Human sexuality and sex steroids

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Abstract

Studies on human sexuality are considered to be extremely difficult. Moreover, their results appear often unclear and contradictory. Sexuality is perceived as the identity, feelings and behavior associated with sex. Different assumptions concerning its mechanisms are made by researchers in the field of neuroendocrinology, endocrinology and psychology, and their tests' results help to describe human sexuality. Since the second half of the XXth century efforts of describing sexuality have been made, but they are still imperfect. There are no current research methods which allow for separation of sexual functions or sex-related behavior in a human, and for their description. It should be remembered, however, that the very awareness of taking part in such examination can have meaningful impact on the tests' results. What is more, the patient's emotional state can also alter the results. In this paper, current results on sexual steroids' place in forming human sexuality and its role in an adult human being life are presented. The cognition of the complete role of testosterone, estradiol and progesterone in forming human sexuality is considered to be the challenge for researchers in the following years.

REVIEW

INTRODUCTION

The concept that hormones, first androgens, influence behavior can be traced back over 2000 years ago, to Aristotle, who observed it in his biological treatise Historia Animalium (cf. Rubinow and Schmidt, 1996). At present, scientists while studying nonhuman primates, manipulate with hormones during early development, and determine the results of these manipulations on sex-related behaviors. For ethical reasons, such experiments on human beings cannot be carried out, as the hormone levels cannot be altered during fetus' early life and in pregnant women (Hines, 2003).

The physiological observation of sexual responses constitutes a precious medical contribution to research about human sexual behaviors. A gynecologist William H. Masters and a psychologist Virginia E. Johnson are most closely associated with this approach. In the 1950s they pioneered research on the nature of human sexuality and published two classic books *Human Sexual Response* and *Human Sexual Inadequacy* in 1966 and 1970, respectively. In these books, not only the first comprehensive description of how men's and women's bodies perform during sexual behavior has been presented, but also the diagnosis and treatment of sexual dysfunctions have been described (Masters and Johnson, 1966, 1970). The neural control mechanisms that mediate sexual arousal and sexual behavior have also begun to be put forward by neuroscientists in the twentieth century. The issue of how sex was determined and what possibly could go wrong with this process has been explored by geneticists (cf. Kula and Slowikowska-Hilczer, 2000, 2003; Levay and Valente, 2006).

The close relation and the full connection between certain parts of human sexuality is confirmed by present day' research results from the field of neuroendocrinology, endocrinology, genetics, and psychology. This close relation among these filds of science is of basic importance in interpersonal relations, human reproduction, and the feeling of quality of life.

WHAT IS HUMAN SEXUALITY?

At the beginning, the meaning of word 'sex' was restricted only to the description of human sex on the basis of lack or presence of the external genitalia, what resulted in the official record: male or female. Now, however, this definiton describes sexual behaviors and differences between men and women, including anatomical and physiological differences between sexes.

Till the half of the twentieth century, sexual activity had been identified only as the appearance of sexual excitement at men, manifesting in occurrence of the penis erection (Bancroft, 2005; Levay and Valente, 2006). After doing the research on human sex-related behaviors, presenting the whole range of appearing mechanisms and manifestations, as well as its role in human's life, the new definition of homo sapiens' species sexuality has arised. At present the human sexuality is being defined as: the feelings, behaviors and identities associated with sex (Fig. 1). Identity is understood in the sense of self-labeling or group affiliation (Levay and Valente, 2006).

It must be remembered that the term 'sexual arousal' referring directly to sexual behavior is not only genital response at men. It involves activities taken up and occurring as changes resulting in the organism, guided towards feelings of sexual arousal, sexual pleasure and probable orgasm.

Human behaviors show individual differences in sexual behavior. Two levels of organization of the sexual phenotype can be distinguished. The first organization is the process of sexual differentiation that is guided by gonadal determination, and the morphological, physiological and behavioral aspects of the sexual phenotype are manifested in this way. Directly related to the above organization, there exists also the second, subsequent level of organization. It constitutes the basis of individual differentation in sexually dimorphic behaviors (Pardridge, 1982; Crews, 1998; Kula and Slowikowska-Hilczer, 2003). Behavioral endocrinologists have concentrated on the problem of sexual differentiation and virtually ignored the problem of individual differences (Crews, 1998).

