Neuronal Pathways and Molecular Mechanisms Behind Sexual Arousal -- Using ETI Formulas to Support Sexual Health∗

In this paper, we will primarily be focusing on neuronal pathways and the molecular machinery involved in the sexual arousal mechanism found in both men and women, specifically concentrating on nitric oxide (NO) functions and how they influence sexuality. The topic is interesting, because it clearly shows the human body as an interrelated system with well orchestrated interconnections between the central and peripheral systems (Abraham, 2002; Holstege, 2005; Mah & Binik, 2005). We will also discuss the importance of the reward system (Parsons & Hurd, 2015) regarding sexual fitness and vitality, as well as a Vital Force Technology (VFT) approach to energetically supporting sexual health. Considerations of the different dimensions of men and women's sexual health will be reviewed in detail later in 2018, highlighted by our exploring the enhancement of women's health and the enhancement of men's health.

In addition, we'll look at sexual arousal from an energetic point of view, particularly our abilities to transform energy on the mental, emotional and physical levels. When these levels are balanced, it's typically an indicator of good health in general, which leads to good sexual health in particular.

1. Multidimensional Models of Sexual Function

Current data support the multidimensional models of sexual function, where the spinal cord sexual reflexes underwent an evolutionary rise to the cerebral level, such that now all the mechanisms and corresponding subjective sexual perceptions of both men and women have a brain-based autonomic presentation.

These models have acknowledged that numerous psychosocial problems, regarding pleasure within the relationship, self-image and previous emotional sexual experiences, have an important impact on male and female sexual behaviors (Chung et al., 2013; Stoleru et al., 2012; Holstege, 2005; Mah & Binik, 2001, 2005; Bancroft et al., 2003). (See Fig. 1).

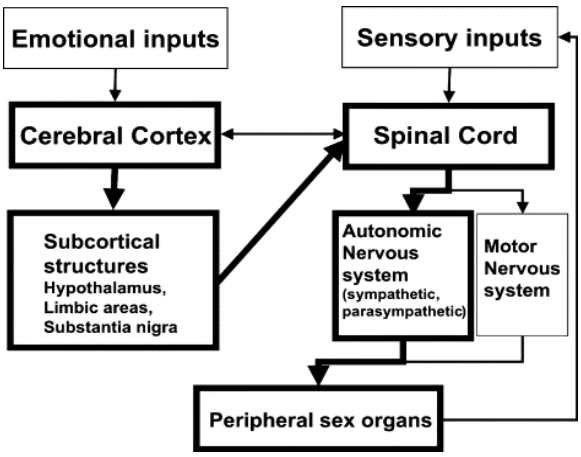


Fig 1. http//:www.sciencedirect.com/science/article/pii/S1043661806000168

A number of the brain's regions, including the amygdala, hippocampus, orbitofrontal cortex and parts of the prefrontal cortex (PFC), are interconnected in complex pathways that involve excitatory (primarily glutamatergic) and inhibitory (primarily GABAegic) projections (Parsons & Hurd, 2015; Koob & Volkow, 2010; Carlezon & Thomas, 2009). "In general terms amygdala circuits contribute to the formation of associative reward- and fear-related memories, hippocampal circuits are critical for declarative memory functions, and frontal cortical circuits mediate control of executive functions. In turn, innervation of each of these circuits allows sensory and emotional information to be converted into motivational actions through the output to motor systems. These same circuits participate in negative reinforcement mechanisms that promote behaviors for avoiding or relieving aversive states" (Koob & Volkow, 2010). (For more details, see Appendix #1.)

2. Complex Interaction of Hormones and Neurotransmitters in Sexual Behavior

There are several brain hormones and neurotransmitters involved, to varying degrees, in human sexual behavior (Fig 2). Among neurotransmitters, the most studied are dopamine (DA), serotonin (SHT), acetylcholine (ACh), glutamic acid and nitric oxide (NO). Among neuropeptides, the best known are oxytocin, adrenocorticotropin (ACTH) stimulating hormone (r-MSH)-related peptides and opioid peptides. Interestingly DA, ACh, glutamic acid and NO appear to assist, while opioid peptides inhibit penile erection by increasing and decreasing, respectively, central oxytocinergic transmission, by acting in the paraventricular nucleus of the hypothalamus (Tang et al., 1998; Lue et al., 1984; Andersson, 2011, Bos et al., 2012).

