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GENDER DIFFERENCES IN BEHAVIOUR: ACTIVATING EFFECTS OF CROSS-SEX HORMONES

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SUMMARY

The relative contribution of organizing and activating effects of sex hormones to the establishment of gender differences in behaviour is still unclear. In a group of 35 female-to-male transsexuals and a group of 15 male-to-female transsexuals a large battery of tests on aggression, sexual motivation and cognitive functioning was administered twice: shortly before and three months after the start of cross-sex hormone treatment. The administration of androgens to females was clearly associated with an increase in aggression proneness, sexual arousability and spatial ability performance. In contrast, it had a deteriorating effect on verbal fluency tasks. The effects of cross-sex hormones were just as pronounced in the male-to-female group upon androgen deprivation: anger and aggression proneness, sexual arousability and spatial ability decreased, whereas verbal fluency improved. This study offers evidence that cross-sex hormones directly and quickly affect gender specific behaviours. If sex-specific organising effects of sex hormones do exist in the human, they do not prevent these effects of androgen administration to females and androgen deprivation of males to become manifest.

Keywords—Gender differences; Sex hormones; Cognition; Aggression; Sexuality; Transsexuals.

1. INTRODUCTION

ANIMAL RESEARCH HAS clearly shown that sex hormones play an important role in many behaviours. In higher mammals this role is less clear, mainly because in these species the influence of the psychosocial environment on behaviour is more prominent and difficult to disentangle from the biological one. The development of internal and external genitalia, sex differences in figure and appearance, as well as sex specific behaviours, like sexual behaviour and forms of aggressive behaviour, are for an important part related to the presence or absence of testosterone during the early, prenatal developmental phases. Women only develop female features in the absence of testosterone as an organising factor, whereas the presence of this hormone during early development steers the

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sexual differentiation into a male direction. The interpretation of hormonal data is, however, complicated by the fact that apart from the organising effects sex hormones also affect somatic and psychological aspects of adult life, the so-called activating effects.

The issue whether sex differences in behaviour are mainly due to organising or activating hormonal effects is a difficult question to answer. Human research on these influences of sex hormones in adulthood is restricted to (a) the study of fluctuations in hormone levels in normal people, as for instance research on the menstrual cycle (for example, Bäckström et al., 1983; Van Goozen et al., unpublished data); (b) the study of people who are treated with low doses of sex steroids, like women on oral contraceptives; or (c) the study of patients with atypical hormone levels.

Although both women and men produce oestrogens and androgens, the ratios of production vary enormously between the sexes. There are indications from nonhuman and human studies that the cross-sex hormones contribute to an important extent to the expression of sex-dimorphic behaviours in adulthood, like for instance aggression and sexual motivation (Archer, 1991; De Jonge & Van de Poll, 1984; Van de Poll & Van Goozen, 1992). It would, therefore, be interesting to thoroughly study effects of exogeneously administered testosterone on women and of anti-androgen deprivation and oestrogen administration on men. However, unlike animal research, experimental research on human behaviour is virtually impossible.

1.1. Androgens and Aggression

Studies on aggressive behaviour in animals clearly indicate that aggression is a predominantly male attribute. Criminological studies also reveal a clear sex difference: men use far more physical violence and are more often the victims of aggression. Biological explanations have often linked these findings to the effects of the male sex hormone testosterone, the most important androgen. Whereas animal studies have demonstrated that the presence of this hormone is a necessary prerequisite for the display of aggressive behaviour, correlational studies in humans of fluctuations in hormone levels and concomitant changes in psychological functions also indicate an association, although less clearly so (Olweus et al., 1988).

Correlations between self-reports of aggressive behaviour and androgen levels in men are generally low (Gladue, 1991; Kreuz & Rose, 1972; Meyer–Bahlburg et al., 1974). However, aggressive behaviour as such (now or in the past) correlated positively with testosterone concentrations in some studies. For example, Dabbs and co-workers (1987) measured saliva testosterone in 89 male prison inmates and found that testosterone concentration was related to type of crime: men convicted for violent crimes (murder, rape, robbery) had higher testosterone concentrations than men convicted for theft or burglary. Ehlers and co-workers (1980), in a similar study, studied 27 female patients in a neurological clinic. A violent subgroup had a significantly higher testosterone level and scored twice as high on a "Feelings and Acts of Violence" questionnaire. As yet it is unclear whether these results can be generalised to testosterone fluctuations in normal women and men. Moreover, these studies can not demonstrate whether higher levels of testosterone are the cause or the effect of aggressive behaviour. In an earlier study, using questionnaire methodology, we found that the administration of androgens to female-to-male transsexuals resulted in a significant increase in anger and aggression proneness, but not in an increase in overt aggressive behaviour (Van Goozen et al., 1994b).

A fair amount of evidence exists for activational effects of sex hormones on adolescent

aggressive feelings and behaviours; most of these associations involve androgenic hormones. Larger effect sizes have been reported for boys than for girls. Several studies found evidence of a mediating role for impatience and impulse control in the association between hormonal levels and aggression (Susman et al., 1987; Warren & Brooks-Gunn, 1989). Olweus and colleagues (1988) reported a causal trajectory for effect of pubertal hormones on aggressive behaviour via increased impatience and irritability.

1.2. Androgens and Sexuality

In animal sexual behaviour, the female's dependence on ovarian hormones is a well-established fact. However, circulating testosterone or exogeneously administered androgens clearly affect aspects of feminine sexuality, especially those related to sexual motivation (De Jonge & Van de Poll, 1984). In addition, it has been established that testosterone administered to female rats may lead to a drastic increase of aggressive behaviour which, interestingly, was accompanied by increased sexual behaviour and thereby introduced a clear ambiguity in the behaviour of these females (De Jonge et al., 1986).