It is more difficult, however, to establish hormonal influences on human behavior than hormonal influences on the external genitalia (Hines, 2003). Hormones are not the only determining factors, although the development of children's interest in sex-typed toys and activities is influenced by hormones, particularly androgens (Crews, 1998; Hines, 2003).

The role of sex steroids in influencing sexual arousal, orgasm, sexual arousability and the post orgasm inhibition of arousability will be reviewed in this paper (Bancroft, 2005).

WHY DO MALE AND FEMALE DIFFER SEXUALLY?

All biological sex differences are initiated by genes encoded on the sex chromosomes.

SRY, the testis-determining gene is a critical gene on the human Y chromosome. Owing to this gene, the embryonic undifferentiated gonad develops into a testis rather than an ovary.

This developmental process has the crucial impact whether a human being is phenotypically male or female (Becker *et al*., 2005; Goto *et al*., 2006; Levay and Valente, 2006). DAX-1, another crucial gene relating to sexual differentation, is located on the X chromosome. According to the latest research' results, it appears that SRY works in contradistinction to DAX-1 (Levay and Valente, 2006).

The embryonic testes secrete three hormones: testosterone, Mullerian-inhibiting hormone, and IGF-3 (Becker *et al*., 2005; Goto *et al*., 2006). Masculine features are caused by testosterone, which acts on the urogenital primordia resulting in formation of a penis rather than clitoris, and a scrotum rather than vaginal labia (Becker *et al*., 2005; Goto *et al*., 2006). Male and female external genitalia develop from the same precursors (Levay and Valente, 2006).

SRY and testosterone have also an indirect impact on the possible background to be experienced by a young person. Soon after sex determination, a baby boy or a girl is treated differently, according to their sex (Becker *et al*., 2005; De Vries, 2005; Levay and Valente, 2006).

After the gonad starts to differentiate into a testis or an ovary, the developmental process of sex differentiation of the fetus takes place. The gonadal ridge is a thickening on the primitive me neighbouring to what will become the adrenal cortex (Warne and Kanumakala, 2002). Sexual differentiation of the external genitalia is a fundamental aspect of human development, tied by the phenotype of CYP 21 (P450 21-hydroxylase) deficiency to the fetal adrenal cortex (Warne and Kanumakala, 2002; Goto *et al*., 2006).

Watzka *et al*. (1999) demonstrated for the first time an age and sex dependent expression of CYP11A1 mRNA in different regions of the human brain. They showed that the expression levels are low in children and reach adult levels at puberty. Moreover, they are higher in the cortex of women than of men.

Goto *et al*. (2006) show that cortisol was synthesized by the human fetal adrenal cortex much earlier than it had been previously believed, an effect associated with transient expression of the orphan nuclear receptor nerve growth factor IB-like (NGFI-B) and its regulatory target, the steroidogenic enzyme type 2 3-beta-