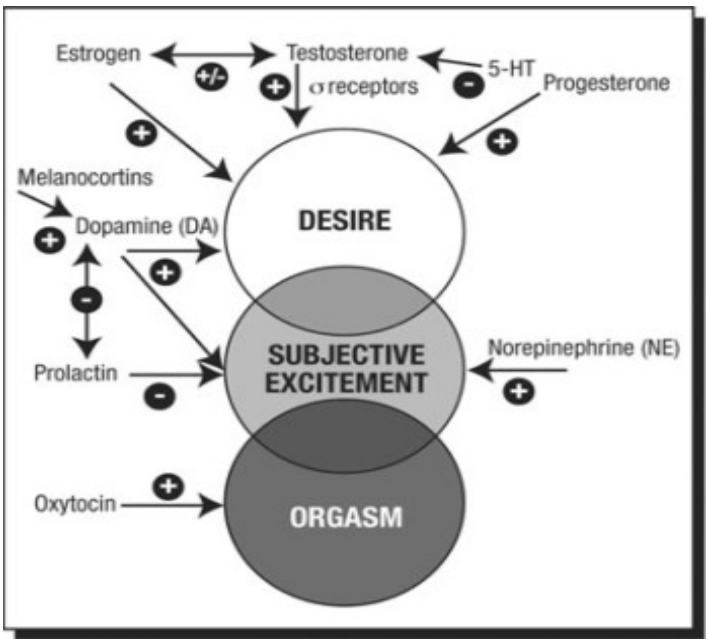


Fig 2.
http://www.jsm.jsexmed.org/article/S1743-6095(15)31783-5/fulltext

3. Nitric Oxide, Testosterone, Oxytocin and Dopamine Involvement in Sexual Function

Nitric Oxide

Nitric oxide (NO) is one of the most studied molecules in medical literature. NO has been shown to be involved in and affect neurotransmission, memory, stroke, glaucoma and neural degeneration, pulmonary hypertension, penile erection, angiogenesis, wound healing, arthritis, nephritis, colitis, autoimmune diseases, tumors, asthma, septic shock, platelet aggregation and blood coagulation, sickle cell disease, gastrointestinal motility, hormone secretion, gene regulation, diabetes, stem cell proliferation and differentiation, and bronchodilation (Jamaati, et al. 2017; Neseem, 2005; Rush, Denniss & Graham, 2005; Azevedo, 2017; Cannon, et al., 2001; Fox-Robichaud, et al., 1998; Rassaf, et al., 2002; Lundberg, et al., 2004; Modin, et al., 2001; Kozlov, Staniek & Nohl, 1999).

Physiologically, penile erection occurs by dilatation of penile arteries and relaxation of the trabecular smooth muscles located in the corpus cavernosum (CC). The main mediator of this smooth muscle cell relaxation is NO. Due to the complexity and significance of NO's role in orchestrating the mechanism of penile erection,, we've placed the details in Appendix #2.

Mostly, NO is synthesized from its precursor L-arginine by nNOS in nitrergic nerve terminals, in response to a sexual stimulus, and by eNOS in endothelium, in response to acetylcholine and shear stress elicited by increased blood flow in the corporeal sinusoids (Tang et al., 1998; Lue et al., 1984).

Remarkably, the body has an alternative source of NO, especially during hypoxia when the oxygen-dependent L-arginine-NO pathway can be altered. Inorganic nitrate (NO_3^-) and nitrite (NO_2^-) are part of the nitrogen cycle in nature. Studies show that nitrate and nitrite can be metabolized in vivo to form nitric oxide (NO) and other bioactive nitrogen oxides (Kleinbongard, et al., 2003; Lundberg & Govoni, 2004). The nitrate content in food can be very high, for example, in green leafy vegetables and sometimes in drinking water (Lundberg, et al., 2004).

