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Aos meus pais,
Aos meus irmãos
À minha família e amigos

Biological Determinants of Sexual Desire in Women

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Abstract

Sexual desire, commonly referred to as libido, is an important component of the sexual response cycle, frequently overshadowed by other aspects of sexual behaviour and activity. Pheromones are thought to be involved in social attraction and recognition and thus in sexual behaviour, since it has been proven to be the case in other species. Furthermore, neurotransmitters are also mediators in the sexual response cycle through both excitatory and inhibitory pathways, each of them with different neuropeptides. Other factors of a woman's physiology and biology may also affect her libido, namely fluctuations throughout the menstrual cycle and menopause. They are most likely due to sexual hormones variations, although, in light of what is known today, none can be pinpointed. This is further suggested by the fact that women with both surgically and naturally induced menopause report a decrease in the quality of life greatly due to the decline in the quality of their sexual life, especially in desire and arousal.

Key Words: sexual desire; women´s biology

Introduction

Sexual desire involves a complex interplay between cognitive and peripheral physiological mechanisms resulting in sexual arousal. (1) The sexual response cycle was initially divided into four phases: desire, excitement, orgasm and resolution. Sexual desire differs from sexual excitement in the sense that the first is defined by spontaneous sexual thoughts, the alertness to sexual cues, fantasies about sexual activity and the desire to engage in them, whereas the latter is defined by the subjective sense of sexual pleasure and accompanying physiological changes, which, in women, are essentially vasocongestion in the pelvis, vaginal lubrication and expansion, and swelling of the external genitalia. (2, 3) However, it has become clearer in recent years that sexual desire doesn't always precede arousal, it may happen synchronously or even afterwards, more so for women in long-term relationships. It has been documented that women's sexual response frequently emerges from intimacy needs, such as reinforcing the pair bond, pleasing the partner, feeling of closeness or preventing the partner from drifting away, rather than a need for physical sexual arousal, seeing that the biological urge to release sexual tension isn't as preponderant as in men. (3, 4)

Basson proposes a cyclic sex-response model, where sexual desire is oftentimes more of a responsive event rather than a spontaneous one, since it habitually ignites by sensing sexual stimuli, an opportunity to be sexual, and/or by the benefits mentioned above. Therefore, women shift from a sexual neutrality to being receptive to or searching stimuli necessary to prompt sexual desire, which consciously or unconsciously arouses women and, in turn, increases desire. (4, 5) It then becomes easy to comprehend that desire and arousal are hard to differentiate, since the two are so intimately related.

Naturally, spontaneous sexual desire may also occur at times, which is in accordance with the traditional sex cycle response, but it may apply more to the beggining of relationships, and not so much to long term ones. (5) And so, since women are motivated to be sexual for other reasons (increased intimacy) than merely the release of tension, a pleasurable physical experience, likely accompanied with time spent in nongenital and genital nonintercourse stimulation, is imperative to permit this motivation to be present throughout long term relationships (5).

In light of most recent studies and developments, the concept of sexuality is being broaden and adjusted to a better and more integrated term, since the modification of the traditional sex response cycle and the realization that there is a very wide spectrum included in this concept, has allowed professionals and even the own individual to have a different perception of what is sexuality and what theirs is. Asexuality is an orientation many consider to have where, according to the Asexual Visibility and Education Network (AVEN), they don't experience sexual attraction. There is no consensus in its true definition, because some consider to be asexual because of their lack of interest in sex and not necessarily in the lack of attraction, since they enjoy engaging in physical intimacy such as hugging, kissing and cuddling (6).

