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Steroid Hormones, Behavior and Sexual Dimorphism in Animals and Men: the Nature-Nurture Controversy

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1. Introduction

During the nineteenth and at the beginning of the twentieth century, the idea that sex differences affect the properties of the brain was generally accepted. Women were thought to be less intelligent than men and to have brains similar to those of male children (see Swaab and Hofman, 1984; Durden-Smith and DeSimone, 1984). Until the period after World War I, this idea justified the social dominant status of European males.

Then arguments of biologic destiny became unpopular and a new ideology took the place of the old one. Experience and culture were thought to be basic to the development of gender differences. The idea that differences between men and women were only the product of learning and experience and not of biology gained popularity and has influenced our thinking for several decades (Freud, 1910; Money, 1961; Hampson and Hampson, 1961; Mead, 1961; for a review: Durden-Smith and De Simone, 1984).

However, on the basis of numerous scientific data, it is becoming more and more evident that both experimental and biological factors influence gender differences in humans. Indeed, a bias of the behavioral sex phenotype by the action of pre- and postnatal hormones does not exclude influences of the environment and of learning. Both experiential and hormonal factors interact and modulate the response of the organism.

It is in fact relevant that even in lower mammals like rodents, in which neonatal hormones determine the adult phenotype by acting on the brain (see below), environmental factors play an important role in the process of sexual maturation and differentiation. For example, female rats lick the anogenital region in male pups more frequently than in female pups. Stimuli originating from this anogenital licking contribute to the development of some elements of male sexual behavior. Neonatal androgens (endogenous in normal males or exogenous in androgenized females) affect the properties of the pups urine and in this way stimulate licking from the mother (Moore and Morelli,

1979; Moore, 1982; 1984; 1985). Thus in rats, perinatal hormones modify urine pheromones of male pups which in turn change the social interaction of the pups with their mother so that adult behavior becomes sexually differentiated. In rats also maternal stress influences the endocrine status of the embryo as well as mother-infant interactions which in turn affect the process of sexual differentiation (Ward, 1984; Moore and Power, 1986).

In all animal species studied so far, including guinea pigs, rats, cats, dogs and rhesus monkeys, social deprivation in early infancy has deleterious effects on sexual behavior in adulthood and the action of hormones varies with prior experience of mating (for review: Larsson, 1978). Thus even in animals, interactions between hormonal and experiential factors are complex and obviously higher levels of complexity can be expected in men.

Several environmental factors like the influence of the own body image, the influence of parents, the social class and the culture are known to affect sexual maturation and differentiation in men (Hampson and Hampson, 1961; Mead, 1961; for a detailed review: Maccoby and Jacklin, 1974). Parents often exhibit different behaviors towards a baby who is dressed as a boy and has a male name than towards the same baby dressed as a girl and with a female name (Will et al., 1976). Even immediately after delivery, mothers are emotionally more involved with a son than with a daughter (Out and Vierhout, 1983). However, like in animals, the observation that social factors are important in the establishment of the behavioral dimorphism does not rule out the possibility that gonadal hormones are critically involved. The aim of the following paper is to review the relevant literature on this subject in humans in relation with animal models. The data suggest that steroid hormones influence human behavior by having some permanent effects during pregnancy or by acting in some reversible manner in the adult.

2. Activating Effects of Steroid Hormones on Sexual and Aggressive Behavior

a) Male Sexual Behavior

In male mammals and birds, sexual activity rapidly declines after castration and treatment with testosterone (T) restores copulation (Larsson, 1979; Beach and Inman, 1965; Balthazart et al., 1983). However some males still copulate several weeks after orchidectomy (Larsson, 1979; Södersten et al., 1980; Deviche and Schumacher, 1982; Balthazart and Schumacher, 1984). This maintenance of sexual activity might be related to the low levels of steroids secreted by the adrenal glands but it is also likely that it reveals the relative independence of the behavior from its hormonal control.

Androgens activate copulation in higher vertebrates not only by affecting the growth of the genital organs but also by acting on the preoptic area (POA) as shown by using intracerebral implants of hormones (e.g. Davidson, 1966; Lisk, 1967; Hutchison, 1967; Barfield, 1969). Other brain parts are also involved in the control of male sexual behavior (for review: Larsson, 1979). In the POA, T is metabolized into several active and inactive metabolites (for review: Balthazart and Schumacher, 1983; Hutchison and Steimer, 1983). As estrogens administered both in periphery or as hypothalamic implants also activate copulation in rat, it has been suggested that aromatization of T into estradiol (E2) at the hypothalamic level is a necessary step for the activation of male sexual behavior (= "aromatization hypothesis"; Södersten, 1973; Dörner, 1980; Lisk and Greenwald, 1983). However, even in species where aromatization of T into E2 is necessary for the activation of copulation (e.g. rat and quail: Adkins and Nock, 1976; Christensen and Clemens, 1975; Morali et al., 1977; Adkins et al., 1980), non-physiological high amounts of E2 are generally required to activate the behavior (Balthazart et al., 1985).

Several studies suggest that in rats, rabbits and quail non-aromatizable androgens like 5α-dihydrotestosterone (5α-DHT) are also implicated in the activation of male sexual behavior. At low concentrations, androgens and estrogens might act synergistically on the brain (Baum and Vreeburg, 1973; Larsson et al., 1973; Beyer et al., 1975; Baum et al., 1982; Schumacher and Balthazart, 1983; Balthazart et al., 1985). The relative importance of androgens and estrogens in the activation of male sexual behavior varies however among species and strains. Thus 5α-DHT alone is sufficient to activate copulation in guinea pigs (Alsum and Goy, 1974) and in some strains of mice (Luttge and Hall, 1973).

In rhesus monkeys, characterized by complex social interactions, castration decreases male sexual activity. The suppression is greater in unexperienced males than in experienced ones. Administration of T or 5α-DHT restores copulation to precastration levels (Michael and Bonsall, 1979). In male monkeys, initiation of sexual behavior, penile erections as well as the refractory period following ejaculation are related to changes in neuronal activity in the median POA (Oomura et al., 1983) and electrical stimulation of the preoptic area evokes penile erections and seminal ejaculation (Robinson and Mishkin, 1966). Thus the POA is also involved in the control of male sexual behavior in non-human primates.

There is little doubt that like in many species of birds and mammals, testicular hormones affect reproductive behavior in men. Castration is one of the earliest surgical techniques ever performed. Human males have been castrated for diverse purposes such as to supply safe guards of ladies in ancient Egypt, to punish enemies or criminals or to prolong usefullness of choir boys in the medieval church. Castration in men is still performed to treat prostatic cancer and to deter sex offenders (see Davidson, 1972). It reduces or even suppress male sexual behavior.