While it is well-established that testosterone affects male adult sexual interests and arousal (Cohen-Kettenis & Gooren, 1992), it may in fact be that women are more responsive to minor variations in circulating testosterone levels (Paikoff & Brooks-Gunn, 1990; Sherwin, 1988). Female sexual arousal does not decline significantly postmenopause when oestrogen levels drop but androgens remain constant. A relationship between higher levels of testosterone and increased sexual motivation in normal women has been suggested by several studies. Women differ in baseline levels of testosterone (measured over the whole menstrual cycle), but also in the level at ovulation, at which point there is a notable increase in testosterone (Sherwin, 1988; Van Goozen et al., unpublished data). A relation between the height of testosterone level at the time of ovulation and frequency of sexual behaviour in couples has been demonstrated (Persky et al., 1978b). In addition, female sexual desire, excitement, sexual initiative and responsivity correlated significantly with (mid-cycle) levels of testosterone (Adams et al., 1978; Morris et al., 1987; Persky et al., 1978a, 1978b). Exposure of women to exogenous androgens has, however, yielded only conflicting results so far (Carney et al., 1978; Mathews et al., 1983; Sherwin & Gelfand, 1987; see also Sanders & Bancroft, 1982).

1.3. Sex Hormones and Cognition

Evidence has been accumulating for sex differences in cerebral lateralisation and cognitive functioning (Geschwind & Galaburda, 1985; Hines, 1982; Maccoby & Jacklin, 1974; McGlone, 1980; Reinisch et al., 1991). Women are reported to perform better than men on tasks involving verbal skill, perceptual speed and fine manual dexterity, whereas men outperform women in visuospatial and mathematical ability (Gouchie & Kimura, 1991). Whether these differences are primarily related to genetic, perinatal organising effects of sex hormones, or activating effects in adulthood has not yet been determined.

There is strong evidence that the two hemispheres are specialised for different cognitive processing. In the majority of humans the left hemisphere is specialised in verbal processing and the right hemisphere in spatial processing. Overall, this lateralisation pattern is stronger in men than in women. It has been suggested that this sex difference in lateralisation is caused by differences in prenatal hormonal levels (Witelson, 1991). Studies on women with the Turner syndrome (Hines, 1982; Netley & Rovet, 1982; Waber, 1979) indicate that these women have an extreme female cerebral lateralisation pattern (i.e., diminished laterality for verbal stimuli). On the other hand, in a study on DES women

(Hines & Shipley, 1984), who have been exposed to synthetic oestrogenic hormones, it was found that these women were stronger lateralised to verbal stimuli. It must thus be assumed that in normal men testosterone derived oestrogens exert this effect on cerebral lateralisation. For females with congenital adrenal hyperplasia (CAH), there are results on enhanced spatial abilities (Resnick et al., 1986) and preliminary findings on possibly higher IQs of salt-wasting female CAH patients, as compared with those of both simple-virilizing CAH females and a sister control group (Dittman et al., 1993).

To date, research on the influence of sex hormones on cognitive performance has been mainly correlational in nature. A positive correlation with measures of spatial ability and a negative correlation with measures of verbal production was found in a study on the relation between verbal and nonverbal cognitive abilities and circulating androgen levels in a sample of healthy adult men (Christiansen & Knussmann, 1987). Recently, studies in women on the cognitive effects of hormonal fluctuations during the menstrual cycle have shown that women did better in speeded articulation and manual skills in the high or midluteal phase of the cycle, when oestrogen levels are high; the same applied to verbal fluency and perceptual speed (Hampson, 1990; Hampson & Kimura, 1988). Women performed, on the other hand, better on spatial tests in the follicular phase, when oestrogen levels are low, than in the luteal phase. Other research failed to find any fluctuations in cognitive function coinciding with hormonal fluctuations of the menstrual cycle (Gordon et al., 1986). In an earlier study (Van Goozen, Cohen–Kettenis, Gooren, Frijda, & Van de Poll, 1994), we found that administering androgens to transsexual women resulted in an improvement in visuospatial ability, whereas it led to a performance deterioration on verbal fluency tasks.

1.4. Transsexuality: Human Research on Behavioural Endocrinology

Transsexuality is an incongruence between the biological sex and the self-declared gender identity (Cohen–Kettenis & Gooren, 1992; Gooren, 1984). Thus far, no abnormalities have been found in the sexual differentiation of the transsexual as manifested by the chromosomal pattern, the gonads, secondary sex characteristics and hormone levels. Nevertheless, their persistent and compelling feeling of belonging to the opposite sex might have a brain substrate (Gooren, 1990).

In Amsterdam the Free University Hospital is specialised in treatment of transsexuals. As part of sex-reassignment transsexuals are treated with cross-gender hormones for about 1.5–2 years before actual sex-reassignment operation, if so desired, takes place. Thus far, psychological, genetic and hormonal studies failed to demonstrate any difference between male-to-female transsexuals and heterosexual males, on the one hand, and female-to-male transsexuals and heterosexual females, on the other (Gooren, 1984).

The present study concentrates on groups of eugonadal female-to-male transsexuals, who were administered testosterone, and eugonadal male-to-female transsexuals, who were administered anti-androgens and oestrogens. Both groups were followed during the course of a three months hormonal treatment. The effects of the cross-sex hormone treatment on aggression, sexual motivation and arousability, and cognitive performance were investigated. Personality assessment and sex role questionnaires were included to control for the possibility that respondents answered in a manner they believed to be stereotypical of their desired sex. Control women and men were added to control for the effect of repeated testing over a three months interval and to provide baseline data on the questionnaires.

2. METHOD

2.1. Sample

A group of 35 female-to-male (FM) and a group of 15 male-to-female (MF) transsexuals participated who had been referred to the Department of Andrology at the Free University Hospital and were in treatment for a sex reassignment. Nearly all FMs were treated once every 2 weeks with testosterone esters (Sustanon, 250 mg), administered intramuscularly. In four cases, androgens were administered orally on a daily basis (Andriol, testosterone undecanoaat, 40 mg, twice a day). This treatment regimen is comparable to that administered to men with testosterone deficiency. Both anti-androgens (cyproterone acetate; Androcur, Schering; 50 mg, twice a day) and oestrogens (ethinyloestradiol; 50 μg, twice a day) were administered orally to the MFs.