Recent studies have shown that the increase of nitrate could influence not only plasma nitrate, but also nitrite (Kleinbongard, et al., 2003). This result is surprising, because it requires reduction of nitrate to nitrite, a reaction that cannot be catalyzed by mammalian enzymes. The "answer" to this curiosity lies in the entero-salivary circulation of nitrate. When nitrate is ingested, as much as 25% is actively taken up by the salivary glands and secreted into saliva (Lundberg, Weitzberg, Cole & Benjamin, 2004). In the oral cavity, much of the nitrate is reduced to nitrite by commensal bacteria, and this nitrite enters the circulation when saliva is swallowed (Kleinbongard, et al., 2003). Research shows that the use of antibacterial mouthwash drastically reduces the level of NO in the stomach and increases the risk of diabetes (Joshipura et al., 2017).

Interestingly, research has shown NO generation from nitrite and relaxation is further increased by vitamin C (Modin, et al., 2001).

Several studies have strongly demonstrated that respiring mitochondria in mammalian cells (Reutov & Sorokina, 1998; Kozlov, Staniek & Nohl, 1999; Nohl, et al., 2000) and in plants (Tischner, Planchet & Kaiser, 2004) can generate NO from nitrite. Also, it has been indicated through numerous studies that NO stimulates mitochondrial biogenesis in vitro and in vivo, which results in increased mitochondrial function and enhanced ATP formation (Moncada & Erusalimsky, 2002; Beltran, 2000; Nisoli, 2004).

Testosterone

Testosterone, a member of the androgen family of steroids, is secreted in the testes of males and the ovaries of female, as well as small amounts from adrenal glands. A complex chain of events known as the hypothalamic-pituitary-gonadal axis (Corradi P, Corradi R & Greene, 2016) regulates production of testosterone. Gonadotropin-releasing hormone (GnRH) is secreted by the hypothalamus, via the hypophyseal portal system; it travels to the anterior pituitary, which then releases luteinizing hormone (LH) in order to stimulate the production of testosterone in the testes (Fig. 3). Starting at puberty, GnRH release from the hypothalamus occurs in small pulses every 1-3 hours in both females and males. Production levels of testosterone are controlled by negative feedback (Constantin, 2017).

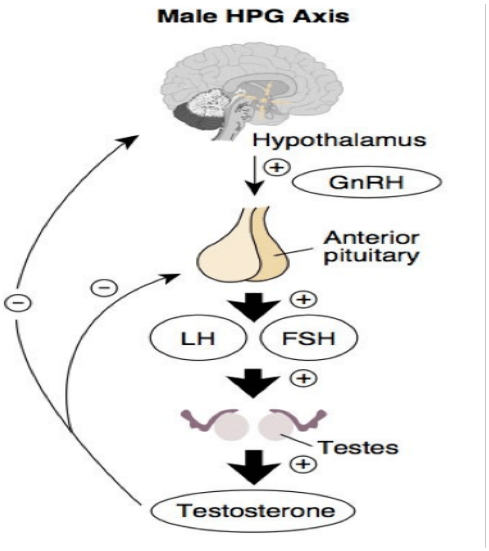


Fig. 3.
http://robertsontrainingsystem.com/blog/serum-testosterone

Low testosterone levels are associated with delayed ejaculation, whereas high levels are associated with premature ejaculation. Testosterone assists in the control of the ejaculatory reflex through its androgen receptors in the medial preoptic area (MPOA) and other areas in the central nervous system (Yildiz, et al., 2005). As well, pelvic floor muscles involved in ejaculation are androgen dependent (Cairrao, Alvarez, Santos-Silva & Verde, 2008). Interestingly, testosterone levels can increase by approximately 10% in males, even though they do not consider some women attractive (Van der Meij, et al., 2011).