Some castrated men still have sexual activity for several years after castration. Like in animals, this could reveal independence from the hormonal control and/or be related to steroid production by the adrenal glands. Low levels of androgens and estrogens can indeed be measured in castrated individuals (Wilson, 1982). Some reports also suggest that castration has more drastic effects on behavior if performed before than after puberty (Money and Ehrhardt, 1972).

Treatment with exogenous hormones increases sexual activity in gonadectomized men (Wilson, 1982) and in patients showing hypogonadism (e.g. XXY patients; Money, 1961; Rubin et al., 1981; Kwan et al., 1983), but not in impotent men (Money, 1961). Steroid treatment of hypogonadic men increases their spontaneous libido (erections, sexual interest and motivation) (Kwan et al., 1983). Antiandrogens such as cyproterone acetate (CA) and medroxyprogesterone (MP) have been used with some success in the treatment of sexual offenders (e.g. XYY men). These compounds would reduce sexual thoughts and behavior (Money et al., 1975; Meyer-Bahlburg, 1978; Rubin et al., 1981).

The effects of T on sexual behavior in men are also suggested by correlations between plasma levels of steroid hormones and behavior. In 60 impotent men, Legros et al. (1973) found decreased levels of T. At puberty, between 12 and 16 years of age, plasma T levels increase markedly. This is correlated with the first nocturnal ejaculations, the beginning of masturbation and sexual phantasms (Beach, 1974a). A correlation between beard growth (which is androgen dependent; Money, 1961) and the anticipation of sexual activity is reported by an anonymous observer (Anon, 1970). There is also a relationship between REM sleep and spontaneous erections and it is known that plasma T is increased during REM sleep (Evans et al., 1971).

However, the relationship between androgenic hormones and sexual behavior is not always so clear in men. In one study, subjects with low plasma T did not suffer from more "castration feeling" than patients with normal androgen levels, whereas the scores "depression" and "anxiety" were significantly higher in the normal T group than in the

low T group (Legros et al., 1975). Such a tendency for a positive relationship between T plasma level and intensity of depression was also found later in a larger study devoted to psychoendocrine relation in 101 patients suffering from "psychogenic sexual impotence" (Legros et al., 1978).

In that study, however, a positive correlation was found between plasma T and sexual interest (Mf MMPI score) in the sexually impotent patients suffering also from a glucose intolerance (r: 0.43) but not in those patients without metabolic abnormalities (r: −0.13). Recent data confirm the high percentage of glucose intolerance in patients suffering from so-called "psychogenic" sexual impotence: the author related the slight metabolic abnormalities to hypercortisolism (Marchesi et al., 1985).

It therefore appears that the relationship between androgenic hormones and sexual behavior can be different according to the metabolic status of the individual, whereas the relationship between T plasma levels and more general psychopathological findings is more constant in that clinical condition.

We do not known whether aromatization of T into E2 is involved in the activation of male sexual behavior in humans as it is in species like rat and quail. Generally the treatment of sexual offenders and of men suffering from prostatic cancer with estrogens causes an important decrease in the erectile response to sexual stimuli and in libido (Money, 1961; Bancroft et al., 1974; Bancroft, 1978; Meyer-Bahlburg, 1978). However, estrogens administered in periphery decrease gonadotropin levels and thus cause a regression of the testes with a concomitant decrease in plasma T levels (Meyer et al., 1981). Moreover, estrogens increase the concentrations of circulating androgen-binding globulins in humans (Murray et al., 1975). Thus estrogens diminish male sexual behavior by reducing the amount of androgen available to the target cells. As peripheral E2 also weakly activates male sexual behavior in species like the quail where the hypothalamic aromatization of T into E2 is an important step of action (Balthazart et al., 1985), it is difficult to interpret data in humans and a possible role of E2 in the activation of male sexual behavior cannot be excluded.

b) Female Sexual Behavior

In the female rat, mounting and palpation of the flanks by a male elicits a stereotyped behavior called lordosis. The head and the perineal regions are elevated thus facilitating penile intromission (Harlan et al., 1979; Pfaff, 1980). This behavior pattern depends on the activating effects estradiol (E2) and progesterone (P). In the guinea pig, both hormones are required (for review: Harlan et al., 1979; Feder, 1984) but in other species such as the vole, E2 alone can be active (Carter and Getz, 1985). Both estrogens and progestagens act at the level of the ventromedial hypothalamus (VMH) as shown by the use of intracerebral hormone implants (Davis et al., 1979a; Rubin and Barfield, 1980; Dörner, 1980; Davis et al., 1982; Howard et al., 1984; Gibson and Cheng, 1979). Other brain parts are also implicated in the regulation of female receptivity in rats (for review: Harlan et al., 1979; Pfaff, 1980; Dörner, 1980).

Lordosis behavior does not exist in non-human primates. However, in female rhesus monkeys, ovariectomy reduces sexual activity and abolishes the rhythmic changes in sexual activity associated with the menstrual cycle (Michael and Bonsall, 1979). In contrast to lower mammals and prosimians, many species of monkeys copulate throughout the menstrual cycle (for review: Goy and Resko, 1978). This suggests that female monkeys may possess neural mechanisms which support sexual behavior and which are less dependent on hormones (Michael and Bonsall, 1979).

In contrast to what is seen in other species, ovariectomy does not affect sexual activity in women (see Davidson, 1972 and Bancroft, 1978 for references). However, the removal of the ovaries only partly diminishes circulating hormone levels in women

because adrenal glands produce about one third of the circulating estrogens (see Wilson, 1982). Ovariectomy accompanied by adrenalectomy inhibits libido in women (Waxenberg et al., 1959; Money, 1961; Wilson, 1982). Gonadectomy has more drastic effects in men than in women, probably because the human testes produce about 98% of the total amount of T (Wilson, 1982).

Androgens might also have facilitating effects on women sexual behavior. Many women for whom androgen therapy is prescribed report an increase of sexual desire (Money, 1961; Bancroft, 1978). This effect seems to be secondary to an increased clitoridial sentiment, however, it cannot be ruled out that androgens exert also these effects as such or after their aromatization to estrogens at the central level.