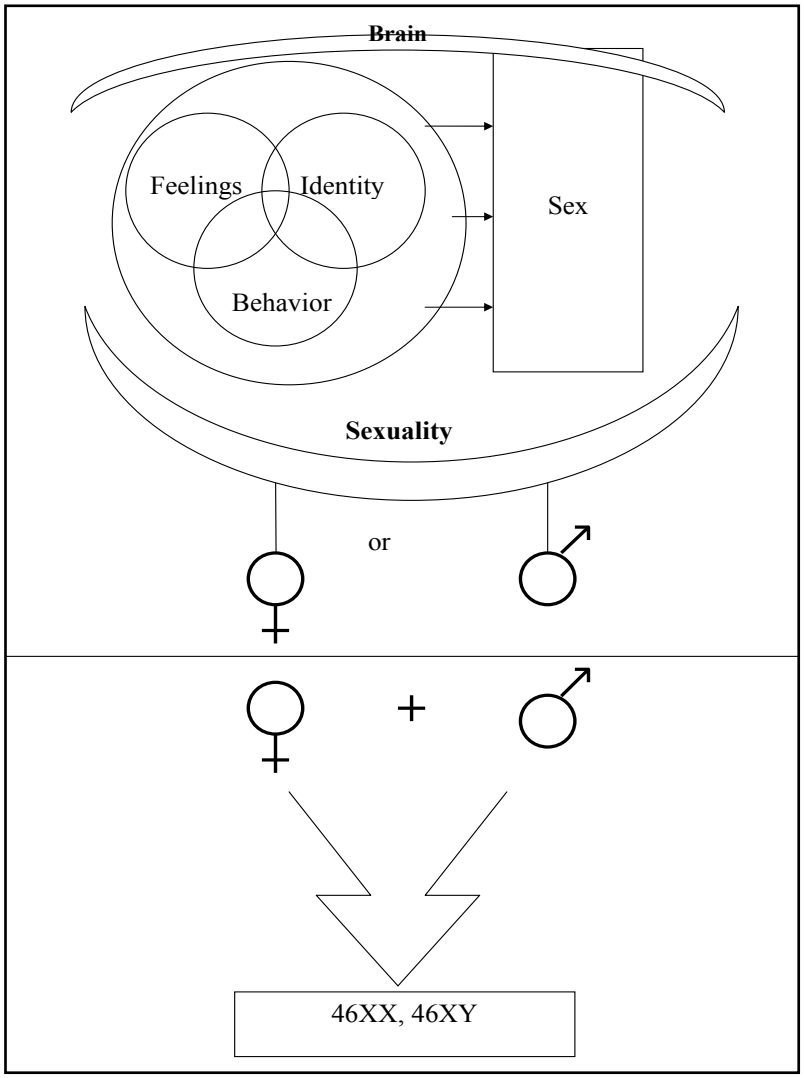

Fig. 1. ***Human sexuality***

hydroxysteroid dehydrogenase (HSD3B2). Under the stimulated adrenal gland to secrete androstenedione and testosterone, the cortisol biosynthesis was maximal at 8–9 week post conception. Taking to account these data, a distinctive mechanism for normal human development whereby cortisol production, determined by transient NGFI-B and HSD3B2 expression is presented, providing feedback at the anterior pituitary to modulate androgen biosynthesis and protecting normal female sexual differentiation (Becker *et al*., 2005; Goto *et al*., 2006).

In humans, early cortisol biosynthesis provides a mechanism to safeguard female sexual development.

DO FEMALE AND MALE BRAINS DIFFER ANATOMICALLY AND MORPHOLOGICALLY?

Human brains show sex differences in the volume of several brain structures, including the corpus callosum (De Vries and Boyle, 1998) anterior commissure, the left planum temporale, and several nuclei in the hypothalamus and (bed nucleus of the stria terminalis – BST). Additionally, some neurotransmitter systems are sexually dimorphic. These differences are mainly connected with differences in behavior, which can be normanlized by them, e.g. differences in cognitive abilities are associated with difference in the cortex, or differences in sexual behavior and sexual orientation are related to differences in the hypothalamus and associated telencephalic nuclei (Fitch and Denenberg, 1998; De Vries and Simerly, 2002; Bartels and Zeki Semir, 2004). Fundamental differences in the organization of cortical and subcortical areas function were evident in functional MRI (De Vries and Boyle, 1998; Bartels and Zeki Semir, 2004; Cahill, 2005).

The region of human brain commonly referred to as the amygdala communicates via fibers of the stria terminalis to the BST. The amygdala is intimately involved in sex and sexuality. It is important to note that the male amygdala is slightly bigger than that of the female (Cahill, 2005; Salamon *et al*., 2005). Most sexual dimorphic brain features, even if they are dependent on sex steroids' influence, have the character of constant

differences and cannot be inverted by introducing hormonal stimuli, therefore they show a sign of the actual sexual differentiation (Kula and Slowikowska-Hilczer, 2000, 2003; Skalba, 1998).

The hormonally triggered dimorphism constitutes the current hypothesis to explain the sexual dimorphism of structure and function in the brain of vertebrates. According to this hypothesis, the epigenetic action of gonadal hormones is responsible for sexual dimorphism in the brain of vertebrates. To be more accurate, the exposure to androgens during a critical period of brain development is responsible for the male-type circuitry, while the female one results from the absence of testicular secretions regardless of chromosomal sex. Circulating testosterone in human beings shows two peaks. The first one appears in the second trimester of gestation and the second one in the first year of post –natal life (Rubinow and Schmidt, 1996; Benvenga, 2005).

In Holland, the research on postmortem brain material, obtained by autopsy, from different groups of people, was carried out by Krujver and colleagues. Among these groups were the following: homosexual and heterosexual men and women, transsexuals, aged castrated and noncastrated men. Thus heterosexuals, homosexuals and transsexuals' brains were examined (Kruijver *et al*., 2001). Both, structural and functional differences between the sexes, and between homosexual and heterosexual men have been described in many areas of the human hypothalamus. In addition, it has been found by Krujver and colleagues, that the central part of the bed nucleus of the stria terminalis (BST) is sexually dimorphic, i.e. smaller in women, with a female volume and neuron number in male-to-female transsexuals. Different areas of the preoptic area (POA), bed nucleus of stria terminalis (BST), and suprachiasmatic nucleus have been proved to be greater in men that in women, while the anterior commissure was found to be the opposite.