The testosterone-induced vasodilation has been demonstrated in isolated animal and human blood vessels, and involves the activation of rapid nongenomic signaling pathways (Malkin, et al., 2006; Rowell, et al., 2009; Seyrek, et al., 2007; Yildiz, et al., 2005) (Fig. 4). Current studies in cultured human vascular smooth muscle cells have demonstrated that testosterone stimulates NO production by nNOS, and then stimulates calcium activated potassium channels (BK_{Ca}) and potassium channels (BK) through cGMP-stimulated protein kinase G (Deenadayalu, et al., 2012; Cairrao, Santos-Silva & Verde, 2010).

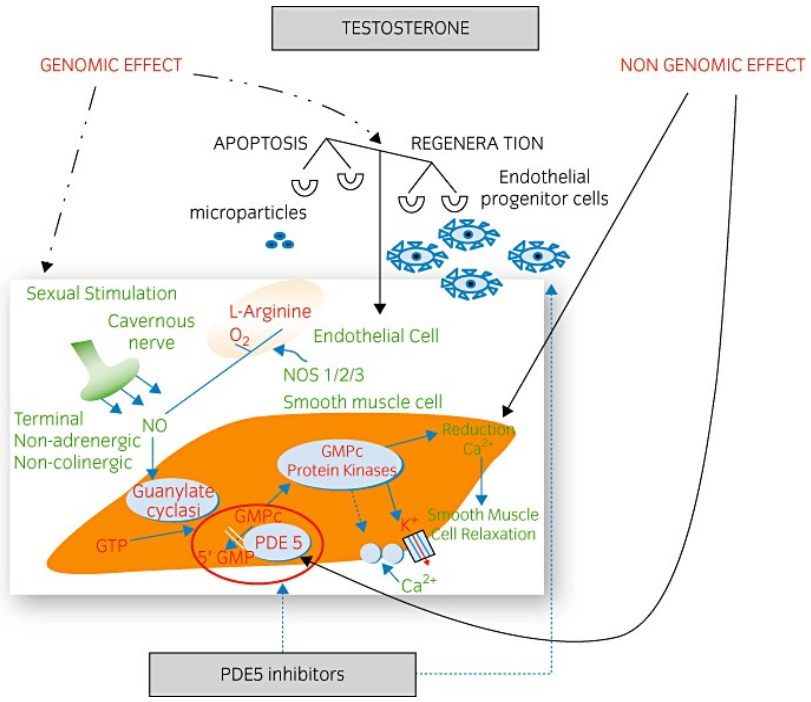


Fig. 4.
https://www.researchgate.net/publication/40680141_Endothelial_dysfunction_and_erectile_dysfunction_in_the_aging_man_Review_Article

Testosterone also can affect the initiation of erections by altering the release of brain neurotransmitters, such as dopamine, oxytocin or NO, from the medial preoptic area (Hull et al., 1999; Suzuki et al., 2007).

Oxytocin and Dopamine

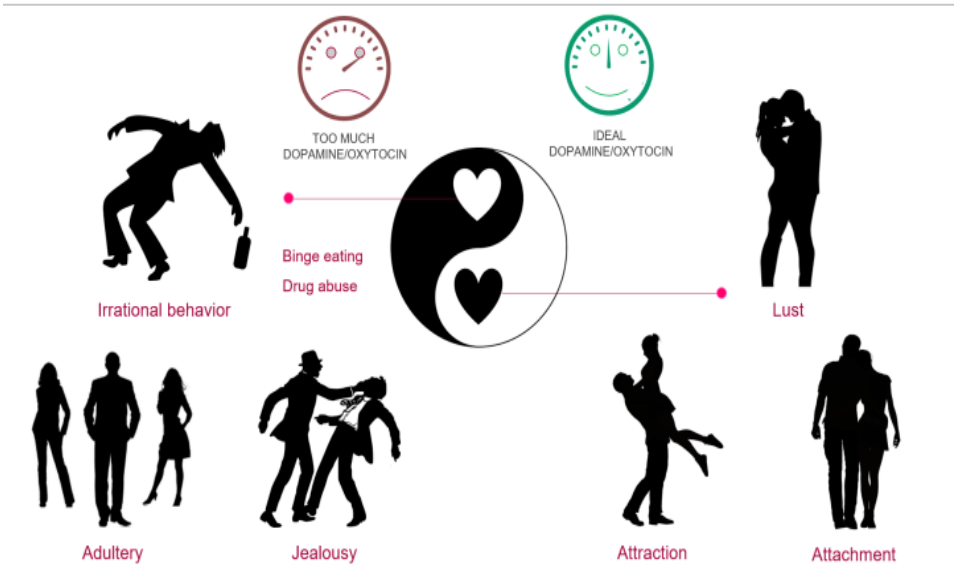
Oxytocin is an oligopeptide synthesized in the supraoptic and paraventricular nucleus (PVN) of the hypothalamus and released from the posterior pituitary gland. Oxytocin serum levels increase after male ejaculation to levels ranging from 20%–360% of normal levels, before reaching baseline at 10 minutes after ejaculation (Corona, 2012). Peripheral oxytocin receptors were found to be highly expressed in the epididymis and tunica albuginea (in smooth muscles more than epithelial cells), and to a lesser extent in the vas deferens and seminal vesicle (Filippi, Vannelli & Granchi, 2002). Despite these encouraging findings and some anecdotal evidences suggesting that intranasal oxytocin can facilitate orgasm in a male (Ishak, Berman & Peters, 2008), a double-blind placebo-controlled clinical study failed to demonstrate an effect of intranasal oxytocin on sexual behavior.