There is lack of normative age- and gender-related data on frequency and degree of sexual desire, which poses a complication in diagnosing disorders of this nature. (2) In addition, it is postulated that brain function and structure may be altered or fortified by experience and behaviour (experience based plasticity), which may encourage disorders of sexual desire nature. (7)

Deepening to a more anatomical and neurologic base, sexual stimuli activate the cognitive state, where they are identified as sexual (1), and somatic afferent pathways activate autonomic cerebral centres (8), causing an increase in specific cortical areas by neural activity, namely the right frontal and inferior temporal cortex, anterior cingulate, insula area and hypothalamus (9, 10). In fact, brain scans and physiological literature indicate the existence of two different systems, one that mediates sex drive and another that mediates pair-bond formation. More specifically, women demonstrated in neuroimaging tests, a weaker activation of the hypothalamus (strongly observed in men), which is associated with intense sexual arousal (11), and higher activation of the caudate head, most likely via oxytocin and vasopressin (12) and ventromedial pallidum, which are involved in subconscious emotional attachment and pair bonding. (13)

Bearing this in mind, it becomes a challenge to analyse only biologic determinants involved in sexual desire, since there seem to be other factors involved which act simultaneously and symbiotically with one another. For instance, age, mental health and psychosocial factors were identified as major contributors to changes in middle-aged women's sexual desire (14). Therefore, it has been proposed that there's an interplay among biological (genetic) influences, experiences and current circumstances. (15) These last two are just as important as biological factors and may even be decisive in the sexual life (15). In fact, the presence of a sexual partner was associated with a lesser likelihood of having low sexual desire (16). Furthermore, psychosocial factors may even block desire, since it has been demonstrated a link between reports of low sexual desire and nervousness (16).

Studies on sexually receptive female rats have shown that when given the choice between spending time with a sexual partner (sexually competent male) or a non-sexual partner (a same-sex conspecific or castrated male), female rats will choose to spend more time with

the sexual partner when he is placed behind a wire mesh, restricting physical contact, relatively to when physical contact and mating is possible. This difference in attitude, related to a restricted or unrestricted physical contact, suggests that other aspects of a sexual partner such as auditory, visual and olfactory characteristics are enough for approach behaviour and trigger a preference in the female rat. (17)

Amidst all these factors, hormones also play a major role in sexual motivation which seems to control libido's intensity and sexual behaviour (18). Their impact on sex drive still isn't quite well understood, but studies have in fact shown an influence which will be approached later on.

The main biological determinants of sexual desire studied and investigated up to date on women will be discussed in this review.

1. Pheromones and Libido

1.1 Pheromones

Pheromones are chemical messengers defined as "substances which are secreted to the outside by an individual and received by a second individual of the same species, in which they release a specific reaction, for example, a definite behaviour or a developmental process", contributing to attract the partner (19). In mammals, these pheromones are detected by the vomeronasal organ, which is part of the accessory olfactory system, where they are processed through G protein-coupled receptors, expressed by sensory neurons (20). However, in humans, there still remains doubts on whether or not this organ is functional, since evolutionarily speaking, there has been a decrease in specific receptors in this structure, leading to a collapse of chemoreception during human evolution (19).

Nevertheless, if pheromone action does occur in humans it is most likely through the main olfactory system, which has shown to detect and process certain chemosignals.

Pheromones may be present in humans in bodily secretions, namely urine, semen, vaginal secretions, breast milk and even saliva. However, the most attention has been given to axillary sweat, originated from eccrine and apocrine sweat glands and sebaceous glands. Pheromones in these secretions are steroid-structure components, in particular the odorous 16-androstenes: androstadienone, androstenone and androstenol (21), linked to signals processed by the accessory olfactory system through the medial preoptic area and anterior hypothalamus, and by the main olfactory system via amygdala, orbitofrontal and insular cortex (22).

1.1.1 Androstadienone

Androstadienone is most likely to have the most exuberant effects on both sexes, but predominantly on females (21). This component seems to be much more concentrated on male axillary sweat rather than womens' and women seem to be more sensitive to androstadienone than men, although, naturally, the effect of this component depends on factors such as duration of exposure and perceptive threshold. Studies have shown an increased positive-stimulated mood and decreased negative mood after exposure to male axillary extracts (23) and purified androstadienone (24, 25), this last one dose-dependent (26). Furthermore, women also report feeling more focused and physically more aroused after exposure to androstadienone (25). This improvement in mood and focus may be significant in women's sexuality.