Also hypothalamic differences have been undergiven observation in connection with sexual orientation. Furthermore, the suprachiasmatic nucleus and the anterior commissure have been observed to be larger in homosexual than in heterosexual men, whereas the interstitial nucleus of the anterior hypothalamus is smaller in homosexual than in heterosexual subjects (Kruijver *et al*., 2001; Monvada, 2006).

This huge load of information and plentiful data confirming that sexual orientation and gender identity do not differ with adult endocrine changes shows that precise analysis of great amount of brain areas is a necessary condition to understanding the biological basis of sex differences, sexual orientation, or gender identity (Kruijver *et al*., 2001; Kula and Slowikowska-Hilczer, 2000).

HOW DO SEX STEROIDS INFLUENCE THE SEXUAL DIFFERENTIATION OF THE BRAIN?

Testosterone masculinizes the brain permanently by acting during early critical periods of neuronal development. When testosterone concentrations are low, as occurs typically in genetic females, the development of the brain is feminine (Becker *et al*., 2005).

Sex steroids are connected with the tissue characteristic for themselves by the means of a receptor. There are three different kinds of sex steroid receptor molecules, named the androgen receptor, estrogen receptor, and progestin receptor (Levay and Valente, 2006). The androgen receptor (AR) is a member of the nuclear receptor superfamily. It is localized in both the cytoplasm and the nucleus of cells in all tissues of the body, but is present in higher concentrations in tissues of the external genitalia and other androgen target tissues, and acts as a transcription-regulator (Warne and Kanumakala, 2002). Androgen receptor (AR) immunoreactivity (AR-ir) in a number of hypothalamic areas in men has been lately founded to be stronger than in women. What is more, in the anterior hypothalamus only moderate sex differences were found, whereas a conspicuous sex difference appeared in the posterior hypothalamus, i.e. the medial mamillary nucleus (MMN) and lateromamillary nucleus (LMN) of the mamillary body (MB) complex (MBC) (Kula and Slowikowska-Hilczer, 2000; Bancroft, 2005). Clear sex differences in nuclear AR-ir expression in neurons of the MBC were confirmed in studies of Kruijver *et al.* (2001). It was shown, for the first time, that circulating levels of testosterone are responsible for this sex difference rather than sexual orientation or gender identity.

Until 1996 only the estrogen receptor (ER-alfa) was known, although abundant in the uterus and the hypothalamus, it was sparsely scattered in other non-reproductive organs and regions of the brain. Later, the second receptor, ER (beta) was discovered. It is considered that the mRNA for ER-beta is more widespread than for ER-alfa. It can be found in the cerebral cortex, hippocampus, and the cerebellum, as well as in the cardiovascular and immune systems and other tissues (Fitch and Denenberg, 1998; Melton, 2000). Estrogen and androgen receptor mRNA containing neurons are not limited to the hypothalamus, but are distributed throughout the adult human brain (Hulshoff *et al*., 2006).

Estrogen-androgen-related signaling molecules medicate amygdale regulation of the male and female sexual cycle. Also ovulation and sexual behavior is respectively influenced by them via coupled NO release (Salamon *et al*., 2005).

Two studies in teenage boys were carried out by Udry and colleagues to study testosterone levels in relation to various aspects of sexuality. In the first a cross-sectional study (Udry *et al*. (1985), an important factor predicting sexual motivation was proved to be the free tes-

tosterone index, while it was impossible to predict the stage of pubertal development. Interestingly enough, in the second Halpern *et al*. (1993), a longitudinal study over 3 years, with 6-monthly assessments, quite opposite state of matters was confirmed. According to this study, it was much easier to predict of sexual interest and behavior the stage of pubertal development than the free testosterone index. This obvious contradiction can be only explained in one way- the influence of testosterone on sexual arousability (and hence behavior) undergoes different stages of development, thus involving changes in receptor numbers or sensitivity, therefore individual differences in receptor sensitivity will also influence this process.