Dopamine is known to be important for normal male sexual response (Hull, Muschamp & Sato, 2004; Peeters & Giuliano, 2007). Several research studies have suggested that dopamine and oxytocin interactions are involved in the neuromodulator of the activation of the sexual response, as well as may increase prosocial behaviors in both paternal and romantic engagements (Theodoridou et al., 2009; Baumgartner et al., 2008 & Rimmele et al., 2009). One mechanism to

explain the prosocial effects of oxytocin is that the oxytocin system reduces anxiety, especially social anxiety (McCarthy et al., 1996; Heinrichs & Domes, 2008).

Also, experimental data in vitro have shown that oxytocin-dopamine pathways are involved in the activation of penile erection (Arletti et al., 1985; Hull & Dominquez, 2007; Martino et al., 2005; Melis et al., 2009).

Bos and colleagues proposed an interesting model in 2011. They suggested that "gonadal steroids and neuropeptides together influence the motivation for social behavior through their action on the amygdala, where testosterone acts to reduce fear and increase sympathetic efferent via amygdala output to the brainstem and motivation to act, while estradiol and oxytocin increase parasympathetic efferent and inhibit amygdala output to the brainstem, enabling greater prefrontal activity and oxytocin-dopamine interactions, which would function to facilitate relationship" (Bos et al., 2011).



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4. VFT's Approach in Supporting Sexual Function

The Vital Force Technology (VFT) lab is constantly working on the creation of formulas that will support not only healthy sexual functioning and the increase of a person's libido, but also facilitate all multidimensional human reactions in encouraging directions, thereby harmoniously influencing partners' reward systems, increasing deep feelings of love and compassion, and bringing greater harmony and unity into the relationship.

Currently, to enhance the range of energy-infused formulas we offer: Sexual Vitality, Chi Men, and Chi Women, to add to VFT's proven classics, Oxytocin and Healing Love.

1. Sexual Vitality Formula

Description:
This formula was created with the intention of helping the body manage better all functions related to reproductive and sexual activities. It can be used as a general tonic for increasing stamina, decreasing fatigue and/or supporting healthy male/female sexual glands. Also, it can help to open emotional channels for sexual energies, revitalize feelings, convert negative expectations into positive ones, and increase deep feelings of love and compassion.
Dosage:
10-15 drops diluted in 2-4 oz. of water. Drink 2-3 times per day until you have the desired effect, or use whenever it is necessary.
Precautions:
No precautions or side effects, if used with the recommended dosages.

