Androgen and Psychosexual Development: Core Gender Identity, Sexual Orientation, and Recalled Childhood Gender Role Behavior in Women and Men With Congenital Adrenal Hyperplasia (CAH)

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We assessed core gender identity, sexual orientation, and recalled childhood gender role behavior in 16 women and 9 men with congenital adrenal hyperplasia (CAH) and in 15 unaffected female and 10 unaffected male relatives, all between the ages of 18 and 44 years. Women with CAH recalled significantly more male-typical play behavior as children than did unaffected women, whereas men with and without CAH did not differ. Women with CAH also reported significantly less satisfaction with the female sex of assignment and less heterosexual interest than did unaffected women. Again, men with CAH did not differ significantly from unaffected men in these respects. Our results for women with CAH are consistent with numerous prior reports indicating that girls with CAH show increased male-typical play behavior. They also support the hypotheses that these women show reduced heterosexual interest and reduced satisfaction with the female sex of assignment. Our results for males are consistent with most prior reports that boys with CAH do not show a general alteration in childhood play behavior. In addition, they provide initial evidence that core gender identity and sexual orientation are unaffected in men with CAH. Finally, among women with CAH, we found that recalled male-typical play in childhood correlated with reduced satisfaction with the female gender and reduced heterosexual interest in adulthood. Although prospective studies are needed, these results suggest that those girls with CAH who show the greatest alterations in childhood play behavior may be the most likely to develop a bisexual or homosexual orientation as adults and to be dissatisfied with the female sex of assignment.

Human psychosexual development involves three primary components: core gender identity, the sense of self as male or female; sexual orientation, erotic interest in individuals of the same or the other sex; and gender role behaviors, the myriad characteristics that are associated with being male or female or that differ on average for males and females (Green, 1974; Hines, 2004). Determinants of these components are thought to be both biological (genetic and hormonal) and social-cognitive (involving reinforcement and modelling of gender typical behavior; Hines, 2004). This paper focuses on the role of androgens, the primary hormones produced by the testes, in psychosexual development.

The hypothesis that androgens influence human psychosexual development is based on evidence that androgens influence sex-related development in other mammals. During critical periods of early life, high levels of androgen promote male-typical neural and behavioral characteristics, whereas low levels produce female-typical characteristics

(see De Vries & Simerly, 2002; Goy & McEwen, 1980, for reviews). These hormonal effects have been demonstrated most clearly for reproductive behaviors, such as the mounting of female animals by males and the receptive lordosis posture adopted by females in response to these mounts. For example, female rodents and nonhuman primates who are treated with testosterone or other androgens during early development show increased male-typical behavior (mounting) and decreased female-typical behavior (lordosis) in adulthood. Similarly, male animals denied testosterone during early life show decreased mounting and increased lordosis as adults. Early manipulations of androgens also influence other behaviors that show sex differences. For instance, treating female rats or rhesus monkeys with testosterone during early development increases subsequent rough-and-tumble play, a behavior that normally is more common in males than in females (Goy & McEwen, 1980; Meaney & Stewart, 1981).

Hormonal influences on human development have been harder to document than those on other species, because true experiments in which participants are randomly assigned to be treated with hormones or placebo are generally not possible. However, some information has come from studies of individuals who developed in unusual hormone environments for other reasons—for example, because of genetic disorders. Information also has come from studies relating normal variability in the early hormone environment to subsequent variability in behavior.