The use of contraceptive hormones and the fluctuations of mood during the menstrual cycle represent another source of information about the effects of hormones on women behavior. Thus pills containing P reduce sexual interest. This reduction might however be secondary to general depressive conditions (for a discussion of this question, see Bancroft, 1978; Rubin et al., 1981; Herrenkohl, 1980; 1984). "Sexual appetite" is maximal during the estrogenic pic before ovulation (see Legros, 1974).

c) Aggressive Behavior

In mice, males are more aggressive than females. Castration in adulthood abolishes intraspecific aggressive behavior and androgens restore fighting (Edwards, 1969). Estradiol also increases aggression in castrated male mice (Bowden and Brain, 1978; Simon and Gandelman, 1978). Estradiol and 5α-DHT appear, to act synergistically at this level (Finney and Erpino, 1976). However, intraspecific aggression and its hormonal control are highly variable among species. In rats, both sexes exhibit considerable aggression although males fight more than females. Castration affects aggressive behavior only after several weeks. In hamsters, females exhibit more aggression than males and combined treatment of female hamsters with E2 and P results in a profound reduction of aggression (for references and reviews, see Beatty, 1979). In adult rhesus monkeys, T activates aggressive behavior in females (Goy and Resko, 1978).

Many data suggest that T also activates aggressive behavior in men. In normal subjects, no correlation has been detected between aggressivity, as evaluated by interviews, and circulating levels of T. This failure, however, probably reflects the importance of short-term changes in behavior (interviews were not conducted in a "hostile" environment). Indeed, correlations between plasma T and aggressivity were found in prisonners who had commited violent actions. It was for example shown that violent criminals (men imprisonned for murder or rape) had higher T levels than thiefs (Rubin et al., 1981). It thus seems that in men, like in animals, hormonal factors are not independent of sexual and aggressive activities, although their role is by far smaller in the former than in the latter compared to the effects of social environment.

3. Sexual Dimorphism in Behavior

Reproductive characteristics like gonadotropin release and sexual or aggressive behavior are sexually differentiated in most birds and mammals. Female rats are characterized by a cyclic pattern of LH secretion by the pituitary, whereas males show a more tonic pattern of LH release (Brown-Grant, 1974). Females seldom or never show male mounting behavior, whereas males seldom or never show female behavior patterns (for review: Dörner, 1980; Balthazart and Schumacher, 1983).

Most of the work on reproductive behavior in animals is limited to the observation of copulation in males and lordosis behavior in females. Only a few studies take into account sexual orientation (= sexual preferences; rat: Meyerson and Lindström, 1973;

Hetta and Meyerson, 1978; Davis et al., 1979b; dog: Beach et al., 1977; rhesus monkeys: Michael et al., 1972; ferret: Baum et al., 1985). Thus in rats, males preferentially approach females and females preferentially approach males. This sexual orientation is under the control of gonadal hormones (Meyerson and Lindström, 1973; Hetta and Meyerson, 1978).

Parental behavior as well as many non-reproductive behaviors like open-field activity, activity in a running wheel, play and learning are also sexually differentiated in rodents (Beatty, 1979; Ichikawa and Fujii, 1983).

In humans, sexual identity, gender role, sexual orientation, parental and aggressive behavior as well as many cognitive and intellectual functions are sexually dimorphic (see Maccoby and Jacklin, 1974; Bancroft, 1978; Money and Schwartz, 1978; Ehrhardt and Meyer-Bahlburg, 1981; Wilson, 1982 for data and definitions). The sexual identity is irreversibly established between 2 and 4 years of age (Money, 1961; Bancroft, 1978). This process is heavily influenced by the experience and the social environment of the child (Money et al., 1955; Money and Schwartz, 1978; Ehrhardt and Meyer-Bahlburg, 1981). Gender role is related to a large variety of behaviors and characteristics such as choice of games and clothes, attitude towards family and professional activity. "Gender role means all those things that a person says or does to disclose himself or herself as having the status of boy or man, girl or women, respectively" (Hampson and Hampson, 1961). Thus boys spend more energy, have higher athletic performances and are more aggressive than girls. These as a mean are more interested in babies and dolls, are more romantic and show a relatively higher preference for family life versus professional achievement (Ehrhardt et al., 1968; Ehrhardt and Baker, 1974; Money and Schwartz, 1978; Meyer-Bahlburg and Ehrhardt, 1982). Finally, as an example of cognitive and mental sexual dimorphism, one could cite the greater verbal ability of women and the better spatial perception and aptitude for mathematical reasonning of men (Witelson, 1976; Meyer-Bahlburg and Ehrhardt, 1980; Benbow and Benbow, 1984).

4. Biological Basis of the Behavioral Dimorphism

Sexual and aggressive behavior are activated by steroid hormones in the adult. The presence of different endogenous hormones in the two sexes (T in males and E2 + P in females) might explain the observed sexual dimorphism. However, numerous experiments show that a different endocrine milieu cannot account for all the differences observed between males and females. In rat and quail for example, ovariectomized females show only little male sexual behavior in response to T treatment in contrast to castrated males (Adkins and Adler, 1972; McEwen, 1978; Balthazart et al., 1983). Testosterone is also very ineffective in inducing mounting behavior in adult female rhesus monkeys (Goy and Resko, 1978). This sex difference affecting the behavioral response to T is not due to a different peripheral catabolism of the administered hormone in males and females as shown by the assay of circulating T during hormone treatment (Balthazart et al., 1983; Schumacher and Balthazart, 1986; Roselli et al., 1984; see also Mode et al., 1984) nor to differential effects on the genital organs as shown by the use of intracerebral hormone implants (Christensen and Gorski, 1978).

Estradiol activates receptivity in both male and female quail (Adkins and Adler, 1972; Adkins, 1978), but it is more difficult to induce lordosis behavior in male than in female rats (Arén-Engelbrektsson et al., 1970; McEwen, 1978; Dörner, 1980). Such species differences exist also for the regulation of gonadotropin release. In rats, estrogens cause a temporary elevation of circulating LH by a positive feedback on the hypothalamus in females but not in males. As a consequence, males are unable to luteinize ovarian grafts (Gorski and Wagner, 1965; Brown-Grant, 1974). By contrast, castrated male

rhesus monkeys will release LH after estrogen treatment in a manner similar to that observed in females (Karsch et al., 1973; Resko and Ellinwood, 1984).

In birds and mammals, differences in brain sensitivity to the activating effects of hormones could thus be responsible for the observed behavioral dimorphism. This different brain sensitivity in males and females has been related to both biochemical and neuroanatomical differentiation. Biochemical and morphological sex differences are not at all exclusive. A neuroanatomical difference implies a biochemical one and a biochemical difference between sexes might correspond to a morphological difference. Moreover, a biochemical differentiation of brain parts may be needed to complement the morphological sex differences (McEwen et al., 1984).