Two control groups of 20 women (Fem) and 20 men (Male) were composed. These control subjects were contacted in a large supermarket in Amsterdam and asked to participate in this study. The controls were considered to be a representative cross-section of the normal population. All subjects were in good physical health. All female subjects (Fem and FM) reported normal menstrual cycles on the first test session. Subjects were between 20 and 45 years of age (mean age FM = 25.3; MF = 32.4; Fem = 29.6; Male = 29.0). The age differences between the four groups turned out to be significant, a result caused by the noticeable higher mean age of the MF group [$F(3, 86) = 3.57$, $p < .05$].

2.2. Instruments

Aggression and anger proneness questionnaires. The VAG (the "Vragenlijst over Agressief Gedrag"), an adapted version of the Buss–Durkee Hostility inventory (Buss & Durkee, 1957), translated into Dutch in our own laboratory, contained four subscales (Van Goozen, 1990): Assault (11 items), Irritability (13 items), Indirect aggression (12 items), and Verbal aggression (14 items), each item having a 5-point answering format. The Anger EXpression (AX) scale (Spielberger et al., 1986) consists of three subscales, measuring anger-out (i.e., overt anger expression, like verbal behaviour, variable "AX-Out"), anger-in (i.e., the suppression of anger expression, AX-In), and anger-control (AX-Control), each subscale having eight 4-point items. Individual scores on the AX consist of summed scores on all items. On the basis of scores of these three subscales an index of anger proneness is calculated, called AX-EX. The ASQ (Van Goozen et al., 1994a, 1994b) was administered to establish the anger proneness of the subject. An anger proneness score (ASQ-sum) is calculated as the sumscore of two subscores: the percentage of items checked for anger (variable "Anger") and the percentage of items checked for assertive (variable "Assert") and aggressive behaviour (variable "Aggres"); this subscore is called "Angry Readiness." Finally, "Anger-In" is the percentage of items checked for indirect or delayed angry behaviour.

Sex questionnaires. Three questionnaires on different aspects of sexuality were administered, all questionnaires being developed at our own laboratory. These are the Sexual Interest Questionnaire (SIQ), Sexual Attitude Questionnaire (SAQ), and the Sexual Arousability Questionnaire (SOQ). The SIQ consist of 33 items, each having a 5-point scale and the respondent is asked to indicate how often s/he involves in 22 sexually motivated behaviours and 11 sexual fantasies. Two example items are: "Walking down the street I notice attractive persons passing by" and "Fantasizing about making love with a colleague or fellow-student is something I do." A behaviour subscore (SIQ-B), a fantasy

subscore (SIQ-F), and a total score (SIQ-Tot) are calculated on the basis of these answers. The SAQ contains 33 opinions on different sexual behaviours and values. These opinions express either a conservative or liberal attitude towards sexual matters, and the respondent is asked to indicate on a 5-point scale how strongly s/he agrees with each opinion. Two example items are: "Within a sexual relationship it should be possible for both partners to have sexual relations with others" and "You shouldn't have sexual fantasies about other persons than your own partner." A total score (range 33–165) is calculated with high scores representing a very liberal attitude and low scores representing a very conservative attitude towards sex. The SOQ contains descriptions of 44 sexual acts and the respondent is asked to indicate on a 5-point intensity scale how strongly engaging in these behaviours would arouse her/him. Two example items are: "When you masturbate in the presence of your partner" and "When your partner kisses you passionately." An arousability score is calculated ranging from 44 to 220.

Assessment of female and male characteristics and behaviours. A gender role questionnaire was included to control for the possibility that transsexuals answered in a manner they believed to be stereotypical of their desired sex. This questionnaire, the Dutch Sex Role Questionnaire (NSRV; Willemsen & Fischer, 1992), consists of 15 female and male personality characteristics (for example, adventurous, dependent, modest, dominant), and 16 female and male behaviours (for example: "Which programme would you prefer to watch on the TV: western, documentary, sports, talk show, romantic movie?"). All items have a 5-point scale and four subscores are calculated: FemChar and MaleChar (score range: 15–75), FemBehav and MaleBehav (score range: 16–90). For the NSRV gender differences were expected, but the scores were predicted to remain stable and not to change over the course of the 3 mo of treatment.

Cognitive skills. To measure spatial ability the *Card Rotations* test was used (Ekstrom et al., 1976). It consists of a set of six 2-dimensional figures: one is a standard figure, the other five are either rotations or mirror-images of it. Correct responses are selections of the rotated version of the standard figure. Seven minutes are allowed to complete the 30 items; the maximum possible score is 150.

In the *Verbal Reasoning* test (Luteijn & Van der Ploeg, 1983), the subject has to identify the relationship common to two word-pairs. This relationship must then be applied to a third word on the basis of which the respondent chooses its pair from a list of five possibilities. This test consists of 20 items and the subject's score is the number of correctly chosen words. This test was administered to get an indication of the general intelligence of the respondent. In addition, unlike tests for verbal fluency (Hampson & Kimura, 1988) there is no evidence that performance on this particular verbal ability is influenced by sex hormones.

Verbal fluency was measured by two tests adapted from Gordon et al. (1986). The *Word Production, Categories* test requires the subject to write as many words as possible in two minutes for each of four categories. At each testing session two categories were presented (session 1: animals, places; session 2: professions, food); the subject's score is the sum of the two categories (variable "Verbal fluency-W"). In the *Sentence Production, Letters* test the subject is given 5 min to write as many sentences as possible that use each of three given letters at least once as word initials (session 1: E, V, L; session 2: a, W, B). The subject's score is the total number of sentences written (variable "Verbal fluency-S").

Diary. At a later stage in the data collection process the transsexuals were requested to complete a dairy consisting of daily forms concerned with moods and sexual interest. Each form consisted of the following 15 items, each item having a 10-point intensity rating scale: cheerful, tired & flat, easy to get on with, energetic & lively, tense & nervous, (quickly) irritated, aggressive, gloomy & depressed, relaxed, bad-tempered & grumbling, active, satisfied, changeable mood, interested in sex, and sexual fantasies. The forms had to be filled out for 15 successive days per month of treatment. Since we started this procedure in the last year of the data collection process, data of only 10 FM and 11 MF transsexuals were collected.

