

Oxytocin, Vasopressin and Sexual Activity

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Hypothalamus is a part of our brain which has lots of different functions, located below the thalamus and above the pituitary gland. One of the most important functions is connecting the nervous system to the endocrine system via the pituitary gland. There are two important neurotransmitter hormones that are produced by the hypothalamus and stored in the posterior pituitary gland until their release into the bloodstream. They are called Oxytocin (OXT) and arginine vasopressin (AVP) or antidiuretic hormone (ADH).^[1-3]

Oxytocin and AVP express magnocellular neurons in the hypothalamic-neurohypophysial system (HNS) and these hormones have been the most studied of all the neuroendocrine cell types. Phenotypes of OXT and AVP in the magnocellular neuronal population have conventionally been assessed by either immunocytochemical or in situ hybridization histochemical methods because of the view that these genes are never co-expressed. In addition, more sensitive methods show that most OXT cells also express some AVP mRNA (messenger RNA), and most AVP cells contain some OXT mRNA.^[4] It is suggested that AVP and OXT evolved from a single primordial neurohypophysial hormone, which is called arginine vasotocin

ABSTRACT

Hormones regulate our body's functions, emotions, or behaviors. Two of these regulators are Oxytocin (OXT) and arginine vasopressin (AVP) or antidiuretic hormone (ADH). They are produced by the hypothalamus and stored by the pituitary gland. It is known like OXT is a feminine hormone, but it has lots of effects on males, too. It has roles in psychology and behaviors including sexual and social behavior, sexual activity or arousal, paternal and maternal feelings, or reproductive system. Due to some of these effects, it's known as the 'love hormone'. On the other hand, AVP has roles on kidneys or retaining osmolality but beyond them, on social choices, fidelity, pair bonds, and aggression. Furthermore, there is an interaction between them, and they generally control each other's functions. Their secretion amount changes during lots of situations such as hugging, kissing, or sexual activity. These changes may lead us to decide, love, or hate. In this article, the conception of social and sexual behavior, the impacts of OXT and AVP on emotions and behaviors, the relationship between OXT and AVP, the conception of sexual activity, and changes in OXT and AVP secretion during sexual activity were discussed.

Keywords: Behavior, oxytocin, sexual activity, vasopressin.

(AVT). OXT is known as the 'hormone of love' because of its effects on psychology, emotions, and maternal behaviors.^[1,5] Furthermore, OXT has a lot of functions in males and females. It regulates sexual behaviors and is stimulated for secretion as a result of sexual activity or orgasm. In females, it helps contractions of the womb during labor by stimulating the uterine muscles to contract, so labor begins.^[6] It also increases the production of prostaglandins, which causes more contractions. Because of this impact, synthetic oxytocin is used to start labor if women can not do it naturally or the women's labor is getting slower. Also, it provides milk from the milk ducts to the nipple during breastfeeding. If the baby stops feeding, OXT production stops until the next feeding. In males, it has a role in male fertility. It affects the production

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of testosterone in the testes. It makes men sexually attracted to women.^[5,7,8]

In humans, it has been also shown to increase trust and generosity, strengthen emotional and cognitive empathy, and reduce social anxiety and fear-related behavior.^[9,10] The therapeutic effects of the oxytocin hormone have been studied in a variety of pathological conditions, both in vitro and in vivo. According to the results of a study, Erbaş et al. claimed that after acute hypercapnic-anoxia exposure, chronic OXT treatment has a long-lasting therapeutic potential on rats, by reducing the gloss with its anti-inflammatory feature and by activating the γ -aminobutyric acid (GABA) pathway.^[11,12]

The main function of the AVP is to regulate procedures in the kidneys, this hormone also has an effect on the cardiovascular system and the central nervous system. It has a role in retaining osmolality and the volume of water in the out-of-cell fluid. The release of this hormone occurs in response to hypertonic in bodily fluids. Furthermore, this allows the kidneys to reabsorb water and return it to the blood from nephron tubules, normalizing the tonicity of bodily fluids.^[7,10] It is suggested that both AVP and OXT have effects on the psychology of animals such as rats and birds but recently several experiments show us that these hormones have serious effects on our psychology and behaviors, too.^[13,14]

Beyond these effects of OXT and AVP, there are many other molecules such as dopamine, serotonin, GABA, and opioids that interact with these two peptides to influence behavior, and other functions. OXT, AVP, and their receptors are epigenetically regulated, genetically changeable, and sensitive to stressors and diet across the lifespan. Sex differences in OXT and AVP are common, and some steroids such as estrogens, androgens, and glucocorticoids play a major role in the regulation of the actions of OXT and the availability of receptors for oxytocin across the lifecycle.^[15,16]

This review first introduces the concept of social and sexual behavior, impacts of OXT and AVP on emotions and behaviors, the relationship between OXT and AVP, the conception of sexual activity, and finally focuses on changes in OXT and AVP secretion during sexual activity.