2. Chi Men Formula

Description:
This formula directly supports healthy male sexual function and improves sexual desire.
The following are the benefits Chi Men formula can bring to you, seen from the energetic point of view:

- Better coordination of complex interactions between several central and local neuro-transmitters and neuropeptides that determine the presence/absence of healthy sexual behaviors.
- Cleaning of any stagnant sexual channels; also, may be effective in cases of erective dysfunctions, premature ejaculation and/or infertility.
- Supporting production of nitric oxide (NO), which affects neurotransmission, memory, mitochondria biogenesis and penile erection.
- Opening of the heart chakra, thereby bringing increased experience of unconditional love.

Dosage:
10-15 drops diluted in 2-4 oz. of water. Drink 2-3 times per day for 3-5 days until you have the desired effect. Increase the dosage to 20-25 drops whenever it is necessary.
Precautions:
No precautions or side effects, if used with the recommended dosages.

3. Chi Women Formula

Description:
Chi Women Formula is designed to support healthy female sexual function and reawaken sexual libido. This formula helps to create a greater vital power that deeply nourishes women of all ages, tones the female reproductive system, increases stamina, decreases fatigue, and creates more emotional stability. Overall, it can awaken in you the possibility of feeling more vital, energized and in harmony with the rhythms of your body and the energy you're receiving.
Dosage:

10-15 drops diluted in 2-4 oz. of water. Drink 2-3 times per day for 3-5 days until you will have the desired effect. Increase the dosage to 20-25 drops whenever it is necessary.
Precautions:
No precautions or side effects, if used with the recommended dosage.

5. *Oxytocin*

Description:
Using this formula, any man or woman may improve their energetic appearance and enhance their sociability. They can look more vibrant, and experience more feelings of charm, love and harmony. For more information, https://practitionerstore.energytoolsint.com/e-commerce/show-item/Oxytocin-258.
Dosage:
10-15 drops diluted in 2-4 oz. of water. Drink 2-3 times per day whenever it is necessary.
Precautions:
No precautions or side effects, if used with the recommended dosages.

6. *Healing Love*

Description:
An excellent formula for supporting your energetic field. Can assist you and your partner (both consciously and unconsciously) in being more open, happy about each other, as well as contributing to greater senses of unity and love. For more information, go to: https://practitionerstore.energytoolsint.com/e-commerce/show-item/Healing-Love-24.
Dosage:
10-15 drops diluted in 2-4 oz. of water. Drink 2-3 times per day whenever it is necessary.
Precautions:
No precautions or side effects, if used with the recommended dosages.

Appendix #1
Sexual Patterns in the Brain

Normal, healthy sexual functioning is, at least in part, a result of the culmination of several different neural mechanisms, each of which is controlled by different areas of the brain and activated at different times during sexual experience. The euphoric and pleasurable experience of sex is drawn primarily from the limbic cortex. It regulates emotion and repetition of pleasurable experiences, and encourages the avoidance of painful or aversive stimuli.

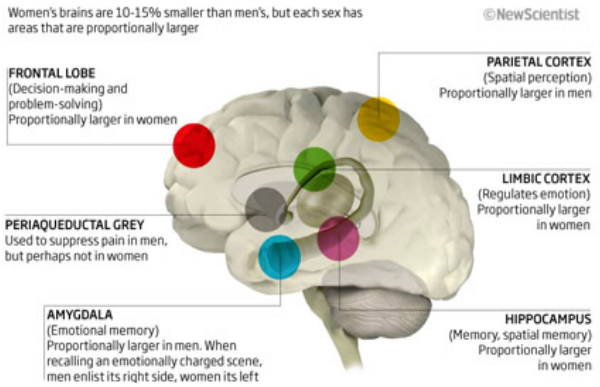

Fig. 1

From a physiological perspective, sexual arousal is controlled by the parasympathetic portion of the autonomic nervous system and manifests itself as vasodilation in sexual organs, along with several other physiological phenomena, including an increase in heart rate. An orgasm, and in particular a male ejaculation, is controlled by the sympathetic portion of the autonomic nervous system, which is also accompanied by deactivation of many areas in the brain relating to external stimuli, in particular fear, allowing the mind to focus on the task at hand (Fig.2).