2.3. Procedure

Each individual was tested twice with a test–retest interval of at least 12 weeks. The transsexuals were tested shortly before and 3 months after the start of sex hormone treatment. On each testing occasion the battery of tests was administered individually in the presence of an experimenter. The test procedure typically lasted 2–2.5 h. The sessions of the transsexual subjects took place at the hospital, the sessions of the control subjects at the Psychology Laboratory of the University of Amsterdam. All subjects were informed that the purpose of the study was to investigate the effects of hormone fluctuations on a number of psychological functions; none of them was aware of the specific nature of our hypotheses concerning the psychological effects. The hospital ethical committee approved the protocol. Subjects were paid for their participation in the study.

2.4. Statistical Analysis

For each subject subscale values for the different questionnaires administered on each test session were entered. Data were analysed by means of multivariate analyses of variance (MANOVA) with "Group" (control vs. transsex) and "Sex" (female vs. male) as between-subjects factors and "Time" (= treatment) as within-subjects factors (time1 vs. time2).

Diary data (n = 10 FMs and 11 MFs) were averaged across the 15 days of each of the 3 mo and analysed using a repeated measures analysis of variance, with "Group" (FM vs. MF) as between-subjects factor and factor "Month" as within-subjects factor with mean monthly values per item taken as data (mean1, mean2, mean3).

3. RESULTS

3.1. Aggression and Anger Proneness

There were strong gender differences in anger proneness, as measured by the AX scale and ASQ (Table I). Biological females (FM and Fem) scored higher on anger proneness (AX-EX, Irritability, ASQ-sum) and different forms of aggressive behaviour (AX-out, Assault, Verbal aggression) than the biological males. Biological males (MF and Male) scored higher on anger control. There were also significant group differences between the controls, on the one hand, and the transsexuals, on the other. For example, controls scored higher on AX-out, AX-EX, Verbal aggression, Assertiveness and Anger Readiness. MF transsexuals differed more from control males than FM transsexuals differed from control females (see the significant interactions between "Group" and "Sex"). As compared to control males, MFs scored very low on Assault and Irritability.

The effects of hormone therapy and/or repeated testing over time were reflected in the results on the subscale Assault of the VAG and the ASQ (interactions of Sex ×

TABLE I. DIFFERENCES BETWEEN FOUR GROUPS ON THREE ANGER AND AGGRESSION QUESTIONNAIRES (AX, VAG, ASQ), AND RESULTS OF MANOVAS, WITH FACTORS GROUP (TRANSSEX VS. CONTROL), SEX (MALE VS. FEMALE) AS BETWEEN-SUBJECTS FACTORS, AND TIME (t-1 VS. t-2) AS WITHIN-SUBJECTS FACTOR

Instrument	Fem	Male	FM	MF	Group (*df* = 1,86)	Sex (*df* = 1,86)	Group × Sex (*df* = 1,86)	Time (*df* = 1,86)	Group × Time (*df* = 1,86)	Sex × Time (*df* = 1,86)	Group × Sex × Time (*df* = 1,86)
AX-out											
t-1	17.7	15.4	16.1	13.7	5.28†	9.19‡	0.29	0.00	0.07	0.15	1.89
t-2	17.3	15.9	16.2	13.3							
Ax-in											
t-1	16.1	17.8	17.1	17.6	0.18	0.56	0.93	0.50	4.48†	1.83	0.26
t-2	16.9	18.0	16.8	15.9							
AX-con											
t-1	18.0	23.2	19.8	23.7	1.32	23.41‡	0.27	0.11	0.11	0.00	0.29
t-2	18.4	23.2	19.6	23.9							
AX-EX											
t-1	31.8	26.0	29.3	23.6	3.85†	14.95‡	0.20	0.43	1.33	0.40	1.48
t-2	31.8	26.7	29.4	21.4							
Assault											
t-1	29.4	29.1	31.7	21.7	1.44	9.46‡	12.91‡	0.57	0.46	0.03	3.29*
t-2	27.2	29.3	33.1	20.3							
Indirect											
t-1	28.2	28.7	28.2	24.2	2.16	2.07	1.17	0.02	0.23	0.06	2.08
t-2	28.8	27.4	27.7	25.1							
Irritab											
t-1	36.1	35.9	36.8	28.8	2.99*	8.54‡	8.89‡	0.10	0.29	1.37	2.38
t-2	35.7	36.1	39.2	27.5							

Verbal											
t-1	46.0	45.2	44.1	38.5	6.20†	6.77‡	1.75	0.41	0.42	1.33	0.31
t-2	47.1	44.0	45.4	39.0							
ASQ-Anger											
t-1	46.1	41.3	49.2	39.3	0.53	9.37‡	1.16	0.03	2.29	4.79†	0.64
t-2	45.8	37.7	54.3	37.4							
Anger-In											
t-1	8.4	8.7	8.7	9.8	1.58	2.51	4.29†	0.01	1.42	3.16*	9.31‡
t-2	8.4	6.9	6.1	14.0							
Assert											
t-1	53.7	46.8	40.8	35.1							
t-2	55.0	46.8	43.0	31.3	18.29‡	7.09‡	0.04	0.00	0.32	1.99	0.82
Aggres											
t-1	10.8	13.4	17.5	17.3							
t-2	12.4	12.8	21.5	13.7	3.62*	0.23	1.03	0.12	0.02	5.66†	1.72
Ang-Read											
t-1	64.5	60.2	58.3	52.3							
t-2	67.4	59.6	64.5	44.9	5.96†	8.60‡	1.10	0.04	0.43	10.03‡	3.49*
ASQ-sum											
t-1	110.6	101.5	107.6	91.7							
t-2	113.1	97.3	118.8	82.3	0.93	11.54‡	1.45	0.00	0.21	12.41‡	3.18*

*$p \leq .10$; †$p \leq .05$; ‡$p \leq .01$.

Time, and/or Sex × Group × Time): the MF group reported more indirect or delayed anger tendencies at posttest [Anger-In; $F(1, 86) = 9.31, p < .01$], whereas in the female group (FM and Fem) feelings of anger proneness and tendencies towards aggressiveness and angry readiness had increased (significant interactions between Sex × Time), but more so in the FM group [significant interactions between Sex × Group × Time for Assault: $F(1, 86) = 3.29, p < .10$; Ang-Read: $F(1, 86) = 3.49, p < .10$; and ASQ-sum: $F(1, 86) = 3.18, p < .10$].