THE CONCEPTION OF SOCIAL AND SEXUAL BEHAVIOR

Sexual behavior is a process by which humans and other animals demonstrate and/or express

sexuality.^[17] Women's and men's brain structures and chemical pathways that control their sexuality are different, but human sexual behavior is one of the parts of interpersonal relationships and is cognitively mediated despite the differences. These behaviors change according to genders and species.^[18] Social behavior is a kind of behavior between two or more organisms in the same species and involves any behaviors in which a member affects the other one.^[19] Some factors affect social behaviors such as gender, abilities, race, and culture also, metabolism of humans', and hormones.^[20]

Sexuality is expressed through means learned by socialization therefore, social context has effects on sexual behavior. Socialization is the lifelong process of inheriting and spreading traditions and ideologies and ensuring an individual with the skills and habits necessary for attending within one's society. For these reasons, social behaviors that are affected by socialization ensure communication about sexuality. Eventually, it can be said that there is a relationship between social and sexual behavior. They affect each other in our lives.^[21]

EMOTIONS AND BEHAVIOR; EFFECTS OF OXYTOCIN AND ARGININE VASOPRESSIN IN HUMANS

It's suggested that oxytocin has lots of impacts on our emotions and behavior. There are some common impacts of OXT on females and males, such as facilitating bonding with children, enhancing romantic attachment, or playing a role in the reproductive system. Also, there are some different impacts. In males, OXT improves the ability to define competitive relationships and navigate their fight or flight response. Females generally lack this response. Instead, oxytocin tends to increase feelings of kinship. These differences are due to the fact that OXT behaves differently in the amygdala of both sexes, which are part of the brain and are responsible for emotions and behavior.^[22]

According to a study by Karen Parker and her friends, oxytocin treatment enhances social abilities in children with autism spectrum disorder (ASD). They tested the efficacy and tolerability of four-week intranasal OXT treatment (24 International Units, twice daily) in thirty-two children with ASD aged between six and twelve using a double-blind, randomized, placebo-controlled, parallel design. The individuals with the lowest pretreatment

OXT concentrations showed the greatest social improvement, but they did not see a decrease in repetitive behaviors, or anxiety. Eventually, as with many trials, some placebo-treated participants showed improvement on the social responsiveness scale (SRS).^[23]

IMPACTS OF OXYTOCIN ON FEMALES

Women generally have higher oxytocin levels than men.^[24] Oxytocin has an impact on females' behaviors and emotions. It's known that OXT has a big role in labor and lactation. It ensures that the baby and mother bond with each other. Pregnant women have a high level of OXT, and they are bonded to their children during their first trimester. During their pregnancy and in the first month after birth, they engage in more behaviors such as singing, feeding, and bathing their infants in a specific way than the other women.^[25]

Researchers compared the rates of oxytocin and its associated AVP hormone in the urine of biological children and adopted children. When children communicate with their biological mothers, they look for a rate of oxytocin, while the rate of oxytocin remains constant in adopted children. The fact that adopted children have confidence problems is also due to the deficiency of this hormone.^[25]

An increase in the level of endogenous oxytocin causes an increase in plasma endorphins, natural painkillers that can reduce pain in women who experience dyspareunia due to insecurity or anxiety to their spouses in the early stages of their relationship [26]. Despite these, research has suggested that endogenous oxytocin may not be high before the oncoming of sexual activity and may not be the main trigger for sex drive and desire preceding the initiation of sexual activity. Accordingly, the level of endogenous oxytocin increases after the woman receives proper stimulation and begins to enjoy sexual activity.^[27] This claim is supported by data from self-declaration studies showing that some women may enjoy sexual activity and reach orgasm when sexual arousal and intercourse occur,^[28] but even if they are not initiators of sexual activity.^[29,30]

Another study revealed the positive emotional responses of some girls who suffered from anorexia were given oxytocin via spray. After treatment, these girls would have shown a more positive attitude towards food and improvement in the expression characteristics of the face through the modification

of emotional processes such as fear, anger, and anxiety.^[31]