This is further supported by studies that show that adoption of a positive mood (27) facilitated further mental and genital arousal, even in women with low baseline mood. Lastly, sniffing of androstadienone at high concentrations, was found to enhance positive mood defined by

calmness, contentment, confidence, happiness, interest and amusement, and decrease negative mood defined by embarassment, fear, disgust, anger, anxiousness and stress, when exposed to emotionally neutral vídeos. (26)

2. Neurotransmitters and Libido

There are specific regions in the brain that modulate sexual desire through neurotransmitters. This modulation may be excitatory or inhibitory. It seems that the first one is mediated by dopamine, melanocortin, oxytocin, vasopressin, and norepinephrine. On the contrary, the inhibitory modulation is mediated by opioid, serotonin, endocannabinoid and prolactin. (28, 29)

2.1 Dopamine and Serotonin

Dopamine and serotonin have been studied for its role on biological influence on sexual behaviour, especially on male rodents (30, 31). Neurons containing dopamine and serotonin are stimulated, releasing their respective neurotransmitter into the synaptic cleft to bind to the postsynaptic neuron and exert its effects on the brain. In female rodents, it is harder to study the biological roles of these neurotransmitters since they usually receive sexual advances of males.

2.1.1 Dopamine

In human and animal studies, the release of dopamine has been linked to motivation and reward-related behaviours, and rising levels of this neurotransmitter even increases sexual motivation and engagement in sexual behaviours among male rodents. (30-32) In these animals, a relationship between dopamine release and precopulatory period has been established when a female in placed behind a perforated barrier. Such release wasn´t

detected when a male was in that same position. (30) The fact that this increase in dopamine was detected before copulation, indicates that this neuropeptide is implicated in sexual motivation.

There may be a genetic influence on the variations of neurohormone concentrations, because if there are variations in genes encoding the receptors and transporters responsible for sensing these transmitters and for reuptaking or hydrolysing them, it could explain some physiological disparities in human sexual behaviour and experience. Dopamine receptor D4 (DRD4) 7+ allele has been linked to greater sexual desire, arousability and engagement in sexual behaviour (33), although results have been controversial, emphasizing the need for more studies.

2.1.2 Serotonin

On the other hand, serotonin has an inhibitory effect on sexual behaviour, where its levels' increase results in decreased engagement in sexual activity among males (30, 31). Regarding the influence of 5-hydroxytryptamine (5-HT), also known as serotonin, 5-HT1A receptor agonist showed a reduced activation of sexual inhibitory mechanisms in the prefrontal cortex. The blockade of its presynaptic transporter by selective serotonin reuptake inhibitors (SSRIs), which increases the presence of serotonin in the synaptic cleft, is a frequently used therapy for depression. Women on this therapy experience decreased sexual desire and other side effects regarding sexual life (34). There are two types of SSRIs, one which is highly selective for serotonin autoreceptors and one which isn't as selective. Since serotonin autoreceptors also bind to other neurotransmitters, such as norepinephrine, the effects of the two different SSRIs will affect norepinephrine's action. The highly selective one will naturally inhibit norepinephrine's effects more strongly in comparison to the other SSRI. Norepinephrine is the major neurotransmitter of the Sympathetic Nervous System,

which essentially mediates peripheral actions. Therefore, when taking highly selective SSRIs and ephedrine (a synthetic molecule similar to norepinephrine), Sympathetic Nervous System effects weren't inhibited, translating to increases in sexual arousal and orgasm. Sexual desire was also assessed, but no effects were demonstrated, since it is a function where the Central Nervous System has a more dominant role (35), and therefore most likely not affected directly by norepinephrine´s actions.