3.2. Sexuality

There were no differences between the sexes in different aspects of sexuality (no main effect for "Sex") (Table II). However, as expected, there were large group differences, with the transsexuals scoring lower in sexual interest, sexual attitude, and arousability than the controls.

The effects of hormone therapy and/or repeated testing over time were reflected in the results on the SIQ and the SOQ. Generally, feelings of sexual interest and arousability increased in the female groups (significant interaction effects between Sex and Time for SIQ-B, SIQ-F, SIQ-Tot, and SOQ) whereas these feelings remained more or less stable in the Male group and decreased considerably in the MF group. However, the increases in sexual interest and arousability were much more pronounced in the FM group as evidenced by the significant interactions between Sex × Group × Time for SIQ-Tot: [$F(1, 86) = 2.90, p < .10$] and SOQ [$F(1, 86) = 10.42, p < .01$]. Time or hormone treatment had no effects on sexual attitude as measured by the SAQ.

3.3. Cognition

Biological females performed better in verbal fluency (significant main effect for "Sex" on Fluency-S), however, contrary to other findings, there was no sex difference in visuospatial ability (Table III). Furthermore, the control group was more intelligent (Verb. Reas) and performed better on the word categories test (Fluency-W) than the transsexual group (significant main effects for "Group").

Repeated testing had a strong effect on all the cognitive skills (significant main effects for "Time"). In particular, performance on the Rotated Figures test had clearly improved during the second test session in the Fem, Male, and FM groups, which is likely to be a task familiarity effect. Of all groups performance on the word categories test (Fluency-W) was worse at posttest.

Some intriguing differences occurred between the groups in cognitive performance as the result of the hormone therapy (highly significant interaction effects between Group × Sex × Time): (a) although the performance on the rotated figures test of the controls and the FMs improved, the increase in performance was strongest in the FMs, whereas the MF group scored slightly worse at posttest [$F(1, 86) = 6.61, p < .01$]; (b) performance on verbal fluency tests deteriorated (Fluency-W, Fluency-S), but the performance deterioration on both verbal fluency tests was stronger in the FM group, whereas the MF group scored only slightly worse on Fluency-W and clearly better on Fluency-S [$F(1, 86) = 14.74, p < .01$, and $F(1, 86) = 18.49, p < .01$, respectively]. On the verbal reasoning test, no such interaction effect was found.

3.4. Gender Characteristics and Behaviours

There were no gross differences between the four groups in self-ascribed female and male characteristics (no significant main effects for "Group" and "Sex" on FemChar and MaleChar) (Table IV). There was a significant sex difference in the attribution of

TABLE II. DIFFERENCES BETWEEN FOUR GROUPS ON THREE SEXUALITY QUESTIONNAIRES (SIQ, SAQ, SOQ), AND RESULTS OF MANOVAS, WITH FACTORS GROUP (TRANSSEX VS. CONTROL), SEX (MALE VS. FEMALE) AS BETWEEN-SUBJECTS FACTORS, AND TIME (t-1 VS. t-2) AS WITHIN-SUBJECTS FACTOR

Instrument	Fem	Male	FM	MF	Group (df = 1,86)	Sex (df = 1,86)	Group × Sex (df = 1,86)	Time (df = 1,86)	Group × Time (df = 1,86)	Sex × Time (df = 1,86)	Group × Sex × Time (df = 1,86)
SIQ-B											
t-1	64.7	68.9	56.9	54.7	13.55‡	0.34	2.97*	3.29*	2.98*	8.78‡	2.31
t-2	66.0	67.8	63.7	53.9							
SIQ-F											
t-1	27.8	28.8	24.2	24.9	5.67†	0.01	0.25	3.08*	0.03	4.10†	1.73
t-2	29.1	29.4	26.6	24.0							
SIQ-Tot											
t-1	92.5	97.7	81.1	79.5	11.87‡	0.22	1.92	3.28*	0.96	8.87‡	2.90*
t-2	95.1	97.2	90.3	77.2							
SAQ											
t-1	113.2	108.9	103.9	102.5	7.15‡	1.03	0.10	2.43	0.98	0.04	0.65
t-2	112.8	110.1	106.4	104.1							
SOQ											
t-1	132.3	137.1	118.9	118.9	11.36‡	0.35	2.02	0.15	1.46	12.00‡	10.43‡
t-2	135.2	139.2	128.2	107.0							

*$p \leq .10$; †$p \leq .05$; ‡$p \leq .01$.

TABLE III. DIFFERENCES BETWEEN FOUR GROUPS IN COGNITIVE ABILITIES, AND RESULTS OF MANOVAS, WITH FACTORS GROUP (TRANSSEX VS. CONTROL), SEX (MALE VS. FEMALE) AS BETWEEN-SUBJECTS FACTORS, AND TIME (t-1 VS. t-2) AS WITHIN-SUBJECTS FACTOR

Instrument	Fem	Male	FM	MF	Group (df = 1,86)	Sex (df = 1,86)	Group × Sex (df = 1,86)	Time (df = 1,86)	Group × Time (df = 1,86)	Sex × Time (df = 1,86)	Group × Sex × Time (df = 1,86)
Card Rot.											
t-1	86.2	97.3	84.5	101.9	0.00	1.69	0.05	22.07‡	0.43	11.32‡	6.61‡
t-2	97.2	105.5	102.4	98.5							
Verb. Reas											
t-1	14.9	15.8	13.1	13.9	6.85‡	2.88*	0.04	6.03†	3.08*	0.22	0.00
t-2	14.9	16.1	13.9	14.9							
Fluency-W											
t-1	55.9	56.2	50.3	45.5	6.74‡	0.02	0.17	129.95‡	3.03*	7.77‡	14.74‡
t-2	44.8	43.1	35.3	42.7							
Fluency-S											
t-1	8.1	7.0	9.2	5.4	0.15	4.84†	0.02	10.55‡	0.03	11.13‡	18.49‡
t-2	7.5	5.8	6.1	6.6							

*$p \leq .10$; †$p \leq .05$; ‡$p \leq .01$.

