

EDITORIAL



Hormones and sexuality: navigating the complex terrain of the interplay between endocrinology and sexual function

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Exciting advances in the field of the endocrinology of sexuality are continuing to shed light on the multifaceted nature of human sexual function and its profound implications for individual health and well-being.

The effect of thyroid hormone derangements on sex life has been the topic of well-designed population-based and prospective controlled cohort studies in the last decade. The interest hinges on the fact that thyroid disorders, besides being quite common in the general population, can also affect sexual function both in males and females. In this special issue, Morenas et al. [1] carried out a comprehensive review of the literature on this intricate relationship published from 1963 to 2022, elucidating how hyperthyroidism and hypothyroidism disrupt various aspects of male sexual health. In hyperthyroidism, male sexual dysfunction may result from mood disorders, including anxiety, up-regulation of the β -adrenergic receptor density, impaired generation of cavernous penile nitric oxide (NO), and reduction in bioavailable testosterone with relative hyperestrogenism due to increased levels of sex hormone binding globulin (SHBG) [2]. Building upon this exploration, Cihan and Esen [3] emphasized the reversible nature of these mechanisms, quantifying, in their meta-analysis, the prevalence and treatment outcomes of sexual dysfunction in men and women with hyperthyroidism. Among men with hyperthyroidism, the prevalence of erectile dysfunction (ED) was confirmed to be notably higher compared to healthy controls, with an odds ratio (OR) of 9.16 (95% CI: 5.0, 16.5). Of note, treatment of hyperthyroidism alone led to improvements in erectile function, along with an increase in mean intra-vaginal ejaculation latency time (IELT) and a significant decrease in the prevalence of premature ejaculation (OR: 0.11; 95% CI: 0.04, 0.28). Similar findings concerned the relationship between hyperthyroidism and female sexual dysfunction. Moving to the opposite pole of thyroid dysfunction, Morenas et al. [1] also described how a deficiency in thyroid hormones can result in both psychic (fatigue, depressed mood) and metabolic/cardiovascular disorders (metabolic syndrome), exerting detrimental effects on sexual health. Furthermore, hypothyroidism can directly disrupt the regulation of the hypothalamus-pituitary-gonadal axis, resulting in reduced circulating levels of sex hormones [2]. Part of this complex relationship involves a dysregulation of prolactin (PRL) secretion. Thyrotropin releasing hormone (TRH) can exert a nonspecific effect in stimulating the release of PRL that, in turn, results in the suppression of gonadotropins: in primary hypothyroidism, the lack of negative feedback by thyroid hormones on TRH secretion leads to both increased circulating levels of thyroid stimulating hormone (TSH) and hyperprolactinemia (HPRL).

The study by Corona et al. [4] outlines the framework of HPRL and its correlation with male sexual desire and ED by employing a dual methodological approach, meta-analytical and observational clinical analysis on a series of 4215 men consulting for sexual dysfunction. Clinical and meta-analytic data confirmed a stepwise negative influence of PRL on male sexual desire, whereas the relationship between HPRL and ED has proven to be more uncertain, partly mediated by the lowering of testosterone levels and/or to the reduction of sexual desire itself. Noteworthy, treating HPRL with any means was associated with a restoration of sexual desire, with a lesser effect on erectile function.

Overall, although thyroid dysfunction and HPRL can affect sexual health in different ways, both highlight the importance of hormonal balance, from the hypothalamus to the peripheral organs, in regulating sexual responses and behavior. Indeed, the neuroendocrinology of sexual behavior remains an extremely stimulating field of research and is the topic of the paper by Ågmo [5]. Gonadal hormones play a key role in attraction to sexual stimuli and in the execution of motor patterns necessary for genital stimulation, albeit with significant differences between species. In female rodents, the pivotal role of estrogen is demonstrated. These hormones, acting on hypothalamic estrogen α receptors, in the presence of tactile stimuli from the male, control lordosis behavior, which is essential for mating and occurs only during a short period of the estrous cycle. The activation of estrogen receptors, other than androgen receptors, is also necessary in male rodents for the maintenance of sexual behavior. On the contrary, in humans and other primates, the control of female sexual behavior by ovarian hormones appears to be less stringent, and androgens would be the main endocrine mediators of sexual motivation and desire in both males and females. Studies on rodents and non-human primates have also provided valuable insights into the possible brain sites involved in the control of sexual behavior, a topic that still remains largely unknown.

