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Review

Relationship between Hunger and Sex: Interaction between Leptin and Estrogens

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A B S T R A C T

The hunger and sex hormones like many other hormones in human body work in coordinated way to complete the assigned physiological task. Some of the primary functions they do independently e.g. Leptin plays a crucial role in regulating energy balance and appetite but it directly or indirectly coordinates with estrogen to participate in reproductive functions. Experimental studies provided enough evidence unequivocally that the circulating estrogen may be responsible for the elevated levels of leptin in blood circulation. In addition to this coordination, estrogen is also capable of stimulating the leptin levels in the serum which peak at mid-cycle synchronising with luteinizing hormone pulses. Gonadotropins and growth factors are responsible for promoting ovarian granulosa and theca cells functions and oocyte maturation if the normal range of serum leptin levels is maintained. Estradiol, primarily inhibits appetite and promotes satiety, leading to reduced food intake though in some cases, like after fasting or low blood sugar, it may actually promote re-feeding. This is thought to be due to the way estradiol influences meal size and onset of satiety. Based on the nutritional status, estradiol, a potent form of estrogen, induces bidirectional actions on feeding.

Keywords: Gonadotropins, Oocyte maturation, Satiety, Human behaviour

1. Introduction

Hormones are signalling molecules produced by endocrine glands placed at different sites in the body. These hormones have a pivot role in regulating physiological processes as well as behavioural activities in humans such as digestion, metabolism, respiration, sensory perception, sleep, excretion, lactation, stress induction, growth and development, movement, reproduction and mood manipulations, in other words most of the important physiological functions. They exhibit a significant role to play everything from sleep and stress to food cravings and weight loss¹⁻³. Hunger and sex are also controlled by co-ordination of different sets of hormones^{4,5}.

Leptin, a hormone primarily produced by adipocytes that plays a crucial role in regulating energy balance and appetite⁶.

Leptin is a signalling molecule to communicate between fat stores of the body and the brain thereby influencing hunger, metabolism and other physiological processes. Leptin also impacts neuroendocrine function, immune responses and other metabolic processes⁷⁻⁹. A number of endocrine glands release hormones when stimulated by hormones released by other endocrine glands. There is a relationship between leptin and estrogen¹⁰, though they are produced in the two different organs performing entirely different functions and belonging to different body systems.

Leptin also affects ovarian function, since studies suggest that it may directly influence granulosa cells to reduce estradiol production indirectly playing a role in reproductive health. Estrogen can interact with other hormones that influence appetite,

such as leptin and ghrelin, which regulate hunger and satiety. For instance, estrogen can help regulate leptin levels, which signal satiety¹¹. The developing ovarian follicles (granulosa cells) contributes to an increase in estrogen levels during follicular phase in turn there is an increase in circulating leptin.

Evidence from studies provides a clue that leptin can also directly influence the ovarian function, potentially by acting on granulosa cells to regulate estradiol production as well in addition to its influence on the development and maturation of ovarian follicles. This conclusion is possible because higher leptin levels have been observed during controlled ovarian hyperstimulation. The role of estrogen in elevating the circulating leptin concentration in humans and rats^{12,13} as well as the reduction in leptin expression in ovariectomized rats can be reversed by estrogen administration confirms the relationship between leptin and estrogen¹⁴⁻¹⁶.

Estradiol, a form of estrogen, though inhibits and promotes satiety, its effects depend on the nutritional status of the host^{17,18}. Estradiol also promotes bidirectional actions on feeding primarily inhibits appetite and promotes satiety, leading to reduced food intake, but in some cases, like after fasting or low blood sugar, it may actually promote re-feeding. This is thought to be due to the way estradiol influences meal size and onset of satiety. Santollo J, et al, suggested that that estradiol (E2) inhibit food intake through estrogen receptor alpha (ER α) transcriptional activity (t-a) via hypothalamus¹⁹.

During mid cycle estrogen stimulates an increase in the titre of serum leptin, thereby synchronizing with nocturnal luteinizing hormone pulses. Serum leptin levels (normal range (10-20 ng/mL) promote ovarian granulosa and theca cell functions and oocyte maturation in combination with gonadotropins and growth factors¹⁷.