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The strongest evidence of hormonal influences on human behavioral development has come from studies of childhood play. Girls with the genetic disorder congenital adrenal hyperplasia (CAH) are exposed to high levels of androgen prenatally (Pang et al., 1980; Wudy, Dörr, Solleder, Djalali, & Homoki, 1999). This androgen exposure causes partial to complete masculinization of the external genitalia in utero, and the masculinized genitalia in the newborn female typically lead to diagnosis within days of birth. Postnatally, androgen levels are regulated by hormone treatment, and the external genitalia are surgically feminized, usually in infancy. Despite postnatal treatment, girls with CAH show altered play behavior (see Hines, 2002, 2004, for reviews). They are more likely than other girls to prefer toys that are normally preferred by boys (e.g., cars) and less likely to prefer toys that are normally preferred by girls (e.g., dolls). They also show increased preferences for boys as playmates and for boytypical activities. These differences in play behavior are seen on questionnaires, in interviews, and in direct observation of toy choices. They also are seen when girls with CAH are compared to unaffected female relatives, as well as to controls matched for background factors like age and parental socioeconomic status. Similar outcomes have been seen for girls exposed to high levels of androgenic hormones prenatally because their mothers were prescribed hormones during pregnancy (Ehrhardt & Money, 1967). In addition, normal variability in maternal testosterone levels during pregnancy has been found to relate positively to male-typical play behavior in female offspring at the age of 3½ years (Hines et al., 2002a).

Androgen levels prenatally also may influence sexual orientation and core gender identity, although fewer studies have been conducted in this area. Women with CAH have been found to be more likely to say they are bisexual or homosexual than female controls with other endocrine disorders (Money, Schwartz, & Lewis, 1984), to score higher on a measure of homosexual interest and lower on a measure of heterosexual interest than their unaffected sisters (Dittmann, Kappes, & Kappes, 1992), and to show less heterosexual interest as well as less sexual interest in general than unaffected female relatives (Zucker et al., 1996). Two studies have not reported reduced heterosexuality in women with CAH (Kuhnle & Bullinger, 1997; Lev-Ran, 1974). However, the author of one of the studies (Lev-Ran, 1974) suggested that social prohibitions in the then Soviet Union, where the study was conducted, may have inhibited participants from discussing their sexuality frankly. The methodology of the second study (Kuhnle & Bullinger, 1997) may have limited its power to detect relationships between androgen and sexual orientation. It included a substantial number of women with late-onset CAH, whose androgen elevation would have begun after the presumed critical prenatal period for hormonal influences, and it classified women as either heterosexual or homosexual based solely on whether they were currently living with a female partner.

In regard to core gender identity, although most women with CAH identify as females, they may be at increased risk of gender identity disorder (GID). In one study, one woman with CAH from among 53 seen at a single clinic had requested a change to the male sex in adulthood (Zucker et al., 1996), and in a second, four women with CAH living in the New York City area were found to be gender dysphoric as adults (Meyer-Bahlburg et al., 1996). Because gender identity disorder is rare (occurring in 1 in 30,000 to 1 in 100,000 women), these observations of gender dysphoria in women with CAH were deemed to exceed expectations based on chance. Younger girls with CAH also may experience reduced satisfaction in their assigned sex. They have been found to be less likely than control girls to say they are content to be or prefer to be a girl (Ehrhardt, Epstein, & Money, 1968) and more likely to to say that they might have chosen to be a boy or might be undecided as to whether to be a boy or a girl, if given the choice (Ehrhardt & Baker, 1974). In addition, a study of 18 girls with CAH found that 2 met the diagnostic criteria for GID, as did 5 of 29 girls with other intersex diagnoses involving elevated androgen prenatally (Slijper, Drop, Molenaar, & de Muinck Keizer-Schrama, 1998).

There is little information on psychosexual outcomes in males with CAH. Most studies of childhood play suggest no differences from males without CAH (Berenbaum & Hines, 1992; Ehrhardt & Baker, 1974). Although one study reported reduced male-typical play (Slijper, 1984), this was seen only in comparison to unrelated boys, not when boys with CAH were compared to unaffected brothers. A second study found reduced male-typical rough-and-tumble play in boys with CAH (Hines & Kaufman, 1994), but the same boys did not show alterations in preferences for male playmates (Hines & Kaufman, 1994) or in toy preferences (Berenbaum & Hines, 1992). Finally, one study reported a difference in the opposite direction, finding that boys with CAH showed increased male-typical behavior in the form of intense energy expenditure (Ehrhardt & Baker, 1974), although other male-typical behaviors, such as toy and playmate preferences, were unaltered. There is essentially no information on core gender identity or sexual orientation in men with CAH.