This points to a role of serotonin, as well as dopamine, in sexual behaviour and activity, although there still lacks conclusive results for females. Also, animal models regarding central control of sexual behaviours, are far more advanced than human models. (29)

2.2 Oxytocin

Oxytocin is produced in the hypothalamus then transported to the posterior pituitary gland and finally released into the circulation. Its known effects are on the breastfeeding reflex in the lactation process and helping contraction during labor. Regarding its role in sexual desire, there is still some doubt on whether or not oxytocin is involved. A double-blind, placebo-controlled naturalistic study, concluded that sexual drive, and other aspects of sexual activity such as sexual arousal and erection/lubrication were not significantly altered by intranasal oxytocin administration. However, it demonstrated an increased intensity of orgasm and contentment after sexual intercourse, and women reported being more relaxed afterwards and showed signs of slightly improved abilities in terms of partner interaction (36). Bearing in mind that the sexual desire model has in consideration reward seeking motivations, it could indicate that oxytocin does in fact promote desire. The author does mention that effects of altered hormonal states (contraception method and pregnancy, for instance) may have had an impact and altered results, further proving that more studies and investigations should be conducted.

2.3 Prolactin

Another neurotransmitter involved is prolactin. It is known to be an important hormone in the regulation of lactation, although it has other biological functions, since its receptors are widely distributed throughout the Central Nervous System and peripherally as well. The main known locations are cortex, hippocampus, amygdala and hypothalamus, centrally, which are involved, as mentioned previously, in the regulation of sexual behaviour and activity. Peripherally, receptors are located in sexual organs, both in men and women, such as testis, epididymis, prostate, ovaries, uterus and fallopian tubes. Dopamine exerts an inhibitory control over the secretion of prolactin and vice-versa, and since dopamine has a predominant role in sexual function including libido, it is likely to assume that prolactin has a role in sexual function (37).

However, the true physiological importance of this hormone isn't well understood, although literature suggests a link between sexual activity and prolactin secretion and, therefore, action. A marked and persistent increase in its levels is observed after an orgasm which may be a peripheral mediator of the feedback control stimulating engagement in more sexual activity afterwards, resulting in an indirect mediation for sexual desire and arousal. The relationship between prolactin and sexual function, both centrally and peripherally, is better understood in men, which indicates that in women it is expected to have similar actions (37). Chronic hyperprolactinemia has been associated with inhibition of sexual behaviour and activity, although its mechanism isn't fully comprehended, most likely concerning the hypothalamus-pituitary-gonadal axis. In women with this condition, decreased libido is one of the main reported symptoms, although the specific phases of female sexual function affected aren't well described. Studies in this field are lacking and required in the future (37).

In addition, patients with Chronic Kidney Disease reported sexual difficulties, including decreased libido (38). In this condition, hormonal changes occur and particularly in End-Stage Renal Disease, women have high levels of prolactin, FSH and LH, often reversible by kidney transplantation (39), reporting concomitantly improvement in libido (38).

2.4 Melanocortins

Melanocortins are small protein hormones derived from the polypeptide precursor proopiomelanocortin (POMC), that, when cleaved, results in biologically active components such as a-, b-, and g-melanocyte stimulating hormone (MSH), adrenocorticotropic hormone, and opioid b-endorphin. These peptides have shown to have effects on sexual behavior of rats, such as penile erection in males and lordosis in females, a position female rats adopt to facilitate penile insertion. MSH binds to central and peripheral melanocortinergic receptors (MCRs), such as MCR3 and MCR4, which can be found in the hypothalamus and limbic system (40).

Bremelanotide, an analogue of a-MSH with high affinity to the MCR-4 (thought to be important in sexual function), was proven to be implicated in sexual behaviour by prompting sexual activity in the presence of an appropriate sexual stimulus. Furthermore, subcutaneous injections of this analogue increased dopamine release in the medial preoptic area (a region in the hypothalamus), indicating that dopamine transmission may be relevant in increasing solicitation, which was reversed by administration of dopamine D1 receptor antagonist in this area. This suggests that melanocortin neurons make presynaptic contact with dopamine terminals and stimulate its release in this region (40).

Very recently, bremelanotide has been approved for the treatment of hypoactive sexual desire disorder in premenopausal women in the USA (41).

2.5 Others

Other hormones such as cortisol, thyroid hormones and growth hormone have been poorly studied for its effects on libido, making it hard to affirm with certainty about its effects, especially on women. However, patients with Cushing's syndrome, and therefore cortisol excess, have reported a decrease in sexual desire (42).