Considering low endogenous oxytocin levels and different mechanisms of action of intranasal and intravenous synthetic oxytocin in women experiencing sexual problems, researchers tried to solve women's sexual problems using synthetic oxytocin intranasal spray, which is expected to give lower doses of synthetic oxytocin to the body compared to intravenous synthetic oxytocin administered during childbirth. A case report by Anderson-Hunt and Dennerstein^[32] showed plenty of vaginal transudates followed by intense sexual desire two hours after the use of intranasal synthetic oxytocin spray to facilitate breastfeeding. However, the findings of their report may not be usually general to the entire population, as they only studied one woman over a short period.^[29-33] Another study showed that intranasal implementation of synthetic oxytocin improves attachment-related behaviors such as eye gazing,^[30-34] interpersonal trust, compassion, and positive communication.^[35]

IMPACTS OF OXYTOCIN ON MALES

Oxytocin is often thought of as a female hormone because it has multiple effects and roles on females. Despite this, OXT has endocrine and paracrine roles in male reproduction. Furthermore, it has some impacts on males' psychology.^[36]

In ejaculation, an oxytocin burst from neurohypophysis to the systemic circulation is released and stimulates the contractions of the breeding path, which helps release sperm. There is definitive evidence that OXT is synthesized in mammalian testis, epididymis, and prostate, and the presence of OXT receptors (OXTRs) through the reproductive system supports a local action for this peptide. OXT has a paracrine role in stimulating the contraction of seminiferous tubules, epididymis, and prostate gland.^[36]

It's suggested that oxytocin has roles in social behaviors and bonding. An experiment was conducted with 110 participants. These participants intranasally self-administered OXT or placebo after this, they rated medium attractive peoples' pictures according to their romantic and sexual interests. 2 types of results were revealed. First, a dating strategy among males was less selective than females including romantic and sexual dating. Second, this unselective strategy was more obvious in inexperienced males, but it was restored to the

level of experienced males by OXT. Behaviors during social interactions are regulated by OXT to help every person adapt to social environments.^[37]

In males, a comparable physiological stimulation is a sexual activity that is possible to trigger a high level of activity of the endogenous brain oxytocin system. During warm social contact with someone or a partner such as hugging, and orgasm an increment of plasma OXT levels was found.^[38]

It is suggested that oxytocin makes the lover attractive to men. Within the extent of research, men were shown photographs of the people they fell in love with, and then volunteers were given the hormone "oxytocin" by nasal spray. After the hormone administration, the same photos were shown again, and they were asked how attractive they found their lovers. Brain MRIs of the participating men were taken to monitor the change. The men who participated in the study voluntarily were shown photographs of women who they did not know or had known for a long time. At the end of the study, brain MRIs determined that men found their partners much more attractive than other women after being given oxytocin. It was argued that the oxytocin hormone acts only on partners and does not cause attraction in friends other than strangers or lovers. German researchers suggest that OXT has a role on achieve monogamy.^[39]

A study conducted in November in the journal *Proceedings of the National Academy of Sciences (PNAS)* supported the theory that oxytocin would strengthen men's early memories of their mothers. In a group of 31 men, those who inhaled a synthetic version of the hormone found that the hormone intensified their mother's loving memories if their relationship was positive. The study showed that those who frayed ties with their mothers reduced their opinions after inhaling oxytocin.^[40]

IMPACTS OF ARGININE VASOPRESSIN

It is known that arginine vasopressin has roles in retaining osmolality and organizing procedures in the kidneys. Beyond these roles, it has also some effects on human psychology and behavior. Furthermore, it has a relationship with OXT when they regulate our body's functions.

According to a recent study, the pain-relieving placebo effect of AVP is particularly perceived by women. Placebos help measure clinical responses or results when analyzing the effects of therapies, medications, or treatments. In the study, an increasing

electrical stimulus was given to participants' hands until reaching shock which was painful but tolerable. Four placebo-based treatments such as AVP, OXT, saline, or no treatment were received to participants randomly. The participants did not know which treatment they received because they were in a double-blind, crossover study but they were told that treatment would eliminate or lessen the pain of shocks. The study demonstrated that the magnitude effects of placebo were affected by a single intranasal administration of AVP. According to the results, AVP increases placebo analgesic effects in women but it does not have an effect in increasing in men.^[41]

It is delineated that the impact of intranasal AVP on hazardous cooperative behavior, placebo-controlled design with using Stag hunt game which is an experimental paradigm that is generally used to study mutually beneficial risky cooperation. According to the findings, AVP's effects on cooperation are specific to the social context of the stag hunt game and are steady with the concept that AVP increases the expected reward of cooperation, rather than social choices, general risk attitudes, or beliefs about the partner's actions.^[42]