The first morphological sex differences described for the rat brain were rather small and affected the size of the nucleus of neurons and the number of synaptic connections (Pfaff, 1966; Dörner and Staudt, 1968; Raisman and Field, 1971; 1973; Matsumoto and Arai, 1980; Nishizuka and Arai, 1981; Ayoub et al., 1983). A major sex difference in brain anatomy related to behavior was first described in the song nuclei of the canary and the zebra finch (Nottebohm and Arnold, 1976). These nuclei are much more developed in males (who sing) than in females (who never sing). A reexamination of the rat brain then allowed the discovery of a big sexually dimorphic nucleus (SDN) in the preoptic area (POA) which is bigger in males than in females (Gorski et al., 1978). Unfortunately, this sex difference has not been associated yet with behavioral characteristics (for review: Gorski, 1984).

Similar sex differences have been described in the POA of Japanese quail (Viglietti-Panzica et al., 1986), ferret (Tobet et al., 1983), guinea pig (Hines et al., 1982), Mongolian gerbil (Commins and Yahr, 1984a), mouse, hamster (Bleier et al., 1982) and men (Swaab and Fliers, 1985). Lesions of the sexually dimorphic area (SDA) in the gerbil disrupt masculine copulatory behavior (Commins and Yahr, 1984b). A similar association between behavioral and neuroanatomical dimorphism has also been described for the spinal nucleus of the bulbocavernosus (SNB), which is more developed in male than in female rats (Breedlove and Arnold, 1980).

Numerous biochemical differences between the male and the female brain have also been described for mammals and birds. These concern the activity of T-metabolizing enzymes (Naftolin et al., 1975; Selmanoff et al., 1977; Roselli et al., 1984; Schumacher and Balthazart, 1984b; Schumacher and Balthazart, 1986), steroid receptors concentrations (Blaustein et al., 1980; Rainbow et al., 1982) and neurotransmitter concentrations and turnover (McEwen et al., 1984) in specific brain parts controlling reproduction. For example, T induces a higher aromatase activity in the POA of male quail than in females (Schumacher and Balthazart, 1986). As T induces male sexual behavior by acting on the POA and as aromatization of T into E2 is a critical step in the activation of copulation in this species (see previous section), the lower induction of aromatase activity in the POA of females is a highly relevant biochemical correlate of their behavioral insensitivity to T.

In humans, data about possible biological bases of sexually dimorphic behavior come essentially from the study of individuals showing a dissociation of the usually correlated sexual characteristics such as seen in homosexuals (reversed sexual orientation), transsexuals (reversed gender identity) or transvesti (partial reversal of the sexual role; see Gooren, 1984 for more definitions) as well as from a direct comparison of biochemical and neuroanatomical data from men and women.

In animals, the presence of different endogenous hormones in males and females cannot account for all aspects of the behavioral dimorphism (see above). Many studies were thus carried out to study the possible relationships between reversed sexual characteristics and circulating hormones in humans. In male homosexuals, plasma T does not

seem to be strongly affected. Three out of 27 studies only mention decreased T levels and these could be a consequence rather than a cause of the homosexuality (different sexual life, frequent association with marijuana consumption: Kolodny et al., 1971; Doerr et al., 1973; Birk, 1973; Meyer-Bahlburg, 1977; Bancroft, 1978; for review: Meyer-Bahlburg, 1984). Some studies also suggest increased estrogen levels in some homosexuals (Newmark et al., 1979; Meyer-Bahlburg, 1984).

Among nine studies on homosexual women, four show higher T levels in a fraction (1/3) of the subjects (for references, see Meyer-Bahlburg, 1984). Elevated levels of T have been found in homosexual women by other authors (Gartell et al., 1977; Sipova and Starka, 1977). In male-to-female transsexuals, the T and E2 production of the testes are normal, while some female-to-male transsexuals have increased T levels (Ehrhardt and Meyer-Bahlburg, 1979).

As a whole, no clear-cut relationship appears between plasma hormone levels and sexual orientation or gender identity, although the existence of some systematic hormonal modification cannot be rejected.

Some observations, however, suggest a relationship between homosexuality and brain sensitivity to steroids. Like in rats (and in contrast to rhesus monkeys; see above), estrogens given to women in adequate doses at an adequate time of the ovarian cycle exert a positive feedback on the hypothalamus and pituitary gland, which results in a surge of LH. This surge cannot be induced in men. However, contrary to what is seen in heterosexual or bisexual men, estrogens partially induce a positive feedback in homosexual men (Dörner et al., 1972; 1975; Dörner, 1980). This controversial result has now been independently confirmed by Gladue et al. (1983) who showed that the LH response to estrogens in homosexual men is intermediate between men and women. Similarly, estrogens only exert a moderate positive feedback in homosexual women (Dörner et al., 1976; see also Seyler et al., 1978). Thus homosexuals possibly have a brain-pituitary unit with an altered sensitivity to steroids which was called "pseudohermaphroditic brain" by Dörner (1980). These brain differences would extend to the areas involved in the control of sexual behavior as suggested by lesion effects (see references cited by Dörner, 1980).

No difference between transsexual and heterosexual men has been found in the response of LH to estrogens (Gooren, 1984; for discussion, see Dörner and Rohde, 1983). It is interesting to mention that estrogen treatment has suppressive effects on libido in heterosexual men, but facilitates orgasm in transsexual men (Meyer-Bahlburg, 1978).

These observations suggest that the brains of men and women differ in their sensitivity to the activating effects of gonadal hormones. Like in other species, this different brain sensitivity might be related to biochemical or neuroanatomical differentiation. Metabolites of androgens present in the human urine supply precious informations about the anabolism and catabolism of hormones in humans. The ratio of 5β-reduced to 5α-reduced metabolites (5β/5α) for 17-ketosteroids (3α,5β-etiocholanolone/3α,5β-androsterone) and for 17β-hydroxysteroids (3α,5β-etiocholanediol/3α,5α-androstanediol) in urine is much higher in individuals suffering from a deficiency in 5α-reductase (which converts T to 5α-DHT) than in normal men (Imperato-McGinley et al., 1974; 1982). This shows that excreted metabolites reflect the enzymatic activities present in various organs such as the liver and possibly the brain.

It is then of interest that the urine content of androgen metabolites is sexually dimorphic. The ratio etiocholanolone/androsterone is about 1:2 in men and 2:1 in women (Pfaffenberger and Horning, 1977; 1978). This indicates a sex difference in the metabolism of androgens which is fairly stable and is namely not affected by menopause in women.