Thus, past research shows that females with CAH show increased male-typical play behavior in childhood and may show an increased risk of gender dysphoria and reduced heterosexual orientation as adults. However, no information is available as to whether sex-typical play in childhood relates to core gender identity or sexual orientation in females with CAH. Also, inconsistent outcomes have been reported for play behavior in boys with CAH, and there are no reports on core gender identity or sexual orientation in men with CAH. The present study assessed recalled childhood play behavior, core gender identity, and sexual orientation in both men and women with CAH. In addition, it examined relationships between recollections of sex-typical play behavior in childhood and psychosexual outcomes (core gender identity and sexual orientation) in adulthood.

МЕТНОР

Participants

Participants were part of a study of psychological, physical, perceptual, and motor development in individuals with CAH. The overall study included 40 females and 29 males with CAH and 29 unaffected female and 30 unaffected male relatives (57 siblings and 2 first cousins), all in the range of 12 to 45 years of age. Because of practical and ethical considerations related to assessments of sexuality, the current study was limited to those participants ages 18 or older, and included 25 individuals with CAH (16 women, 9 men) and 25 unaffected relative controls (15 women, 10 men). This represents all but 9 of the potential participants in the appropriate age range. Three of these 9 (2 men and 1 woman with CAH) were not included because measures of core gender identity and sexual orientation were added after the study began and they had already completed the other aspects of the protocol. The remaining 6 participants (1 man and 4 women with CAH and 1 unaffected female sibling) declined to complete the questionnaire.

Participants with CAH were recruited via pediatric endocrinologists at Middlesex and Great Ormond Street Hospitals in London, England (n=11; 6 women, 5 men) or through a CAH support group in the United Kingdom (n=14; 10 women, 4 men). Unaffected relatives were recruited through the families of individuals with CAH. None of the 25 participants with CAH had the late-onset form of the disorder. Twenty-three of the 25 were deficient in the enzyme 21-hydroxylase; 22 had the salt-losing form of the disorder and 1 (a male) did not. For the remaining 2 participants with CAH, both of whom were female, medical records confirming 21-OH deficiency and salt-losing status were not available.

The overall study involved 6 hours of participation at the university. Subjects were paid £50 (about \$75) for their participation, and their costs of travel to the university were reimbursed. Written informed consent was obtained from all participants prior to conducting the study procedures.

Dependent Measures

We assessed core gender identity and sexual orientation for both the lifetime and for the most recent 12 months using a 10-item questionnaire designed for this purpose (Hines, Ahmed, & Hughes, 2003). Three items targeted gender identity at each time period. These items asked whether the participant enjoyed being a person of his or her own sex, wished to be a person of the other sex, or thought that he or she was psychologically a person of the other sex. The items were answered on a 7-point Likert scale, ranging from 1 (always) to 7 (never). Two items targeted sexual orientation at each time period. These items asked about sexual behavior and about sexual fantasies and desires, and each was answered on a 5-point Likert scale ranging from 1 (exclusively heterosexual) to 5 (exclusively homosexual). We summed items within each

category to obtain an overall score. Thus, two scores were obtained for gender identity (lifetime and past 12 months) and two for sexual orientation (lifetime and past 12 months) for each participant. Higher scores for both gender identity and sexual orientation reflect less sex-typical characteristics (i.e., less identification with the assigned sex or a less exclusively heterosexual orientation).