Gooren (1988), in a study of hypogonadal teenage males, found that boys with primary hypogonadism showed less response to testosterone replacement than boys with secondary hypogonadism.

Basing on research on nonhuman vertebrate brain, it is believed that an important role in human brain development (organizing effects) is played by the interaction between sex hormones and their receptors. Moreover, the adulthood brain function (activating effects) can be altered by them, and these two mechanisms are the causes for sex differences in behavior in the adult life. Both, structural and functional sex differences in the brain can refer to reproduction, sexual orientation and identity (i.e. the feelings of being male or female), cognition and disease (Pardridge, 1982; Kula and Slowikowska-Hilczer, 2000, 2003; Melton, 2000).

HOW DO DIFFERENT SEXUAL BRAINS DEMONSTRATE DIFFERENT HUMANS' SEXUAL BEHAVIORS?

The sexual behavior of a human being in an adult life and anatomical differences between brains of males and females results from differences in levels of hormone during pregnancy (Levay and Valente, 2006).

In men and women, the sexual activity consists of four phases which are guided by sexual desire (libido). The first phase (initial excitation), continues with a phase of constant excitation (orgasm). After a resolution phase (return to normal), a new cycle is ready to start. Male sexual activity is characterized mainly by erection, seminal emission and orgasm (ejaculation).

Female sexual activity is characterized by vaginal lubrication, clitoris erection and orgasm.

Numerous circuits of central end peripheral nervous system controls dimorphism in sexual activity. During embryogenesis, a sex-specific development of some brain structures starts. Sexual desire and arousal of a normal adult male depends on levels of androgens but a necessary condition is an organizational effect of androgens on the above structures of the hypothalamus and limbic system early in the fetal development (Benvenga, 2005).

The crucial role of testosterone in sexual differentiation, both in early development and around puberty cannot be denied, but the influence of testosterone on the appearance of sexual arousability has not been investigated. It is not known however, if the structures of human brain in an adult life can be altered by changing sex hormone levels (Hulshoff *et al*., 2006).

TESTOSTERONE IS A SEX HORMONE IN BOTH MEN AND WOMEN

Testes, ovaries and the adrenal cortex secret testosterone in both men and women. Hormones are presented at different levels in the blood, and a more masculine or a more feminine appearance is a result of these differences (Levay and Valente, 2006).

A period of withdrawal was used as a baseline by most controlled studies of testosterone replacement in hypogonadal men. The administration of testosterone and placebo followed this, using a double-blind crossover design (Bancroft *et al*. 2003). A decrease in the level of sexual interest during testosterone withdrawal is shown in these studies, usually recognizable within 3 to 4 weeks, together with testosterone as a necessary condition for an average level of sexual interest and arousability. If a period of testosterone withdrawal is long enough, seminal emission will eventually be weakened. In such male studies, sexual interest and arousability is restored by testosterone replacement, and placebo has only a small effect.

Psychophysiological studies showed significantly more rigid and longer duration erectile responses with testosterone replacement (Bancroft, 2005). These response would not only show greater rigidity, but would also last beyond the sexual stimulus (Carani *et al*., 1995.

For a healthy man with proper sexual function, nocturnal penile tumescence (NPL) is a characteristic feature, neurophysiology of which is under discussion. NPL is the occurrence of spontaneous erection during rapid eye movement (REM) sleep. The noradrenergic cells in the locus ceruleus are 'switched off' during REM sleep. They are probably connected via their spinal projections with inhibitory tone in the penis. This assumed 'excitatory tone' in the locus ceruleus is regarded to be dependent on testosterone receptors' appearance (Parmeggina and Morrison, 1990).

The effects of exogenous testosterone on NPT in eugonadal men were evaluated by Carani *et al*. (1995). Intramuscular testosterone enanthate neither affected frequency, degree or duration of NPL nor had any effect on sleep parameters, when assessed as penile circumference, they enlarged,however, more or less significantly, penile rigidity during NPT.

It was recommended by Buvat and Lemaire (1997) that in men under 50 years of age, serum testosterone should only be measured in case of an associated loss of sexual interest. Moreover, basing on a large clinical se-

ries, they also claimed that in men over 50 years of age, with ED, testosterone should be measured in all cases.