3. Testosterone and Libido

3.1 Testosterone

Testosterone is a sex hormone produced, in women, by the ovaries, the adrenal glands, and by conversion of androgenic steroid precursors, such as dihydroepiandrosterone (DHEA) and its sulfate (DHEAS). Levels of this hormone are individual among women and vary throughout their life, decreasing drastically after menopause and even more in surgically induced menopausal women (43). Testosterone in circulation can be bound to sex hormone-binding globulin (SHBG) or albumin or circulate freely, the latter being the biologically active one (44). So, it is easy to understand that the effect of the active testosterone depends not only on its production but also on the amount of binding molecules. Testosterone then binds to androgen receptors present throughout the body, namely in the hypothalamus and limbic system, and exerts its actions, one of them thought to be sexual desire.

It has been demonstrated that testosterone affects social behaviours, and sexual behaviour is a type of social interaction, therefore making it a reason for investigations on its effects on sexual function (45). Androgens may exert three different actions on the sexual cycle, the first one being increased susceptibility to psychosexual stimulation, inducing the "sexually activated mental state", common to a good libido; the second being an amplified sensitivity of the external genitalia, facilitating clitoral congestion; and the third being a boost of sexual gratification sensation (46).

In women, the relationship between testosterone and sexual arousal is still debatable. This doubt is in part due to the complexity of the endocrine system and its interplay with psychological factors involved in female sexual behaviour (47). Levels of this hormone have shown to be increased before and right after a sexual encounter, compared to cuddling and exercise in women, indicating that there are anticipatory effects of sexual activity on androgens (48). This demonstrates the impact of these factors in women's sexuality because anticipation of sexual activity seems to heighten the levels of testosterone before intercourse but not before non-sexual activities.

The effect of administered testosterone is still controversial. Some studies with intramuscular injection (49), oral administration (50), gel (51, 52), and transdermal patch (53, 54) have shown an increase in sexual desire in surgically or naturally menopausal women.

3.2 Dihydroepiandrosterone (DHEA)

Studies with DHEA treatments have also been conducted, seeing that it is an indirect precursor of testosterone, it would be expected to find a positive relationship between this hormone and libido. However, once again, results have been controversial. Gudmundur J. et. al., in his study on 38 women with androgen deficiency due to hypopituitarism treated with oral dehydroepiandrosterone, didn't find an effect on sexual interest and activity when compared to placebo, at least not with the tested dose (55), and Clayton Peixoto et. al. even found a negative effect with higher levels of DHEA related to lower sexual desire (56). On the other hand, Arlt W. et. al. when conducting their double-blind study on 24 adrenal insufficient women, found an improvement in well-being and sexuality with DHEAS replacement treatment, most likely due to the direct effect on the nervous system or an increase in peripheral androgen synthesis or both (57).

To conclude, as mentioned before, testosterone has an important role in controlling female sexual activity, yet the true impact on it could be wrongly estimated due to psychologic and affective systems strongly present in females (58).

4. Ovulatory cycle and libido

It has been hypothesized that the hormonal variations inherent to the ovulatory cycle exert physical and psychological effects, including sexual behaviour. Results have been disputed, nevertheless important to mention. Female studies on self reported sexual interest showed it increased days before ovulation (59, 60) with higher levels of sexual arousal (61), and sexual activity, libido and sexual fantasies also augmented around ovulation (62). In addition, one study even reported that women dressed better during their fertile phase (63).

4.1 Estrogens and Estradiol

Estrogens are associated to the perception of the female sex identity, of a satisfying sexual function and to the sensuality and seductivity that increases the quality of sexual relationships. So, when its levels decrease, a progressive loss of libido occurs concomitantly with the auto-perception of a desired entity (64, 65). Also, lack of estrogen causes vaginal dryness and pain that contributes to the inhibition of libido, which further stimulates the cycle.

