oxytocin

Oxytocin is made in magnocellular neurosecretory cells in the supraoptic nucleus and paraventricular nucleus of the hypothalamus and is released into the blood from the posterior lobe of the pituitary gland. Oxytocin is also made by some neurons in the paraventricular nucleus that project to other parts of the brain and to the spinal cord.

In the pituitary gland, oxytocin is packaged in large, dense-core vesicles, where it is bound to neurophysin I as shown in the inset of the figure; neurophysin is a large peptide fragment of the larger precursor protein molecule from which oxytocin is derived by enzymatic cleavage.

Secretion of oxytocin from the neurosecretory nerve endings is regulated by the electrical activity of the oxytocin cells in the hypothalamus. These cells generate action potentials that propagate down axons to the nerve endings in the pituitary; the endings contain large numbers of oxytocin-containing vesicles, which are released by exocytosis when the nerve terminals are depolarised.
Oxytocin is also synthesized by corpora lutea of several species, including ruminants and primates. Along with estrogen, it is involved in inducing the endometrial synthesis of Prostaglandin-F2alpha to cause regression of the corpus luteum.

Oxytocin and vasopressin are the only known hormones released by the human posterior pituitary gland to act at a distance. However, oxytocin neurons make other peptides, including corticotropin-releasing hormone (CRH) and dynorphin, for example, that act locally. The magnocellular neurons that make oxytocin are adjacent to magnocellular neurons that make vasopressin, and are similar in many respects.

References

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