The urine ratio etiocholanolone/androsterone was also elevated in 12 out of 15 homosexual men by comparison to heterosexual men (Margolese, 1970). However, we do not

know whether there is a direct relationship between urine metabolites and brain metabolism of androgens.

More relevant are actually the neuroanatomical differences found between men and women, which may provide a biological basis for the observed sex differences affecting human behavior. A few years ago, a sex difference in the shape of the corpus callosum was described (Lacoste-Utamsing and Holloway, 1982) which might relate to the different lateralisation of brain characteristics in men and women (Witelson, 1976; Kimura and Harshman, 1984). The shape of the suprachiasmatic nucleus (SCN) is also sexually dimorphic in humans and its middle part contains more vasopressinergic cells in men than in women (Swaab and Hofman, 1984). In the rat, this nucleus determines temporal aspects of the brain sensitivity to steroids (Södersten et al., 1981). Recently, Swaab and Fliers (1985) have described a sexually dimorphic cell group in the POA of the human hypothalamus. The volume of this nucleus is larger in men and contains twice as many cells as in women. Homology with the sexually dimorphic areas of other species remain however to be shown. Like in the rat, the spinal nucleus of the bulbocavernosus (SNB) is more developed in men than in women (Forger, N. G. and Breedlove, S. M., 1985).

5. Ontogeny of the Behavioral Dimorphism

It is now well established that the mechanism of sexual differentiation proposed by Jost (1953; 1972; 1983) for the genital organs is also applicable to the differentiation of brain and behavior (for review: MacLusky and Naftolin, 1981; Schumacher and Balthazart, 1985). Chromosomes determine the sex of the gonads as well as the basic organization of the brain and the peripheral structures. In a second phase, gonadal hormones determine the sex phenotype of the genital organs and of the central nervous system (CNS).

In 1935 and 1936, Pfeiffer showed that in rats the sex of the hypophysis is dependent upon the gonad at birth. In 1959, Phoenix, Goy, Gerall and Young established that the behavioral dimorphism in the guinea pig is due to the action of androgens during pregnancy. They proposed that gonadal steroids have two different actions: activational and organizational. According to this concept, gonadal hormones activate their target tissues during adult life in a reversible manner or they differentiate (= organize) their target tissues during early development. These organizing effects of steroid hormones would occur only during limited periods of development, the so-called "critical periods of sexual differentiation".

The sexually dimorphic characteristics mentioned in the previous section for animals are also differentiated by the action of steroid hormones on the brain during critical periods in early development (for review: Schumacher and Balthazart, 1985). In the rat, circulating T levels are higher in males than in females around birth, a period of development which corresponds to the critical period of sexual differentiation (Weisz and Ward, 1980; Gogan et al., 1981). At this time, cells of the hypothalamus are characterized by an immature aspect and testicular androgens probably influence the final phase of cell division and migration as well as the survival and differentiation of hypothalamic neurons (Reier et al., 1977; Arai and Matsumoto, 1978; Lawrence and Raisman, 1980; Matsumoto and Arai, 1980; McEwen, 1982; Gorski, 1984).

Sexual differentiation of song nuclei in the zebra finch corresponds to the death and atrophy of specific neurons in the female brain (Konishi and Akutagawa, 1985). Other neuroanatomical sex differences observed in adults (see previous section) are also due to the organizing actions of gonadal hormones during early development (song nuclei in zebra finch: Gurney and Konishi, 1980; SDN in rat: Döhler et al., 1983; Gorski, 1984; SNB in rat: Breedlove, 1984; SDA in gerbil: Yahr, 1985).

Similarly, neonatal steroids determine the sensitivity of the brain to the activating effects of hormones. In rats, the female sex is considered to be the neutral or anhormonal sex, although weak amounts of estrogens seem to be required for the maturation of female behavior (Döhler et al., 1984; Toran-Allerand, 1984). Neonatal T defeminizes and masculinizes the behavior of males (Beach et al., 1969; Lobl and Gorski, 1974; Christensen and Gorski, 1978; for review: Dörner, 1980). As a consequence, adult males are more sensitive to the activating effects of T on male sexual behavior than females (previous section). Sexual preferences are also influenced by neonatal T in the ferret (Baum et al., 1985).

In rats, aromatization of T into E2 plays a crucial role in the differentiating effects of the hormone. Aromatase inhibitors and antiestrogens prevent the organizing actions of T (McEwen et al., 1977; Södersten and Hansen, 1978; Davis et al., 1979b). In rodents, female embryos are protected against the masculinizing and defeminizing actions of their own and maternal estrogens by circulating alphafetoproteins (McEwen et al., 1975; Mizejewski et al., 1983). Higher P levels in females might also protect their brains against the differentiating actions of neonatal hormones (Shapiro et al., 1976; Hull et al., 1980). Androgens like 5α-DHT also seem to play an important role in the process of masculinization in rats and may act in synergy with estrogens to differentiate the male brain (Hart, 1979; Van der Schoot, 1980; McEwen, 1982; Olsen, 1983).

Neonatal steroids differentiate the regulation of gonadotropin release (positive feedback, see previous section) and other behaviors like intraspecific aggression and parental behavior (Beatty, 1979; Ichikawa and Fujii, 1983). It is interesting to mention that during early development, gonadal hormones differentiate behavior patterns like urinary behavior in dogs, which do not require activation by hormones in adulthood (Beach, 1974b).

In contrast to rats (where the female sex is the neutral sex and the process of sexual differentiation corresponds to a masculinization of male embryos by testicular androgens), the male sex is considered to be the neutral sex in the Japanese quail. In this species, the adult female phenotype will result from the demasculinizing actions of ovarian estrogens during a critical period before hatching (Adkins, 1978). This conclusion is based on experiments showing that injections of estrogens into male eggs cause their demasculinization (they will not copulate in response to T as adults), whereas injections of an anti-estrogen into female eggs will prevent their demasculinization (they will show male sexual behavior in response to T as adults; Adkins, 1979; Adkins-Regan, 1983). Thus two distinct mechanisms will lead to the adult phenotype in mammals and birds: masculinization of males in rats and demasculinization of females in quail would respectively be responsible for the higher sensitivity of adult males to the activating effects of T on behavior (for a detailled treatment of this question see: Schumacher and Balthazart, 1985).