TABLE IV. DIFFERENCES BETWEEN FOUR GROUPS IN GENDER CHARACTERISTICS AND BEHAVIORS (NSRV), AND RESULTS OF MANOVAS, WITH FACTORS GROUP (TRANSSEX VS. CONTROL), SEX (MALE VS. FEMALE) AS BETWEEN-SUBJECTS FACTORS, AND TIME (t-1 VS. t-2) AS WITHIN-SUBJECTS FACTOR*

Instrument	Fem	Male	FM	MF	Group (df = 1,61)	Sex (df = 1,61)	Group × Sex (df = 1,61)	Time (df = 1,61)	Group × Time (df = 1,61)	Sex × Time (df = 1,61)	Group × Sex × Time (df = 1,61)
FemChar											
t-1	48.7	51.6	49.7	54.3	0.67	1.92	0.08	0.48	0.14	0.41	0.10
t-2	48.3	51.0	50.0	53.7							
MaleChar											
t-1	46.2	50.4	53.2	50.3	1.83	0.00	2.20	1.41	0.08	0.87	0.41
t-2	45.5	49.4	53.6	48.8							
FemBehav											
t-1	43.5	43.7	39.2	49.8	0.03	5.15†	5.73†	0.10	0.95	0.12	1.43
t-2	44.3	43.6	37.7	49.9							
MaleBehav											
t-1	42.0	44.6	42.5	38.7	3.74*	0.66	6.39‡	2.56	0.16	1.37	1.05
t-2	41.4	43.9	42.6	36.5							

* For the NSRV, the FM group consisted of 10 subjects.
*$p \leq .10$; †$p \leq .05$; ‡$p \leq .01$.

female behaviours with biological males scoring higher than biological females [$F(1, 86) = 5.15, p < .05$]. This result is clearly due to the scoring patterns of the two transsexual groups, with feminine behaviours being clearly less descriptive of the FM group, but more so of the MF group. Moreover, the MF group attributed more feminine and less masculine behaviours to themselves than either of the other three groups (significant interactions between "Group" and "Sex" on FemBehav [$F(1, 86) = 5.73, p < .05$], and MaleBehav [$F(1, 86) = 6.39, p < .01$]). There were no main effects for "Time," nor any interactions between "Time" and/or "Sex" and/or "Group." Therefore, although both transsexual groups predictably differed in self-evaluation of stereotypic female and male behaviours, with both groups showing the pattern of response belonging to the desired sex, this pattern was stable and did not change over the course of the hormonal treatment.

Summarizing the results, there was a stronger tendency in the FM group to appraise situations in an angry way, an increase in aggressive tendencies and angry readiness and a decrease in indirect angry behaviour after three months of testosterone treatment. At the same time there was an increase in sexual motivation and arousability. With respect to cognitive functioning, visuospatial ability had improved whereas verbal fluency had deteriorated. In the MF group there was a significant increased tendency to indirect angry behaviour, but aggressive tendencies and feelings of angry readiness had decreased. As expected, there was a significant reduction in sexual arousability. With respect to cognition, there was a significant improved performance on the sentence production aspect of verbal fluency, whereas visuospatial ability had marginally deteriorated.

Although the mean level of performance has gone up or down, it has happened in a consistent way across subjects within each transsexual group, which is shown in the size of the rank order correlations. Pearson product moment correlations, calculated between pretest and posttest scores, for rotated figures are 0.81 (FM) and 0.89 (MF), for word production 0.77 (FM) and 0.84 (MF), for sentence production 0.70 (FM) and 0.94 (MF), and for verbal reasoning 0.75 (FM) and 0.84 (MF). All correlations are significant at the level of 5%.

3.5. Diary Data

Ten FM and 11 MF transsexuals completed daily forms containing 15 items concerned with moods and sexual interest (Table V). The diary data were averaged across the 15 days of each of the 3 months that were filled out and analysed using repeated measures analysis of variance, with "Group" as between-subjects factor and "Month" (mean monthly values per item) as within-subjects factor.

Generally, there were no striking mood intensity differences between the two transsexual groups, nor were there large shifts in tonic moods over the three months. As expected, MFs were very low in sexual interest and sexual fantasies. The FMs were higher than the MFs in self-reported aggressive mood, but the intensity of this feeling did not fluctuate over the course of the 3 months. There was a significant interaction between Group and Month on the item "changeable mood," with the MF group generally reporting stronger changes in mood than the FM group. In addition, the FM group had a dip in changeable mood scores in the second month of treatment, whereas the MF group had a peak at this time. More interesting is the fact that despite the high doses of administered hormones the effects on different reported moods were quite small: contrary to what might have been expected, MFs were not depressed and FMs were not in a very irritated or aggressive mood. Generally, both groups were about equally high in cheerfulness, liveliness, and feelings of satisfaction, and equally low in different negative moods.

TABLE V. MEAN VALUES FOR DIFFERENT MOODS OVER 3 MONTHS OF SEX HORMONE TREATMENT, AND RESULTS OF 2-WAY ANOVA USING GROUP AND MONTH AS FACTORS