The importance of the complex regulation that hormones exert on sexuality can be inferred not only from the clinical features of endocrine disorders such as hypogonadism, thyroid disease, and HPRL, but also from physiological conditions, such as pregnancy, and from iatrogenic models, including gender affirming hormone therapy (GAHT) in transgender people.

Pregnancy is one of the most challenging phases in a woman's life, featured by deep changes exposing to psycho-physical adjustments that affect the couple's needs [6]. Overall, sexual function tends to decline during pregnancy [7] when nearly half of women experience sexual dysfunction [8]. The genesis of this phenomenon lies in a complex interplay between hormonal, psychological, relational and social factors. In particular, anxiety, which is a common symptom during pregnancy [9, 10], can contribute to the impairment of sexuality [10]. Within our special issue, Khanjari et al. [11] delved into the topic of pregnant

women's sexuality. Through a randomized clinical trial, they unveiled the potential of omega-3 supplementation in reducing gestational anxiety and improving overall sexual function among pregnant women. The study also discussed potential mechanisms behind these findings, including improved blood flow, especially in the pelvic organs, anti-inflammatory effects, and mood enhancement associated with omega-3 intake. While promising, further research with larger sample sizes is warranted to confirm these results.

While extensive research has been conducted on sexual function in cisgender individuals, understanding and addressing the sexual health and its relationship with endocrine profile and interventions in transgender people presents unique challenges and considerations. Before undergoing GAHT, transgender individuals may experience dysphoria and dissatisfaction with their sexual lives due to incongruence between their gender identity and assigned sex [12]. Hormone therapy and gender-affirming surgeries (GAS) play a pivotal role in aligning physical characteristics with gender identity, with deep implications for sexual function and satisfaction. The review by Marinelli et al. [13] dealt with sexuality of transgender individuals assigned female at birth (t-AFAB) seeking gender affirming care. In this population, testosterone based GAHT leads to physical changes, such as the development of male secondary sexual characteristics, clitoral growth, as well as changes in sexual desire and arousal [14, 15]. GAS, aimed at further aligning an individual's physical appearance with the gender identity, can have profound effects on body image, self-esteem, and sexual satisfaction [12]. However, the impact of gender-affirming treatments on sexual function is complex and multifaceted. While some studies suggest improvements in sexual satisfaction and functioning following GAHT and GAS [12, 14, 15], others highlight clinical challenges such as sexual pain [16]. Additionally, the decision to undergo gender-affirming treatments and the outcomes of these interventions can be influenced by various factors, including personal preferences, cultural norms, access to healthcare, and social support. Moving forward, further research is needed to better understand the impact of gender-affirming treatments on sexual function and satisfaction in transgender individuals. This includes the development of specific tools and measures for assessing sexual health and its determinants in this population. By addressing these gaps in knowledge, healthcare providers can adopt a holistic approach to address the sexual well-being of transgender individuals, considering their unique experiences, needs, and goals.

Overall, this special issue provides an overview of the intricate interactions between hormones and sexual function. The view can only be partial, given the complexity of the topic, but the outlined landscapes extremely stimulating. From thyroid dysfunction and prolactin regulation to pregnancy and hormone therapy for gender transition, the papers presented here give us a sense of the many ways in which hormones affect human sexual health. These studies not only underscore the importance of optimal hormone balance for healthy sexual function, but also the need for a deeper understanding of the underlying mechanisms and clinical implications of these interactions. We hope that this special issue will stimulate further research in this field, thereby contributing to improving the quality of sexual and overall life of our patients.

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COMPETING INTERESTS

The author declares no competing interests.