The existence of "critical periods" is supported by many experiments carried out in several species showing that endocrine manipulations only affect the adult phenotype in a permanent way if performed during short and limited periods of early development (for review: McEwen, 1978; MacLusky and Naftolin, 1981; McEwen, 1982; Schumacher and Balthazart, 1985). However, some experimental evidence shows that the critical period of sexual differentiation does not encompass the entire period during which gonadal hormones contribute to the organization of the brain (quail: Hutchison, 1978; Schumacher and Balthazart, 1984a; Balthazart and Schumacher, 1984; rat: Gorski, 1968; Gustafsson, 1974; Södersten, 1976; Harlan et al., 1979; Stewart and Cygan, 1980). On the basis of experimental work with quail, we recently proposed that sexual differentiation in birds and mammals might be a biphasic phenomenon. A "critical period of sensitization" of the undifferentiated target tissues to the organizing actions

of steroid hormones would be followed by a more "continuous period of organization" (differentiation) extending into adulthood (Schumacher and Balthazart, 1984a; Balthazart and Schumacher, 1984; Schumacher and Balthazart, 1985). Similar ideas have been formulated in the rat literature (Harlan et al., 1979; Weisz and Ward, 1980; Baum et al., 1985).

In rhesus monkeys, plasma from male fetuses in early gestation contains significantly more T than plasma from female fetuses. The origin of this sex difference is the fetal testis (Resko and Ellinwood, 1984). Fetal levels of P are higher in females than in males and may contribute, like in the rat, to the protection of the female brain against the masculinizing actions of androgens (Hagemenas and Kittinger, 1972). If female monkeys are exposed to androgens prior to birth, their mounting and play behavior is masculinized and in contrast to normal adult females, these pseudohermaphroditic females copulate in response to T (Goy and Resko, 1978). The non-aromatizable androgen 5α-DHT has the same masculinizing effects as T and thus unlike in rats, estrogens do not seem to be required (Resko and Ellinwood, 1984).

In contrast to what is seen in rats, the ability to show a LH-surge in response to estrogens (positive-feedback) is not altered by prenatal androgen treatment of female rhesus monkeys (Resko and Ellinwood, 1984) and as we already mentioned, this characteristic is not sexually dimorphic in the adult (Karsch et al., 1973; Phoenix et al., 1983).

In humans, abnormal endocrine conditions during gestation have been associated with alterations in gender identity, sexual role and sexual orientation. It must be stressed that most of the experimental studies in animals have analyzed the development of the motor components of sexual behavior (lordosis and mount) and only in a few instances sexual orientation (see above). There is also no animal model for the study of gender role and gender identity. The variable studied in animals and men are thus not strictly homologous and general principles on sexual differentiation must be taken very cautiously.

Nevertheless, ten principles derived from animal studies, can be considered in the analysis of human sexual development:

1) There are species differences concerning the hormones involved in sexual differentiation and the reproductive characteristics affected by the early endocrine status of the animal (see examples cited above).

2) The organizing effects of steroid hormones depend on their nature. Thus estrogens masculinize the SDN and male sexual behavior, whereas only androgens have masculinizing effects on the SNB in rats (e.g. Gorski, 1984; Breedlove, 1984).

3) The organizing effects of steroid hormones depend on the amount of hormone to which the embryo is exposed (e.g. Harlan and Gorski, 1977; Harlan et al., 1979).

4) The organizing effects of steroids depend on the age when embryos are exposed (e.g. Harris, 1964; Beach et al., 1969; MacLusky and Naftolin, 1981; Davis et al., 1979b).

5) The organizing effects of steroid hormones depend on the duration of the early hormone exposure (e.g. Goy and Resko, 1978).

6) Different behavior patterns such as masculine and feminine sexual behavior develop independently (e.g. Whalen, 1974; Davis et al., 1979b).

7) Steroid hormones act on different brain parts to differentiate different behaviors (e.g. Christensen and Gorski, 1978).

8) Steroid hormones not only organize the brain by acting during "critical periods of sexual differentiation" but still exert permanent effects until puberty. Sexual differentiation might be a biphasic process with a critical period of sensitization and a more continuous period of organization (Schumacher and Balthazart, 1985).

9) The duration of the competent period of sexual differentiation depends on the strength of the exposure during the critical period (Harlan et al., 1978; 1979).

10) The environment of the animal influences its sexual differentiation (e.g. presence of siblings in utero: Vom Saal et al., 1980; 1983; stress: Ward, 1972; 1984; Weisz et al., 1982; treatment by the mother: Moore, 1984; 1985; sexual experience: Larsson, 1978).

These 10 principles may explain why in humans, characteristics such as gender identity, gender role, sexual orientation and gonadotropin release differentiate independently as shown by the study of transsexuals, homosexuals and transvesti.

In humans, like in rats, hormonal signals during early development are synchronized with particular stages of cerebral development. Testosterone levels are elevated in boys but not in girls during the second trimester of pregnancy (period when the genital organs differentiate) and at birth (Wilson et al., 1981a; 1981b; Ewing and Zirkin, 1983). The neonatal peak of T corresponds to a phase of development during which most of the synaptic connections are formed and myelinization of the nerve fibers occurs. During the second trimester of pregnancy, the division of neuroblasts is not completed (for review: Kaplan et al., 1976). Thus like in rodents, steroid hormones might influence the final phase of neuronal division and neuronal maturation in humans.

More direct arguments in favor of permanent organizing actions of hormones on the human brain (= "hormonal imprinting") come from the study of cases of endocrine defects during gestation and from the study of the psychosexual development in children from mothers treated with exogenous steroids during pregnancy.

6. Endocrine Defects during Gestation and Sexual Dimorphism in Human Behavior

In most endocrine diseases which could potentially affect sexual differentiation, the effects of the endocrine modification during gestation are confounded with experiential factors in the post-natal life so that no firm conclusions can be reached. However, in a limited number of cases, these two influences can be tentatively separated and by references to the animal studies, conclusions can be drawn.