Estrogen, though a sex hormone is also capable of regulating appetite and food intake because it can suppress food intake and meal size; influencing the body processes of generating energy from food²⁰. The other sex hormones like progesterone and testosterone also have an influence on the hunger regulation other than reproductive function. The mechanism of regulating hunger by estrogen is a complex mechanism, including actions on the estrogen receptors in the brain particularly in the amygdala and its impact on energy expenditure, which is involved in hunger-enhanced memory for food stimuli. Estrogen can also influence how the body uses energy, by inducing ketabolism as well as the distribution of body fat²¹.

New research indicates that neuroestrogens help suppress appetite since in aromatase knocked out mice that cannot synthesize estrogens in a systemic manner. As a result, in these mice increased food intake and body weight compared with their aromatase-expressing counterparts. When aromatase expression was restored the action of neuroestrogens influencing appetite was observed²².

1.1. Evolution of sex and hunger

Sex and hunger are two distinct physiological functions yet interconnected. While hunger is a fundamental drive for survival, sexual motivation is primarily meant for reproduction and the continuance of species. Evolutionary pressures have shaped both hunger and reproduction^{23,24}, with sex often influencing behaviour in ways that may not directly maximize

individual survival, but enhance the reproductive success of the species. Here are some points to be considered a more detailed look:

1.1.1. Evolution of hunger:

- **Survival:** Hunger drives individuals to seek food, indispensable for energy and survival. The brain regulates hunger through various hormones and neurotransmitters, influencing appetite and satiety²⁵.
- **Adaptation:** The ability to detect food sources and regulate hunger based on available resources has been a key factor in the survival and evolution of species²⁶. This way both the purposes are served very well.

1.1.2. Evolution of sex:

- **Reproduction:** in biological sense sex is fundamentally about the mixing of genetic material to produce offspring with new combinations of genes. In other words, propagation of species, but variation because of combinations. This increases genetic diversity, which can be beneficial in adapting to changing environments²⁷.
- **Beyond reproduction:** Beyond reproduction, sex can also have a vital involvement in social bonding, mate selection and even the development of complex social structures it's a fact that sex plays an important role in human relationships, emotional well-being and overall health. It facilitates intimacy, strengthens bonds and can provide pleasure, relaxation and a sense of connection. Sex can also have a positive impact on physical health, including lowering blood pressure and improving sleep^{27,28}.
- **Sexual selection:** Evolutionary pressure exerted on individuals is responsible to select traits that enhance the ability to find a mate, as well as directly benefit survival value in sexual selection. This can lead to the development of elaborate displays or competitions. Sexual selection is a mechanism operated in nature where members of one sex choose mates of the other sex to mate with (intersexual selection), resulting in completion among the members of the same sex to get the mate of the opposite sex (intrexual selection).

1.1.3. The interconnection:

- **Resource Availability:** In some species, resource availability can influence the timing and frequency of sexual activity predominantly because, individuals normally reproduce when enough resource are at their disposal for the young once especially. Intersexual activity in many species is observed to get reduced due to resource scarcity²⁹.
- **Human Behaviour:** In humans, the relationship between hunger and sex is complex. Both hunger and sexual drive are fundamental human motivations, but they are also linked in various ways, including through brain regions, hormones and even behavioural changes. Hunger, as a physiological drive, can impact sexual behaviour, potentially reducing libido when energy stores are low. Conversely, sex can have appetite-suppressing effects due to the release of hormones like oxytocin. Emotional factors come in to such situation linking psychological well-being³⁰.
- While some studies suggest a correlation between high hunger and increased libido, particularly in males, other

research indicates that severe calorie restriction can suppress sexual desire.

1.2. Sex vs. food

Scientific data suggests that during resource scarcity such as food couples show eagerness to socializing with members of the opposite sex. Depending on situation hunger proves to increase sexual desire. There is a complex interplay between hunger, appetite, socialization and sex drive. However, so far it is not well defined whether higher libido can result due to hunger or appetite suppression. Leptin receptor neurons when activated in mice, social interaction was given priority despite hunger or thirst. Liu Z, et al, suggested from the preliminary study that overeating or rebound eating after calorie-restricted dieting is a better practice³¹.