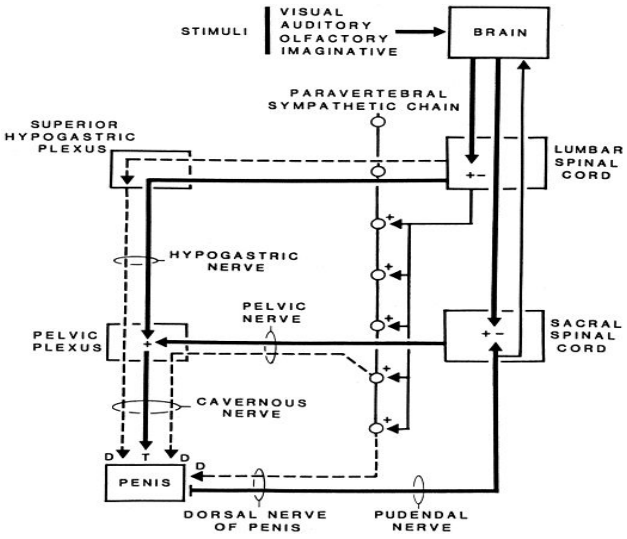

Fig. 2

Amygdala

Prior to the physical stimulation associated with sexual experience, comes sexual desire. Largely mediated by emotions through the limbic system, activation of the amygdala can trigger penile erection, sexual feelings, sensations of extreme pleasure, memories of sexual intercourse, as well as ovulation, uterine contractions, and orgasm. The amygdala projects through three pathways to many areas of the brain, the stria terminalis, the amygdalofugal pathway and the anterior commissure. These pathways influence hormonal and somatomotor aspects of behavior and also emotional states.

The amydalofugal pathway connects the corticomedial nuclei of the amygdala with the thalamus, median hypothalamus, brain stem and nucleus accumbens. This pathway is thought to be responsible for pleasurable feelings. The stria terminalis has projections to and from the hypothalamic-pituitary-adrenal axis and is thought to mediate threat monitoring and the stress response. It is also responsible for sympathetic nervous system activation.

Ventral striatum

Input travels from the basolateral nuclei of the amygdala along the amygdalofugal pathway to the ventral striatum, which is made up of the nucleus accumbens, putamen and parts of the caudate nucleus. The nucleus accumbens plays a role in pleasure and reward, due to a large number of dopaminergic neurons from the VTA (ventral tegmental area) (Fig. 3).

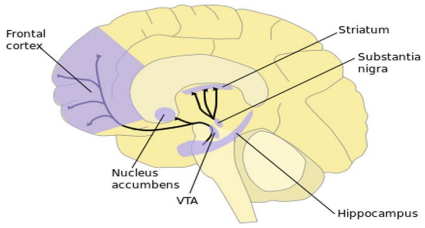

Fig.3

Orbitofrontal Cortex

The orbital frontal cortex (OFC) is located ventrally along the frontal skull and superior to the orbits of the eye. The OFC has a large network of connections that project to various areas of the brain, including all somatosensory modalities, the hippocampus, ventral tegmental axis and amygdala (Fig. 4).

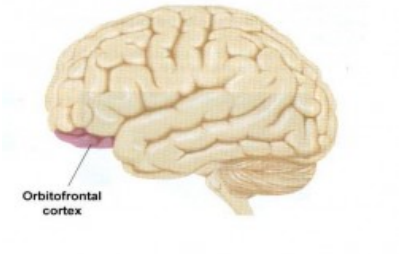

Fig. 4

In contrast to many other cortical regions, the OFC is still poorly understood. Currently, it is held that higher cognitive functions occur in this area, in particular, sensory integration, representing the affective value of reinforcing expectation and judgments based on reward and punishment.

In terms of sexual desire, the OFC is thought to mediate reward and punishment and personal assessment. This relates to mate selection -- whether someone is seen as desirable. Evidence

derived from studies of facial attractiveness and those involving males presented with sexually attractive visual stimuli both support the OFC's involvement in this role.