Two endocrine disorders are especially interesting in the present context because in these cases, the individuals are raised with a sexual experience which is in contradiction with their prenatal condition: it is the deficiency in 5α-reductase activity and the adrenogenital syndrome.

a) The 5 Alpha-reductase Deficiency

In this condition, first described by Nowakowski and Lenz (1961), genotypical males are born with female external genitalia and are usually reared and identified as girls. The enzymatic deficiency indeed prevents T from having its masculinizing effects on the external genital organs, although plasma T levels are normal and the brain is thus presumably exposed to adequate levels of androgens as also suggested by the virilized internal genital organs. At puberty, there is however a masculinization of the external morphology (growth of a penis and formation of the scrotum) due to the very much increased levels of T (Wilson et al., 1981a; 1981b; Imperato-McGinley et al., 1982). The sexual role during infantile life (female) is thus opposite to what would be expected from the prenatal androgenization (male; Imperato-McGinley et al., 1974). Despite their education as girls, in many cases these men revealed a male identity when adult (Imperato-McGinley et al., 1974; Bancroft, 1978). This male gender identity was probably

not formed after puberty when male genitalia became visible as this factor is usually thought to be insufficient (case of transsexuals; Gooren, 1984) and gender identity is determined irreversibly earlier in life (Money, 1961). Males with a 5α-reductase deficiency also have a predominant male role (Wilson, 1982). Their sexual orientation is essentially that of a male and their sexual activity is directed toward females. It is thus reasonable to believe that this male gender identity, male sexual role and male sexual orientation are related at least in part to the prenatal exposure to androgens overcoming the effects of post-natal experience. Alternative views have however been expressed (Feder, 1984) and conceptual as well as methodological problems are present in the published reports (Meyer-Bahlburg, 1984) which would make the above mentioned conclusion no more than tentative.

b) The Congenital Adrenal Hyperplasia (CAH) or Adreno-genital Syndrome

In this condition, an enzymatic defect due to an autosomal recessive gene shifts the steroid hormone production by the adrenals from cortisol to androgens (New et al., 1984). CAH girls are thus born with a male morphology (presence of a penis and scrotum) and are reared as such if the disorder goes undetected. However, if the abnormal endocrine status is recognized, the young girls will be treated with cortisol immediately after birth so that adrenals will stop producing this excess of androgens. Reconstructive surgery will also be applied (clitoridectomy and opening of the vagina) to restore a complete female morphology in the first few weeks after birth. These treated girls will then be reared as females (presumably) and can be fertile woman as adult (Money and Schwartz, 1978; Meyer-Bahlburg, 1984). In the case of the treated girls, the sex of rearing thus agrees with the external appearance but is in contradiction with the hormonal condition during gestation. CAH girls usually have a female identity (Wilson, 1982). However, a study of 17 girls treated with cortisol from birth revealed that 6 of them thought that it would be easier to be a boy (Ehrhardt and Baker, 1974). CAH girls are exposed to high androgen levels only during the end of fetal life and it is thus not unexpected that the effects on gender identity are limited.

The CAH condition is however associated with masculinized sexual role. CAH girls treated with cortisol since birth and reared as girls show, by comparison with control females, an increased energy expenditure, higher athletic capacity and they engage in group sports with boys. They show a decreased interest in dolls and babies and usually show an increased interest for their professional career by comparison to their mother and wife role (Ehrhardt et al., 1968; Ehrhardt and Baker, 1974; Money and Schwartz, 1978). It is usually assumed that this masculinization is not related to education because parents normally encourage feminine traits in these CAH treated girls so that education rather tends to counteract the influence of prenatal hormonal conditions (Ehrhardt and Meyer-Bahlburg, 1981). Some studies show that CAH girls initiate more fights and engage more easily in violent sports than control girls (Meyer-Bahlburg and Ehrhardt, 1982). Money and Schwartz (1978), however, found no differences between treated CAH and control girls in aggressive behavior during infancy.

Sexual orientation is probably not deeply affected in the CAH girls. Reports of increased bisexuality in imagery and in sexual experience are available (Legros et al., 1974), but adequate controls are missing. The majority of the CAH girls are heterosexual (Ehrhardt et al., 1968; Money and Schwartz, 1978; Money et al., 1985; Schwartz and Money, 1983). All these results are thus compatible with a prenatal masculinization in CAH girls but "are also open for social-learning interpretation if one assumes that the awareness of the medical condition on the part of the parents may have influenced psychosexual development" (Meyer-Bahlburg, 1984).

7. Psychosexual Development in Children from Mothers Treated with Exogenous Steroids during Pregnancy

Steroids have been and are still given to pregnant women in order to maintain high-risk pregnancies. In a few cases, estrogens were given alone but most frequently they were associated with progestins (Yalom et al., 1973; Ehrhardt and Meyer-Bahlburg, 1981). As estrogens derived from aromatization of T play a key role in the sexual differentiation of rodents (see previous sections), the case of offsprings born from mothers treated with estrogens (usually the synthetic estrogen diethylstilbestrol or DES) is thus of special interest.

On the basis of animal research, it would be expected that progesterone-related progestins should have a demasculinizing effect in males while androgen-based progestins should have masculinizing effects in females (see previous sections). Recent reviews of the available data can be found in Meyer-Bahlburg (1984) and Reinisch and Sanders (1984).

These predictions have been verified to some extent. Girls exposed to androgen-related progestins during fetal life tend to be masculinized (more violent sports, decreased maternal tendency, more self-assured and independent ...) as reported in interviews with mothers and subjects (Reinisch, 1977; Ehrhardt and Money, 1967; Ehrhardt and Meyer-Bahlburg, 1979; Money and Mathews, 1982). By contrast, boys and girls exposed during gestation to progesterone-related progestins were more feminine than control subjects (see Ehrhardt and Meyer-Bahlburg, 1979; 1981).

DES was used in the States in pregnant diabetic women until 1975 when its carcinogenic effects were recognized. The limited evidence from the children of the treated mothers points to a feminizing or demasculinizing influence (Reinisch and Sanders, 1984; remember that in quail, estrogens exert also demasculinizing effects). These children were indeed rated as less aggressive and assertive and showed decreased athletic skills. They were less individualistic and less self-sufficient than their unexposed brothers or sisters (Reinisch, 1977). Besides sexual role, prenatal DES could also affect sexual orientation. Females whose mother was treated with DES showed an increased incidence of homosexuality and bisexuality compared to controls (Ehrhardt et al., 1985). Two other studies, however, failed to reveal these differences (see Meyer-Bahlburg, 1984).

Many studies also support the notion that prenatal androgenization masculinizes aggressive behavior in humans. Exposure to androgen-based progestins during fetal life increases the aggressivity in girls and boys (Money and Ehrhardt, 1972; Zussman et al., 1975; 1977 in Meyer-Bahlburg, 1984). A recent study compared girls and boys exposed during fetal life to androgen-based progestins to their unexposed brothers and sisters. Experimental subjects were exposed to progestins during at least a part of the period during which differentiation of the hypothalamus takes place (Dörner and Staudt, 1972). Unexposed boys were more aggressive than unexposed girls. Boys and girls exposed to progestins showed more physical aggression than their control brothers and sisters, respectively (Reinisch, 1981). By contrast, children which were exposed to progesterone-based progestins or to DES during fetal life showed less aggressive behavior than control subjects (Yalom et al., 1973; Meyer-Bahlburg and Ehrhardt, 1982; Reinisch, 1981). It thus seems that prenatal androgens masculinize the aggressive behavior while progestins and estrogens have the opposite effect.