It cannot be denied that testosterone plays an important role in sexual interest and associated sexual arousability in men who have gone through normal puberty and who have not yet been affected by effects of aging. The effects of testosterone on central arousal mechanisms are confirmed by this evidence, whereas the peripheral effects of testosterone in the human male, important for sexual arousal, still remain unclear. The research also shows that in the circulation, the levels of testosterone are higher than needed to maintain sexual arousability. That is why, most probably, in the periphery other effects of testosterone require higher levels than are necessary in the central nervous system.

It is still not well known what is the role of testosterone in the emerging sexual arousability of the peripubertal male. Different aging effects, such as altered hypothalamo-pituitary feedback, increased testosterone binding and reduced receptor sensitivity, also complicate the picture in case of the older male (Bancroft, 2005). Shortage of physical capabilities, lack of energy, impaired memory and impaired sex-life can be improved by testosterone replacement therapy (Moncada, 2006).

The effect of testosterone variation within the normal range on mood has remained unclear up till now. It is quite difficult to measure the possible effect of testosterone owing to the fact that some cerebral functions can also be modulated by estradiol (produced by the aromatization of testosterone) and these effects must be separated from the effects of testosterone (Zitzman, 2006).

Two hypogonadal men, assessed with functional magnetic resonance imaging in their response to sexual stimuli, with and without testosterone replacement,were being reported on by Park *et al*. (2001) Testosterone replacement caused greater activation of the inferior frontal lobe, cingulate gyrus, insula and corpus callosum in both men.

Positron emission tomography scan evidence of brain activity during response to sexual stimuli was compared by Redoute *et al*. (2005) Nine hypogonadal men with and without testosterone replacement and eight eugonadal men were put to the examination. Greater activation was found in the controls and the treated hypogonadal men than the untreated, in the right orbitofrontal cortex, insula and claustrum. Also in the controls and treated patients deactivation of the left inferior frontal gyrus was found, suggestive of reduced inhibition of sexual arousal.

Certain components of sexual function are clearly androgen-dependent in the human male. Testosterone treatment restores sexual desire, sexual thoughts, intensity of sexual feelings, and sexual activity reduced in hypogonadal males. The frequency, duration, and magnitude of spontaneous and nocturnal erections, impaired in hypogonadal men, are increased by testosterone treatment. However, it appears that androgen does not cause erections in response to erotic stimuli. Additionally, androgen dependence works as a threshold level, below which libido (sexual interest and arousal) and sexual function are weakened and above which they are not, with no connection between either the ideational or erectile components of sexual function and testosterone levels in the normal range. Thus, increasing androgen levels does not remedy disturbances of libido and erectile function in men with normal gonadal function, and in young men, self-reports of sexual interest or spontaneous erections are not increased due to increasing testosterone (Rubinow and Schmidt, 1996).

Erectile physiology is directly connected with testosterone. Central mechanisms including libido and neurological signals that travel down the spinal cord to exert their effect on the penis are stimulated by testosterone. It also affects the peripheral mechanisms of erectile function, including endothelial production of nitric oxide and endothelial-independent mechanisms that still need explanation. Erectile function does not involve aromatization to estradiol, but it is probable that dihydrotestosteron is the active metabolite responsible for the effects on erectile function (Guay, 2006).

ARE ANDROGENS IMPORTANT IN WOMEN SEXUALITY?

Examination of sexual hormonal dependence in women is more difficult than in men, because sexual arousal constitutes a part of a period cycle syndrome and the endocrinology of reproduction, pregnancy and lactation. It also changes with the age. That is the reason why observations obtained from examinations are often contradictory and unclear. Global loss of sexual desire, decreased sensitivity to sexual stimulation in the nipples and in the clitoris, decreased arousability and capacity for orgasm, loss muscle tone, diminished vital energy, thinning and loss of pubic hair, and dry skin are the symptoms of androgen deficiency (Dennerstein, 2001).

The infant girl has a low level of testosterone, and doubles it through pubertal maturation, compared with an 18-fold increase in testosterone for boys. Udry *et al*. (1986) provided the most important evidence of the relationship between testosterone and emerging sexual arousability in females. According to their studies on adolescent boys, discrepant results between their cross-sectional study of eight to tenth grade girls (approximately 13–15 years of age) were found, showing a relation between testosterone levels and measures of sexual interest and masturbation. It was not connected, however, with experiencing sexual intercourse**.** Moreover, the reverse relation was found in their longitudinal study of girls post-menarche Halpern *et al*. (1997).