The OFC is thought to be responsible for the disassociation of rewarding; that is, the adaptive value of a face can be disassociated from that of an aesthetically pleasing one, in effect, mediating beauty for members of the opposite sex. Another function of the OFC regards managing expectation, particularly those based on memories modulated by projections from the hippocampus. The associated decisions, emotional states and perceived consequences can then be used to modulate sexual desire and its related physiological responses.

Vagus Nerve

Areas of activation via the vagus nerve during and after orgasm include the hypothalamic paraventricular nucleus (PVN), midbrain central gray, amygdala, hippocampus, anterior cingulate, frontal, parietal, temporal and insular cortices, anterior basal ganglia and cerebellum.

Appendix #2
Nitric Oxide Participation in Sexual Function

NO diffuses to adjacent smooth muscle cells, where it activates soluble guanylyl cyclase (sGC) and increases the production of 3' ,5'-cyclic guanosine monophosphate (cGMP) from 5'-guanosine triphosphate, after being synthesized from its precursor L-arginine by nNOS in nitrergic nerve terminals in response to a sexual stimulus, and by eNOS in endothelium in response to acetylcholine and shear stress elicited by increased blood flow in the corporeal sinusoids, (GTP) (Fig. 1).

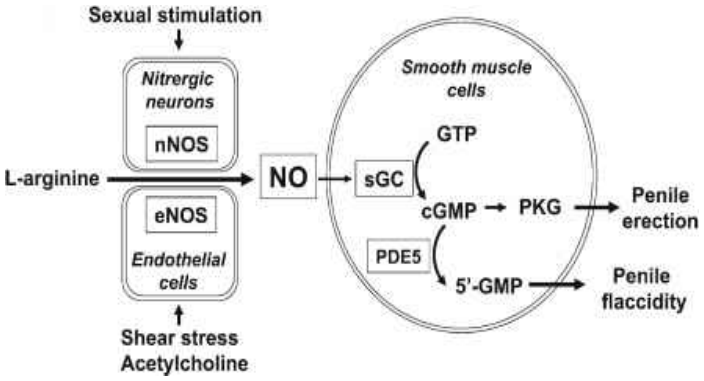

Fig.1

Protein kinase G phosphorylates several key target proteins, including ion channels, ion pumps, and enzymes; all are involved in the control of intracellular calcium level. Among these target ion channels are K^+ channels. Phosphorylation of K^+ channels by PKG leads to their activation with subsequent hyperpolarization and relaxation of corporal smooth muscle cells (Fig.2).

cGMP in the penis is hydrolyzed primarily by type 5 phosphodiesterase (PDE5) to inactive 5 ' -GMP, which terminates NO signaling and returns the penis to the flaccid state smooth muscle and vasodilation of blood. PDE5 inhibitors such as sildenafil, vardenafil and tadalafil inhibit PDE5, thereby boosting cGMP levels and penile erection.

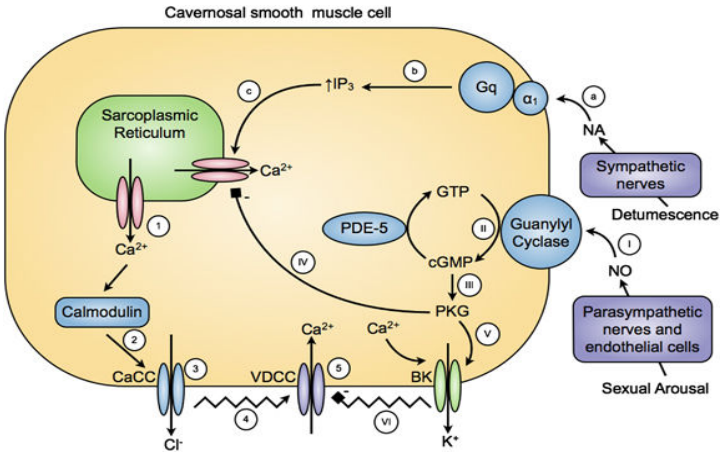

Fig. 2.

∗ **Disclaimer** (i) This information is provided for educational purposes only. (ii) These statements have not been evaluated by the Food and Drug Administration (FDA). The provided information is not intended to diagnose, treat, cure or prevent any diseases or medical problems.

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