High estradiol levels are associated with lower sexual desire, while sexual satisfaction was promoted by high levels of estrogen (66). However, when watching an erotic film, women showed an increase in salivary estradiol, which is associated to self-reported genital arousal, but not with genital arousal measured via vaginal pulse amplitude (67). Nevertheless, in other studies on fertile and postmenopausal women, estradiol was identified as an important positive predictor of sexual interest (68, 69).

4.2 Ovulatory Cycle

A study conducted on 97 women, with and without sexual partners, aged 18-40 years, with regular 25-35 day menstrual cycles, and otherwise healthy, who completed daily questionnaires each evening of their menstrual cycles, strongly supported the theory that even though women are receptive to sexual activity during their menstrual cycles, their sexual behaviour and sexual desire act in accordance at midcycle (59). An important observation for this hypothesis was made when abstinent women, therefore less likely to be influenced by the desires of the sexual partner, reported augmented libido and autosexual behaviour at midcycle, reflecting the physiological fluctuations in sexuality of women. Moreover, this study also concluded that, despite women's sexual orientation, they engaged in more allosexual activity around the time of their follicular and ovulatory phases, during the peak of luteinizing hormone (62), with a second, not as evident peak, premenstrually, in comparison to other days of the cycle.

Another study carried out during a 2 year period on women from five different countries found a positive link between reported sexual desire and intercourse and the basal body temperature, indicating an increase in libido around the ovulatory phase, which the authors consider to suggest that hormones contribute to the timing and/or extension of sexual desire (70).

During the fertile phase, heterossexual pair-bonded women tend to prefer partner characteristics of dominance, symmetry, and masculinity. They give greater importance to physical attractiveness of their sexual partner, report more arousal to male body features, and more interest in sexual encounters with masculine men during their follicular phase (pre-ovulatory), in comparison to their luteal phase (post-ovulatory). For instance, women when fertile, are particularly interested in visual sexual stimuli like the subtle flexion of the arm muscles of an attractive man, which makes attractive and muscular men particularly

interesting to women in a sexual way. However, if their sexual partner possesses these features, women don't feel particularly attracted to other men who also do, whereas if their partner does not possess them, attraction towards other men is common in the fertile phase (71). In addition, women adopt a more short-term mating strategy and pursue partners with good genes in the fertile phase, and adopt a more long-term mating strategy and pursue commitment during the non-fertile phase (14, 71).

A different study conducted on women during their follicular and luteal phases of the cycle showed that in the 24h after testing, women in the follicular phase reported more sexual fantasies and higher levels of arousal to erotic films (72), suggesting once again a predisposition to sexual behaviour in certain phases of the menstrual cycle.

4.2.1 Sexual Fantasies

Dawson S. and his team in another study investigated the role of the menstrual cycle in sexual fantasies and category-specificity of sexual interest using a hormonal measure to determine ovulation (73). As in the previous studies, sexual fantasies were more frequent during ovulation and the magnitude of arousal generated from it was also increased, which means that fantasies in the ovulatory phase are more arousing than in non-fertile phases. However, gender category-specificity of sexual fantasies did not increase. 48% of women were always category-specific across all menstrual cycle phases, reporting only male partner's involvement. The remaining percentage stated fantasies with both their preferred sexual partner (male) and non-preferred (female) partners. Nevertheless, regarding these fantasies, the investigators noticed no change in the number of females during the different phases, in contrary to the number of males which significantly increased during ovulation. Therefore, during the ovulatory phase, women report engaging in more fantasies that include their preferred sexual partners (73).

4.3 Emotional State

On a different note, a relationship between emotions and women's sexuality has also been found. Sexual desire was related to positive affect, although both varied in regards to allosexual behaviour. Libido, exclusively, was positively related to allosexual behaviour, whereas positive affect exclusively, was negatively related to allosexual behaviour. This supports the hypothesis that these two systems are involved in women's sexual behaviour in different ways: one involving sexual arousal and mating behaviour and the other involving affection and attachment behaviour. The authors of this study conclude that this fact helps explain the emotions and motivations involved in sexual desire, since sometimes libido is positively related to sexual behaviour and, concomitantly, negatively related to attraction. (59) This duality had also been shown in a study that found that women in relationships with sexually less attractive men, were more likely to feel attracted to other men in the ovulatory phase (libido and affection acting independently) but not during the rest of the cycle (libido and affection acting together) (74).