We assessed recalled childhood gender role behavior using the Pre-School Activities Inventory (PSAI; Golombok & Rust, 1993). The PSAI consists of 24 items assessing interests in sex-typical childhood toys and activities (e.g., playing with vehicles, weapons, dolls, or jewelry, playing with girls, enjoying rough-and-tumble play). It has been standardized for children 2½ to 7 years of age and is typically completed by a parent to describe the behavior of a child. Participants in the current study completed the inventory retrospectively to describe their own childhood behavior. Higher scores on the inventory represent more male-typical behavior. The PSAI was added to the study after other aspects of data collection had been completed and was mailed to participants, along with a self-addressed stamped return envelope. It was returned by 14 females and 8 males with CAH and 11 unaffected female and 8 unaffected male relatives who also had completed the measures of core gender identity and sexual orientation.

Control Measures

Age and general intelligence were included in the assessments to determine if participants in the four groups were similar in regard to these background factors. Age at the time of testing was calculated from information provided by participants as to their date of birth. The vocabulary subtest of the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981) provided the measure of general intelligence. The dependent measure was the age-scaled vocabulary score.

Statistical Analyses

We designed this study to test specific hypotheses regarding women with CAH. These were that women with CAH would recall increased male-typical play behavior in childhood and would show reduced core gender identity as female and reduced heterosexual orientation in adulthood, compared to unaffected female relatives. We investigated these hypotheses using planned comparisons (one-tailed or directional *t* tests). No differences were predicted in any of these areas between men with and without CAH, and so differences between the two groups of men were evaluated using two-tailed *t* tests. We did not predict group differences in control measures (age and vocabulary), and we analyzed these data using two-tailed tests.

RESULTS

Control Measures

There were no significant differences in either age or intelligence for males or females with and without CAH (Table

1): for age, t (17) = 1.02, p = .32 for males and t (29) = 0.43, p = .67 for females; for vocabulary, t (17) = 0.10, p = .92 for males and t (29) = -1.56, p = .13 for females.

Recalled Childhood Play and Activity Interests

As expected, men scored significantly higher than women on the PSAI, t (17) = -5.45, p < .001, d = 2.90 (Table 1). Also as predicted, women with CAH recalled significantly more male-typical behavior in childhood than unaffected women as reflected in higher scores on the PSAI, t (23) = 3.99, p < .001, d = 1.60. Men with and without CAH did not differ in scores on the PSAI, t (14) = -.31, p = .76, d = 0.16.

Sexual Orientation

Women with and without CAH differed significantly in sexual orientation, both for the past 12 months and for the lifetime: t (16.63) = 2.21, p = .02, d = .92 for the past 12 months and t (17.45) = 2.00, p = .03, d = .82 for the lifetime, both unequal variance (Table 1). For both time periods, women with CAH reported a less exclusively heterosexual orientation than did control women. Men with and without CAH did not differ in sexual orientation for either time period: t (17) = 0.80, p = .44, d = .42 for the past 12 months and t (17) = .09, p = .93, d = .03 for the lifetime.

In addition to looking at mean scores for sexual orientation, we looked at the frequency with which respondents endorsed particular response choices to describe their sexual behavior during the most recent 12 months. Among females with CAH, 5 women (31%) rated their recent behavior as bisexual or homosexual. Of these 5, 1 indicated that her behavior over the past 12 months was exclusively homosexual, 2 that their behavior was mainly but not exclusively homosexual, and 2 that their behavior was half heterosexual and half homosexual. In contrast, among females without CAH, none rated themselves as bisexual or homosexual; all indicated that their behavior had been exclusively or mainly heterosexual. The proportion of women describing themselves as bisexual or homosexual

differed significantly for women with and without CAH (Fisher exact p = .026). None of the men in either the group with CAH or the group without CAH reported bisexual or homosexual behavior at the current time. All of the men indicated that their behavior had been exclusively or mainly heterosexual during the past 12 months.