Discussion

The idea that steroid hormones activate and organize human behavior is still much debated. It is clear that in humans, characterized by a slow maturation, a considerable development of the cerebral hemispheres and correlatively a number of higher mental

functions such as consciousness and long-term memory, experiential factors are very important in the maturation and expression of behavior. As already mentioned in the introduction, cultural factors affect gender identity in humans (Hampson and Hampson, 1961; Mead, 1961; Maccoby and Jacklin, 1974). This does not, however, rule out the existence of a "hormonal imprinting" of the foetal brain and of activational actions of hormones on the adult brain.

There is indeed no reason to believe that the phylogenetically old mechanisms of sexual differentiation and behavioral activation, which are present in all higher vertebrates including non-human primates, completely disappeared in men. The brain parts which control reproductive behavior in vertebrates (especially the preoptic area, the hypothalamus and the limbic system) are very old and phylogenetically stable (Morrell and Pfaff, 1978; Pfaff, 1980). These brain parts contain androgen metabolizing enzymes and steroid receptors in all vertebrate classes (Stumpf and Sar, 1978; Callard et al., 1978a; 1978b; Kim et al., 1978). In species as distant as quail (Schumacher and Balthazart, 1984b), rat (Roselli et al., 1984), rabbits, rhesus monkeys and men (Naftolin et al., 1975), preoptic aromatase activity is higher in males than in females.

From data presented in section 2, it seems clear that gonadal and adrenal steroids affect libido and aggressive behavior in humans. There is however no definite proof that these hormones influence sexual behavior in men and women by acting on the POA and VMH respectively rather than on peripheral structures like the genitalia and muscles or through their general anabolic effects (Kochakian et al., 1956; Kochakian, 1964; Griminger, 1976). However, data based on brain lesion effects in humans (Müller et al., 1974; Dieckmann and Hassler, 1975; cited by Dörner, 1980) suggest that the hypothalamus is still involved in the control of human sexual behavior. Moreover, studies of eroticism in paraplegics and in humans after penectomy or vulvectomy (Money, 1961) suggest an independance of erotic cognition from pelvic stimuli. Even in rhesus monkeys, sexual activity is related to neuronal activity in the POA (Oomura et al., 1983). Thus despite the lack of direct evidence which would be derived from studies using stereotaxic implants of hormones (which will never be carried out for obvious ethical reasons), all the available evidence suggest that gonadal hormones act at the hypothalamic level in humans.

In contrast to other vertebrates, men and women (as well as higher primates) might possess additional neural mechanisms which support sexual and aggressive behavior and which are less dependent (or even independent) on hormonal stimulation. This is namely suggested by the observation that female primates and women, despite cyclic variations, are receptive nearly throughout the whole menstrual cycle (Michael and Bonsall, 1979; Goy and Resko, 1978). Like in several species (Schumacher and Balthazart, 1984a; Södersten et al., 1980; Rosenblatt and Aronson, 1958; 1959), castration has less severe effects in men with than in men without sexual experience (Wilson, 1982).

We still do not know whether T itself or one of its metabolites activates sexual behavior in men. The relative importance of androgens and estrogens in the activation of sexual behavior shows important differences among species. Whereas aromatization of T into E2 is required for the activation of male sexual behavior in quail and rat, 5α-DHT is sufficient in guinea pigs and rhesus monkeys (see section 2). In rat and quail, copulation depends on the activation of an androgen- and an estrogen sensitive mechanism. The simultaneous treatment with E2 and 5α-DHT is more efficient than the treatment with the same doses of the two steroids taken separately. The overstimulation of one of these two mechanisms also gives rise to a behavioral response (Balthazart et al., 1985). Thus during evolution, one or the other mechanism might have become predominant according to the species.

It is obvious that the ability of the female rat or quail to copulate in response to T or the ability of the male rat to show lordosis behavior after E2 treatment are not direct models for the study of human homosexuality or transsexuality (only the few experiments concerning sexual preferences in animals might eventually be related to homosexuality; see Feder, 1984 for discussion). Such simple models have however allowed the formulation of ten basic statements (see section 5) which can enlighten the study of human sexual differentiation.

With all the restrictions resulting from these 10 general principles, it is not surprising that several studies fail to show organizing effects of prenatal hormones on human behavior. It is however encouraging that all the positive results are in agreement with the animal models: a masculinization of male behavior by early testicular androgens whereas progestagens (like in rats) and estrogens (like in quail) have demasculinizing effects. We have, however, to be aware of species differences (principle 10) so that responses observed in animals do not necessarily need to be expected in humans.

There is no need to establish a strict dichotomy between experiential (social) and biological (hormonal) factors in their contribution to the organization and activation of behavior in humans nor in animals. This nature-nurture conflict once became "fashionable" amongst students of animal behavior. It has now become clear that opposing innate to learned aspects in the development of behavior was a sterile counterproductive approach which could only hide the complexity of the interactions between these two types of factors and deter scientist from actually studying these interactions.

In his review published in 1980, Dörner stressed the biological contribution to the control of human sexual behavior and in reaction, Feder (1984) has put the emphasis on the social controls. He has also pointed out the flaws in the experimental studies devoted to the hormonal controls, stressed the lack of direct evidence for hormonal controls in humans and warned against the ideological implications of the literature on this subject.

The above review makes it clear, we believe, that both hormonal and social factors contribute to the organization and activation of human behavior. It is thus critical to study their interaction rather than oppose them in an useless conflict. This approach has proved to be fruitful in animals. For example, in many species major effects of the environment on the development of sexual behavior are mediated through "social imprinting". Social imprinting is in turn influenced by the presence of gonadal or adrenal hormones as shown in several species of birds (Martin, 1978; Balthazart and DeRycker, 1979; Pröve, 1985).

Techniques are now available which permit to study behavior control mechanisms in animals at a level that would have been classified as "science fiction" only two decades ago. Important progress can thus be expected in our understanding of behavior control for the coming years. By combining experimental studies on animals with correlational studies in humans and considering the interplay between hormones and the environment, basic research will provide useful insights on the mechanisms which control human sexuality. This will probably provide treatments to a number of pathologies but will also raise a number of ethical questions which will have to be considered very cautiously.

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