Neuroscientists have found a fidelity gene as a result of their long-standing experiments on mice. This gene, called AVPR1A (arginine vasopressin receptor 1A), is located on chromosome 20 and secretes AVP. It is observed that when the AVP hormone secreted by this gene, which has 334 different forms, is high, mammals are more likely to be monogamous. In fact, animal experiments show that a polygamous mammal can switch to monogamy when the level of AVP hormone is raised.^[43]

The effects of AVP depend on both the person and the content. Intranasal AVP in men induces agonistic facial motor patterns in response to same-sex faces, reducing the intimacy rates of those faces; Conversely, AVP induces connected facial motor patterns in response to same-sex faces in women and increases the intimacy rates of these faces.^[44]

It is suggested that intranasal AVP expedites dishonesty in women. An experiment was performed to prove this concept. In this study, participants displayed dishonest behaviors to avail themselves and others. Interestingly, for the dishonest behavior bringing benefits to both self and others, women lied more than men when they were treated with AVP. After receiving AVP, this behavior of women increased with repetition.

These findings suggest that lies producing mutual benefits and escalation of dishonesty in women can be supported by AVP.^[44]

AVP has effects on social memory in females, and the amount of it is a little bit more in males than females. It affects males more than females. AVP which can be defined as a male hormone decreases sexual desire, in females after birth and increases the tendency of aggression. Also, high levels of AVP decrease sexual motivation in females.^[45]

THE RELATIONSHIP BETWEEN OXYTOCIN AND ARGININE VASOPRESSIN

It is known that two amino acids distinguish OXT and AVP, except that these two hormones are similar to each other genetically and structurally. Also, they evolved from a common ancestral molecule called arginine vasotocin. They have a role in regulating our social behaviors. Furthermore, they affect our psychology, sexual activity, or emotions. Beyond these conditions, they affect each other and act together.

OXT itself does not affect, and AVP's interactions regulate many OXT effects. They might be considered one pathway because they are functionally a part of it. Both of them are susceptible to social and environmental demands in different ways. OXT, which acts alone, appears to be a component of a more social or passive coping strategy, while AVP can allow active and mobilized coping strategies.^[46]

It seems like autonomic and emotional peak experiences such as dealing with an initial exposure to a baby, orgasm, or falling in love are supported by acting together of OXT and AVP. The early stages of relationships or experience of sexual arousal and orgasm could base on the capacity of OXT and AVP to allow enhanced sympathetic arousal without parasympathetic withdrawal.^[46,47]

SEXUAL ACTIVITY, OXYTOCIN, AND ARGININE VASOPRESSIN

Human sexuality is a way to express individuality in human beings or experience themselves sexually, and this concept has an important extent for them. Sexuality involves lots of different feelings and behaviors such as emotional, social, erotic, spiritual, or biological.^[45]

Human sexual activity in a manner to express or experience sexuality for humans. People attempt

various sexual acts because of lots of reasons. A person's interest in sexual activity generally increases in his/her puberty times. Human sexual activity has different aspects such as emotional, behavioral, sociological, cognitive, or biological. These aspects include all forms of sexual behavior, sharing emotions, personal bonding, or the reproductive system's physiology. Sexual activity can pursue sexual arousal. These arousals may cause physiological changes in people, such as changing the number of hormones like OXT and AVP.^[48]

The amount of AVP and OXT^[49] changes during and at the end of sexual activity. Also, they affect sexual activity, sexuality, sexual behavior, or sexual arousal. According to a study in 1990, AVP's amount increased during sexual arousal but not orgasm. The amount of OXT didn't change during sexual arousal, but increased during orgasm in the same study.^[50]

In summary, humans' psychology, sexuality, behaviors, sexual activity, and emotions are affected by hormones such as OXT and AVP. On the other hand, the amount and the releasing time of OXT and AVP are affected by sexual activity. These hormones can be used in the treatment of autism, anorexia, and dyspareunia. They can also be used to strengthen relationships between couples due to their effects on the psychology and reproductive system. These kinds of improvements are hopeful for the pharmaceutical industry and the conception of unities such as families. We know that there is an interaction between OXT and AVP so, a change in the amount of one of them affects the other one which affects our metabolism eventually. Knowing that these metabolic changes are caused by hormones makes us more aware of them and may prompt us to seek medical treatment. Having a consciousness about OXT and AVP is encouraging for humans to research new usage areas and treatments for the hormones.

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