Core Gender Identity

Women with and without CAH also differed significantly in core gender identity over the past 12 months as well as over the lifetime: t (20.52) = 1.83, p = .04, d = .70 for the past 12 months and t (17.03) = 1.99, p = .03, d = .82 for the lifetime, both unequal variance (Table 1). For both comparisons, women with CAH reported weaker identification as females. Men with and without CAH did not differ significantly in core gender identity at either time point: t (14.8) = -1.33, p = .19, d = .64, unequal variance, for the past 12 months and t (17) = -1.61, p = .13, d = .75 for the lifetime. However, effect sizes for these comparisons were moderate to large and in the direction of men with CAH reporting stronger male identity.

As for sexual orientation, the frequency with which particular responses were endorsed for core gender identity (wishing to be a person of the other sex) over the most recent 12-month period was examined. Among women with CAH, 11 indicated that they had never or almost never wished to be a person of the other sex. However, 5 (31%) indicated having had this wish during the past 12 months, with 4 endorsing some of the time and 1 endorsing about half of the time. In contrast, not one of the 15 control women reported wishing to be a person of the other sex. All indicated that they never or almost never had this wish during the past 12 months. The proportion of women who indicated that they had wished to be a person of the other sex at least some of the time during the past 12 months differed significantly for women with and women without CAH (Fisher exact p = .026). None of the males, whether they had CAH or not, indicated a wish to be a person of the other sex during the past 12 months. All men in

Table 1. Control Variables and Psychosexual Outcomes in Women and Men With and Without CAH (Means + SD)

	Women		Men	
	CAH (n = 16)	Control $(n = 15)$	CAH (n = 9)	Control $(n = 10)$
	Control variables			
Age (years)	23.6+6.7	22.7+3.4	28.1+8.4	24.3+7.8
Vocabulary	8.19+1.51	9.07+1.62	9.00+2.45	8.90+2.01
	Psychosexual outcomes			
Recalled childhood gender role behavior a	60.5+16.1***	33.6+17.6	68.3+11.8	69.8+7.4***
Core gender identity b (past 12 months)	5.44+3.01*	3.93+1.28	3.22+0.67	3.80+1.13
Core gender identity 6 (lifetime)	6.75+4.84*	4.27+1.22	3.44+0.88	4.20+1.14
Sexual orientation ^c (past 12 months)	3.75+2.62*	2.27+0.59	2.44+1.33	2.10+0.32
Sexual orientation ^c (lifetime)	3.69+2.60*	2.33+0.72	2.22+0.67	2.20+0.42

^a Numbers of participants for recalled childhood gender role behavior = 14 women with CAH, 11 control women, 8 men with CAH, and 8 control men. ^b Scores can range from 3 to 21. Lower scores indicate stronger identification with the assigned gender. ^c Scores can range from 2 to 10. Lower scores indicate stronger heterosexual orientation.

^{*} Differs from mean for control women, p < .05. *** p < .001.

both groups indicated that they never or almost never wished to be a person of the other sex.

Correlations

We also examined whether recollections of male-typical play in childhood related to increased male-typical sexual orientation or core gender identity among women with CAH. (This analysis was only conducted for women with CAH because the other three groups showed almost no variability in sexual orientation or core gender identity.) Childhood gender role behavior correlated significantly with sexual orientation during the past 12 months (r = .63, p < .01, one-tailed) and over the lifetime (r = .51, p < .05, one-tailed). The correlation of childhood gender role behavior with core gender identity over the past 12 months, although of moderate size, was not significant (r = .30, p = .15, one-tailed), but the correlation with gender identity over the lifetime was (r = .57, p < .05, one-tailed). All relationships were in the direction of more male-typical behavior in childhood predicting less female-typical sexual orientation and core gender identity in adulthood.

Finally, because women's recognition of or willingness to report same-sex erotic interests or dissatisfaction in the female gender might increase with age (Katchadourian & Lunde, 1975), we correlated age with sexual orientation and core gender identity. None of these correlations were significant: r = .08 and .07 for sexual orientation over the past 12 months and over the lifetime, respectively; r = -.16 and .00 for core gender identity over the past 12 months and over the lifetime, respectively.