Dairy item	Mean-1	Mean-2	Mean-3	Group (df = 1,19)	Month (df = 2,38)	G × M (df = 2,38)
Cheerful						
FM	6.42	6.19	6.24	0.31	0.55	0.31
MF	6.61	6.44	6.73			
Tired & flat						
FM	3.87	3.53	3.98	0.28	0.93	1.44
MF	3.43	3.41	3.36			
Easy to get along						
FM	6.37	6.16	5.97	0.43	2.27	1.37
MF	6.67	6.38	6.60			
Energetic & lively						
FM	5.77	5.95	5.61	0.30	0.11	1.26
MF	6.21	6.04	6.22			
Tense & nervous						
FM	2.66	2.34	2.69	0.01	0.08	2.09
MF	2.56	2.73	2.44			
Quickly irritated						
FM	2.88	2.61	2.74	0.24	1.03	1.67
MF	2.54	2.78	2.17			
Aggressive						
FM	2.36	2.42	2.21	3.59*	2.30	0.23
MF	1.57	1.56	1.22			
Gloomy & depressed						
FM	2.18	2.03	2.35	1.09	0.57	2.01
MF	2.51	3.05	2.67			
Relaxed						
FM	5.53	5.41	5.28	1.10	0.64	0.29
MF	6.17	5.93	6.08			
Bad-tempered						
FM	2.37	2.46	2.44	0.07	0.93	0.57
MF	2.26	2.54	2.17			
Active						
FM	5.95	6.00	6.00	0.12	0.23	0.21
MF	6.21	6.08	6.31			
Satisfied						
FM	5.83	5.41	5.63	2.69	0.79	0.34
MF	6.61	6.50	6.75			
Changeable mood						
FM	2.58	2.21	2.34	2.53	0.87	3.89†
MF	3.42	3.79	3.36			
Interested in sex						
FM	4.59	4.75	4.73	4.68†	1.45	0.56
MF	2.15	2.65	2.86			
Sexual fantasies						
FM	3.67	4.36	4.05	2.30	3.64†	0.68
MF	2.26	2.54	2.46			

*$p \leq .10$; †$p \leq .05$.

4. DISCUSSION

Animal studies and research on humans prenatally exposed to atypical sex hormone levels support the idea that aspects of aggressive and sexual behaviour are influenced by sex hormones in an organising and activating way (Archer, 1991; Dittmann et al., 1992; Sherwin, 1988; Van de Poll & Van Goozen, 1992). Furthermore, there is preliminary evidence that the performance on specific cognitive abilities fluctuates as a result of changing sex hormone levels (Hampson & Kimura, 1988). The aim of the present study was to study gender differences in these sex-dimorphic aspects of behaviour in transsexual and control groups, and to find out whether measures of these behaviours show short-term changes as a result of cross-sex hormone therapy.

4.1. Gender Differences

Research on gender differences tends to involve "normal," nonpatient, samples of subjects. Since transsexuals are dissatisfied with the assigned sex, it is interesting to establish whether similar gender differences can be found in these special groups, and whether cross-sex hormone treatment influences variables typically associated with psychological gender differences. Generally, the "Sex" effect was more consistently significant than the "Group" effect. Therefore, transsexuals did not differ in an important way from the normal pattern of gender differences. Two important exceptions are that controls seemed to be more assertive and somewhat more intelligent. With respect to aggression and anger proneness, as well as cognitive performance, transsexual females and control women were quite similar, as were transsexual and control males. However, the Fem and FM groups were clearly more similar than the Male and MF groups. Sexuality is the area in which gross "Group" differences were found: both transsexual groups scored lower on the different sexual aspects measured. As for cognition, on the pretest testing occasion both the FM and the MF group showed a pattern of cognitive performance specific of their *biological* sex.

4.2. Psychological Consequences of Repeated Testing and/or Cross-Sex Hormone Treatment

Repeated testing in itself had practically no effect on the different measures of aggression and anger proneness. It did, however, have a strong effect on cognitive performance: performance on card rotations and verbal reasoning had improved on the posttest occasion (which we attribute to a familiarity effect), whereas it was worse for verbal fluency. Probably, the word categories and letters presented on the second occasion were more difficult and elicited fewer words and sentences than the ones presented at pretest. More important for our research questions are the interaction effects, especially the interaction between Sex × Group × Time. Little is known about the psychological effects of testosterone treatment on females and of androgen deprivation and oestrogen treatment on males. In the present study some clear effects were found of cross-sex hormone therapy on transsexual females and males. After three months of testosterone administration, FM transsexuals were more anger prone and reported more aggressive tendencies, they had a stronger sexual motivation and arousability, and they were better in visuospatial ability and a worse in verbal fluency (significant interactions between Sex × Group × Time). On all these subscales control women, however, showed the same pattern of responding, albeit less clearly so (significant interactions between Sex × Time). By contrast, after three months of oestrogen therapy MF transsexuals were higher on indirect forms of

angry behaviour and lower on anger proneness and aggressiveness, lower on sexual interest and arousability, and their performance on verbal ability improved at the expense of that on visuospatial ability. Therefore, cross-sex hormone treatment resulted in some drastic changes in the pattern of gender differences, with both transsexual groups moving in the predicted direction. For the interpretation of these results it is important to note that no meaningful changes occurred in both transsexual groups in self-assessment of masculinity and femininity (see Table IV: no interaction effects with Time). It can therefore be concluded that the changes in different gender dependent behaviours are likely to be due to the effects of the hormone therapy and not to an unconscious or deliberate move in the direction of stereotypical ideas about personality characteristics and/or behaviours of the desired sex.

In both transsexual groups the clearest results with respect to changes in anger proneness and aggressiveness were found on the ASQ (Van Goozen et al., 1994), in which the respondent is presented with a number of hypothetical aversive situations (Table I). No clear changes were found on the VAG (based on the Buss–Durkee Hostility inventory; Buss & Durkee, 1957) and AX scale (Spielberger et al., 1986). In this respect it is interesting that some FMs in an interview preceding the second testing session reported to feel more relaxed and happy; life in general had become a more positive experience. They attributed this to a greater acceptance and recognition by their (social) environment since the start of the androgen treatment (which is probably partly due to the quick physical changes that occur). This possibly explains the results: When asking people to indicate what they did when angry or how often they have been aggressive recently, as is the case with the traditional inventories, no increases are found. The results on the ASQ however showed a different picture in the two transsexual groups exposed to high levels of cross-sex hormones: against a general background of more happiness and satisfaction, and less tension, there was a clear increase in aggressive tendencies and angry readiness in the FM group, and in indirect angry reactions in the MF group at the expense of assertive and aggressive reactions (significant interaction effects). In other words, when FM transsexuals were asked to imagine being in negative situations, it turned out that these situations were appraised in a more angry way and that they experienced more aggressive tendencies and feelings of angry readiness than before the testosterone treatment. On the other hand, MF transsexuals experienced less aggressive tendencies in favour of more indirect angry reactions after three months of androgen deprivation.