1.3. Leptin influences libido

Neuroscientists observed that both types of neurons one which carry receptors for leptin and the other which produce neurotensin, are involved in hunger and thirst in addition in sexual behaviour³². On activating the neurons with leptin receptors, Martin, et al, observed changed behaviour in the mice in all the three experimental conditions such as well-fed, hungry after fasting overnight and chronically hungry (after spending five days on a restricted diet)³³; and were surprised in activating the leptin neuron did nothing in mice from well fed and fasting. Animals those who had plenty to eat displayed, a priority to find sexual partners, as usual, but the starved mice were indifferent to sex and went for search for food first.

1.3.1. Sex and hunger relationship:

The following conclusions were drawn in the laboratory experiments with mice

- In the mice who had plenty to eat and drink activating the leptin neuron did nothing., as well as in,
- Chronically hungry mice also behaved as mice who had plenty to eat and drink.
- The well-fed mice prioritized finding sexual partners,
- The very hungry mice said no to sex and went for the food.
- Moderately hungry mice shifted their priorities from eating and drinking to sexual desire under the influence of activated the leptin neurons, but in the same group on, activating the leptin neuron shifted their priorities from eating and drinking to sexual desire. They were able to ignore minor hunger or thirst in order to find a sexual partner and have sex.

1.4. Hunger increases sexual desire

Scientific studies established that there is a complex interplay between hunger, appetite, socialization and sex drive. However, the link between hunger and elevated libido is yet to be established. The study also provides a clue that hunger curbs libido but minor hunger easier to ignore when sex becomes priority³⁴. Leptin is not capable of inducing libido. But calorie restriction can improve sex drive, unlike negative impact on sex drive during extreme calorie restriction⁹. This must be the reason for not able to reduce food intake for a longer period though dieting is possible for a short duration³⁵.

1.5. Obesity linked low sex drive

Obesity has a negative impact on libido and sexual desire. Link between body mass index (BMI) with physical limits on sexual activity and reduced sexual life score, sexual desire, frequency of sexual activity and satisfaction with sex has been established.

Obesity has a profound role to play in sexual dysfunction, though weight loss through medication or surgery may help restore sexual function. Scientific research is wanting to have a better understanding³⁶. Excessive leptin production in response to overeating or in states of leptin resistance lead to decreased reproductive function in obese men^{36,37}.

1.6. Improve libido by manipulating hunger

Libido is influenced by many factors such as body image and self-esteem and so sexual arousal is easy to manipulate. Regulating hunger and maintaining a moderate bodyweight can indirectly improve libido. A healthy, balanced diet, rich in lean proteins and vegetables, can help prevent disorders that affect sex drive, while also boosting overall energy levels. Additionally, a stable body weight can positively impact both physical and psychological factors related to libido.

Diet and hunger regulation can impact libido directly by

- **Hormonal balance:** A balanced diet rich in nutrients like zinc, found in foods like oysters and pumpkin seeds, can help boost testosterone levels, which are important for sexual function in both sex.
- **Blood flow:** Foods like watermelon, which contain citrulline, can help improve blood flow, which is crucial for sexual arousal and performance.
- **Energy levels:** A healthy diet provides the energy needed for sexual activity and overall well-being.
- **Stress reduction:** A balanced diet can help reduce stress, which is known factor in low libido.
- **Weight management:** Maintaining a moderate weight can improve physical and psychological factors related to libido.

Gaining Sex Drive by losing weight is possible since obesity is the one of the causes of low sex drive and with the best nutrition both issues can be solved.

The proper selection of nutrient may help to solve both the problem of sex life and weight control.

- **Pomegranate:** Pomegranate helps in improving sex life, by regulating blood flow
- **Vitamin D:** vitamin D helps in strengthening immunity and enhance calcium uptake for strong bones, it also supports testosterone levels which plays a crucial role in male sexual function. Men who suffer with sexual performance also suffer with a vitamin D deficiency.
- **Lemon verbena:** Polyphenols rich lemon verbena promotes weight loss without the unwanted side effects of medication.
- **Whole grain rye:** Weight loss is more pronounced when whole-grain rye is consumed rather than refined wheat bread. Rye bread is rich in magnesium, to maintain healthy blood pressure. healthy blood flow helps during sex, as well as overall heart health.
- **Probiotics:** To maintain overall good health keeping gut microbiome healthy by supplementing probiotics.

Reduced sugar intake is good since sugar creates havoc in our gut.

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