Studies conducted in this field highly suggest an important role of the different phases of the ovulatory cycle in sexual behaviour and activity, especially in sexual desire. These fluctuations are possibly due to variations in hormonal levels, which are known to occur throughout the cycle.

5. Menopause and Libido

The menopausal transition is a change in psychosocial and biological factors, that undeniably affect the sexual life of a woman. These factors vary from the presence of physical or psychological ill health, to the existence of a sexual partner, to partner's age and health, to employment and even to negative attitudes toward menopause (75). In fact,

relationship with the partner has particularly powerful effects. It is well documented that during menopause, there's a drastic reduction in the levels of sex hormones, which leads to physiological alterations of the female body during the sexual response cycle, such as reduction in vaginal lubrication. Various studies stated a decrease in sex drive in menopausal women, both naturally and surgically induced, which doesn't seem to be due to a decrease in androgen levels (58, 68). The amount of biologically active, which means free testosterone, is actually increased throughout the transition, due to a decrease in DHEA levels, which makes it unlikely to be the cause of a reduced sexual function (75).

A study conducted in Australian-born women aged 45-55 years who lived in Melbourne, concluded that 42% of them in the early menopausal transition indicated sexual dysfunction compared to 88% of postmenopausal women at year 8 of follow-up. Correlation between androgen levels and decreased sexual function was not established, however low estradiol levels and decline in estradiol was related to a decline in SPEQ (Short Personal Experiences Questionnaire) levels which translates in a decline in sexual function (68). A different study conducted on the same sample of women reported a decrease in frequency of sexual activities and libido in postmenopausal women, that may be related to the increase in vaginal dyspareunia typical in the postmenopause period.

In addition, hot flashes which are frequently felt by women in this transition, also impact quality of life, including sexual functioning. These hot flashes are a trigger for insomnia, which consequently reduces energy, having a negative impact on sexual function (75, 76). Tiredness, mood changes and anxiety, all symptoms of menopause, may as well contribute to loss of libido (68, 75).

Conclusion

Sexual desire is a pivotal component in sexuality and a fundamental characteristic in sexually active or sexually interested individuals. Women often struggle with lack of libido, which greatly diminishes the quality of life. Thus, comprehensively studying the biological factors underneath it would greatly increase the knowledge and possible future therapies for disorders of this nature. However, because sex drive is a combination and an interplay between various elements, the biological determinants, although of great importance, are hard to isolate and truly investigate. Psychosocial factors and current circumstances deeply affect libido and may even be the main problem in these disorders, making them an important target of therapy as well.

Competing Interests

The authors declare no existing competing interests.

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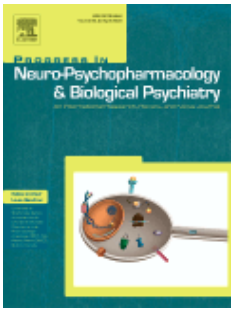

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Confirmation of the functional consequences of a common disease-associated variant is useful information, but does not substitute for a rigorous demonstration of a statistically significant association. Analysis of pathways or candidate regional analysis is encouraged over single gene studies. Candidate gene studies must have strong positional or biological rationale or precedents in the literature that motivate gene choice.

For studies of non-functional variants, there should generally be sufficiently dense marker coverage to allow a relatively comprehensive analysis of common variants within a gene or genes. Analysis of the extent of marker coverage using standard methods to assess linkage disequilibrium should be presented. If rare variants are being tested, the same method of assessment (sequencing, copy number assessment, etc.) should be used in both case and control groups.

We will consider both negative and positive association studies, as well as large replication studies. Negative studies should be based on an attempt to replicate previous studies. Power calculations considering reasonable effect sizes must be provided to show that the study had sufficient power to be informative.

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