With respect to aspects of sexual behaviour supposed to be influenced by sex hormones, it was found that sexual arousability and interest were strongly affected by the changes in sex hormone levels in both transsexual groups: arousability increased in the FM group and decreased in the MF group (Table II). Although both transsexual groups scored significantly lower on different aspects of sexual behaviour than controls on the pretest occasion, of the transsexual subjects who happened to have an intimate relationship with a partner, female-to-males reported a stronger interest in sexual behaviour, no changes in frequency of sexual fantasies, more intense sexual arousal when engaging in sexual behaviour, and a generally more satisfactory sexual life. The male-to-females however reported an almost complete cessation of sexual interest and behaviour and, among others, difficulty in maintaining erection during sexual behaviour.

The results of sex hormone treatment on cognitive performance are intriguing. Although a number of studies have provided tentative support to the idea of hormonally determined fluctuations in cognitive performance, those studies have been correlational

in nature, the evidence is mixed, and it is unclear whether cognitive abilities fluctuate as a result of (relative) changes in androgen or oestrogen levels (Christiansen & Knussmann, 1987; Gouchie & Kimura, 1991; Hampson, 1990; Hampson & Kimura, 1988). By analysing the effects of cross-sex hormone treatment on visuospatial and verbal ability in biologically female and male groups, the present study was able to provide some answers. In both transsexual groups some striking effects on cognitive performance were noted: higher testosterone levels resulted in females becoming better in visuospatial ability and worse in verbal fluency, whereas lower levels of androgens and higher levels of oestrogens had the effect of making males better in verbal fluency and worse in visuospatial ability (Table III). The study demonstrates that gonadal hormones do not have a unidirectional influence on cognitive function but have rather, as suggested by Kimura (1988), a differential effect on different cognitive functions within an individual, such that as one function improves, the other deteriorates. As already mentioned, the results are likely to be hormonally caused and not influenced by stereotypical ideas of the transsexual groups about performance of their desired sex. Moreover, to be submitted to cross-sex hormone therapy transsexuals have to prove that they belong to the opposite gender. On the verbal reasoning test there was no change in performance in the MF group and even a slight performance improvement in the FM group. If the results on the verbal fluency tests would have been caused by (stereotypical) expectations of the FM transsexuals (i.e., men perform not so well on verbal tasks), they would have performed worse on the verbal reasoning test too.

4.3. Mood Effects of Hormonal Changes

Interest in the relation between sex hormones and the experience of emotions has been fairly low. Within this domain, much attention has focused on the menstrual cycle in general, and the premenstrual phase in particular, to find out whether the period preceding the onset of menstruation is accompanied by an increase in negative moods. Despite the fact that there is a clear pattern in the levels of both oestrogens and androgens over the menstrual cycle, evidence for a corresponding temporal pattern in emotional changes has been inconsistent (Abplanalp et al., 1979; Bäckström et al., 1983; Parlee, 1982).

As in other research (for example, van Kemenade et al., 1989), in the present study the diary results indicate that no striking mood changes occurred in either transsexual group over the course of the 3 months of treatment: there were no clear differences between the two groups in intensity of different positive and negative moods, nor were there strong fluctuations over the 3-month interval. The female-to-male group only reported slightly stronger feelings of aggressiveness and stronger feelings of sexual interest; however, these were stable differences (a significant group effect). The male-to-female group reported suffering more from changeable moods, feelings which peaked in the second month (significant interaction effect).

The failure to detect direct links between absolute sex hormone levels, on the one hand, and emotional states, on the other, is not surprising and for an important part related to the methodology of subjective assessment of tonic mood states. It is unclear what subjects are doing when they rate their current mood. They may be comparing themselves with others, or with themselves at a different timepoint. Furthermore, the reference point for making such ratings may shift as a function of factors internal and/or external to the individual. To give an example from another domain, in studies with cancer patients or people living with AIDS, it was paradoxically found that more than

90% of these patients reported positive changes in their lives as a result of the threatening experience (Taylor et al., 1994). On the basis of the diary study we would have to conclude that no gross changes occur in tonic mood levels in either transsexual group undergoing a period of drastic physical and psychological changes.

Current emotion theories (for example, Frijda, 1986) attribute an important role to cognitive processes in the instigation of emotion. How one appraises a situation determines to a large extent which emotion one experiences, and the appraisal in turn depends on one's coping options. This implies that the same situation can elicit, for example, anger, fear, or sadness. Thus, we assume that negative moods or emotions are not generated intrinsically, but are intimately connected to events that are appraised in a negative way. The possible link between hormonal changes and the experience of negative moods is thus mediated by the occurrence of negative life events, which, for instance in the premenstrual phase may be appraised more negatively. In an experimental study we found that the premenstrual phase of the cycle was related to an increased susceptibility to react emotionally to negative life events. The present study demonstrates that much more is happening to the transsexuals than one would have concluded on the basis of the diary study alone. To ascertain whether biological males (for example) become less aggressive after androgen deprivation, it would be preferable to assess their reactions to specific life events (real or imaginary), instead of asking them to make global ratings of the intensity of their aggressiveness.

To conclude, the present study offers some strong and consistent support for the idea that opposite sex hormones have a direct and rapid effect on gender specific behaviours: the administration of androgens to transsexual females results in an increase in anger and aggression proneness, in sexual motivation and arousability, and in visuospatial ability, whereas verbal fluency performance deteriorates. By contrast, the administration of anti-androgens and oestrogens to transsexual males has the complete reverse effects: Anger and aggression proneness, sexual interest and arousability, and visuospatial ability decrease, whereas verbal fluency shows a notable improvement. Clearly, it remains to find out what the long-term effects of cross-sex hormone treatment are for these gender-specific behaviours. We have no reasons to believe that the transsexuals have had an aspecific endocrine history in the sense that the FM transsexuals have been exposed to higher androgen levels than normal females, and conversely, that MF transsexuals have been exposed to lower androgen levels than normal men (Gooren, 1984). The effects of cross-sex hormones on psychological functions are impressive. It would therefore seem that if sex-specific organising effects of sex hormones do exist in the human, they do not prevent the activating effects of androgen administration to females and of androgen deprivation of males to become manifest.

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