The connection between testosterone level and sexuality through the cycle is being described in very few papers, which often do not agree. The possilble explanation for this may be the research' methodology and

lack of objective measures to examine the complexity of the aspects of human sexuality (Bancroft, 2005). Also substantial individual variability in testosterone/behavior relationships may be responsible for these inconsistent findings, involving studies with relatively small numbers of participants.

The timing of the effects of an increase in testosterone on sexual arousal is being described by only one study. The influence of testosterone on women's sexuality was tested on the group of eight healthy women with normal testosterone levels. Sublingual doses of testosterone were given to them in a placebo-controlled experiment. Genital response to erotic stimuli occurred in 3–4 h after the peak increase in plasma testosterone (Tuiten *et al*. 2000). According to these results cyclical variations in testosterone levels in plasma are manifested as cyclical patterns of sexual interest and/or responsiveness.

In women, both a positive connection and the lack of a correlation between testosterone levels and sexual interest and behavior have been observed. Similarly libido is increased by androgen replacement therapy in women who are androgen-deficient (e.g. after surgical menopause) but sexual arousal or behavior is not affected in naturally menopausal women (Rubinow and Schmidt, 1996).

Treating women who lack estrogen with testosterone alone would cause the increase of the already existing high ratios of androgen to estrogen. There is not enough safe or efficacious data for testosterone supplementation for estrogen-deficient women (Basson, 2006; Margo and Winn, 2006).

Testosterone withdrawal and/or replacement has been proved to have effects on women's sexuality, but the evidence is not clear and sometimes contradictory. One obvious reason for this is that women differ in the extent to which testosterone influences their sexuality and several examples of evidence supporting this have been presented. It is also becoming more and more well understood that mood, energy and well-being, as well as other psychological mechanisms powerfully influence the sexuality of women. This might be the reason why, in several studies of younger women, the correlation between testosterone and sexuality was most visible in women without problematic sexuality (Bancroft *et al*., 1980; Tuiten *et al*., 1996; Riley and Riley, 2000).

Although testosterone can play a role in the sexuality of many women, it must be remembered that the co-existence of other psychological or affective factors can easily obscure its effects. It also appears that testosterone has a mood and energy-enhancing effect in women. Hence, testosterone influencing on the mood, may also have the influence on pleasure from sexual experiences (Watzka *et al*., 1999; Warne and Kanumakala, 2002; Zitzman, 2006).

Davis *et al*. (2005) confirmed that no evidence of connection between low scores for any of the sexual domains evaluated and low serum total and free testosterone levels was found.

DOES HUMAN SEXUALITY NEED ESTROGENS?

Estradiol, having a crucial role in the negative feedback control of testosterone, is synthesized from testosterone in both sexes. Evidence of the influence of estrogens on the sexuality of the human male, although limited, consistently suggest a negative effect of exogenous estrogens (Bancroft, 2005). The question arises whether some of the effects of testosterone on sexual interest and arousability may be mediated by aromatization of testosterone to estradiol, in addition to interaction between testosterone and estradiol in negative feedback control of LH. Unlike to other species, where the role of estradiol in mediating many of the central nervous system effects of testosterone on male sexual behavior is well known, its role in human male sexuality remains uncertain, moreover exogenous and endogenous sources of estradiol can manifest different effects, particularly when the endogenous estradiol results from aromatization of testosterone within the brain (Lindzey and Korach (2003).

The importance of estradiol for normal vaginal lubrication has been proved, but it still remains unclear whether estradiol has a direct effect on sexual interest and arousability (Bancroft, 2005). Estrogen seems to have little impact on sexual desire on either males or females. Deficiency of estrogen in women, however, can cause a decrease genital lubrication caused by the thinning of the vaginal epithelium. The physiological and psychological aspects of sexual arousal can be impaired by all these factors (Romero, 2002].

It is poorly understood what are the basis of desire and perceived arousal in women, but interactions among sex hormones, multiple neurotransmitters, and environmental factors seem to be involved (Basson, 2006).

CONCLUDING REMARKS

The research on human sexuality started in the half of the twentieth century and from the beginning it has been very difficult. In humans, there is no simple relationship between endogenously and exogenously administered gonadal hormones and sexuality. Different aspects of human life and sexuality are influenced by sexual steroids (Medvei, 1993; Silber, 1997), but at the time being the impact of certain isolated sex hormones on sexuality is not possible to be found out. While evaluating this impact of sex hormones on human sexuality, one should avoid the interpretation of examinations' results not including psychological factors and quality of life.

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