DISCUSSION

We found that women with CAH recalled more male-typical play behavior in childhood and that, as adults, they were less likely to be exclusively heterosexual and to express satisfaction with being a female compared to a group of unaffected female relatives. These results replicate numerous prior reports of increased male-typical play behavior in girls with CAH (e.g., Berenbaum & Hines, 1992; Dittmann et al., 1990a, 1990b; Ehrhardt & Baker, 1974; Ehrhardt et al., 1968; Hines & Kaufman, 1994; Money & Ehrhardt, 1972; Nordenstrom, Servin, Bohlin, Larsson, & Wedell, 2002; Zucker et al., 1996). They also add to the growing number of studies suggesting that women with CAH may be more male-typical than other women in respect to sexual orientation (Zucker et al., 1996; Money et al., 1984; Dittmann et al., 1992) and core gender identity (Zucker et al., 1996; Meyer-Bahlburg et al., 1996).

We found that men with CAH did not differ significantly from unaffected male relatives in recalled childhood play behavior or in sexual orientation or satisfaction with being a male in adulthood. There are fewer prior studies of behavioral outcomes for males with CAH than for females with CAH. However, most prior studies of boys suggest no changes in childhood play behavior (Berenbaum & Hines, 1992; Ehrhardt & Baker, 1974; Hines & Kaufman, 1994), and our results also support this conclusion. In addition,

our results provide initial evidence suggesting that any prenatal hormonal alteration that might occur in males with CAH does not produce dramatic alterations in sexual orientation or core gender identity in adulthood.

The present study also provides an initial evaluation of relationships between sex-typed behavior in childhood and adult psychosexual outcomes in females with CAH. In this group of women, male-typical scores on the PSAI were associated with reduced heterosexual interest both during the most recent 12-month period and over the lifetime. This finding suggests that those girls who are most behaviorally masculinized as children are also the most likely to evolve a bisexual or homosexual erotic orientation as adults.

Girls with CAH who show more male-typical play behavior as children also may be at increased risk for developing dissatisfaction with the female gender. We found that those women with CAH who recalled more male-typical childhood play behavior, as reflected in scores on the PSAI, reported less satisfaction with the female gender over their lifetime. However, the correlation between recalled childhood gender role behavior and core gender identity over the past 12 months was not significant, suggesting that this dissatisfaction may be reduced in adulthood. This interpretation would be consistent with the relatively high percentage of girls with CAH who have been reported to meet the criteria for GID (Slijper et al., 1998) compared to the relative rarity of gender dysphoria in adulthood among women with CAH (e.g., Meyer-Bahlburg et al., 1996; Money & Daléry, 1976; Zucker et al., 1996).

One limitation of the current study is that it was not longitudinal. As a consequence, some data were based on retrospective reports. In addition, the measure of childhood gender role behavior used, the PSAI, was standardized for parents describing the behavior of their 21/2- to 7-year-old children. In contrast, in the current study, adults used the PSAI to describe their own behavior during childhood. Nevertheless, the size of the sex difference we observed in adults using the PSAI to report retrospectively on their own childhood behavior was very similar to that reported previously for prospective assessments made by parents of children at the age of 3½ years (Hines et al., 2002a). Also, the size of the difference between women with and without CAH in the current study is similar to that obtained for parental assessments of girls with and without CAH in the age range of 3 to 10 years (Fane, 2002). Thus, the retrospective use of the PSAI to assess one's own past behavior appears to produce results similar to those obtained when it is used prospectively by parents to assess their children's behavior. Nevertheless, it will be important to replicate the current findings using prospective assessments of childhood gender role behavior as well as of core gender identity and sexual orientation.

A second limitation of the study is the small sample. Such small samples are not unusual in research on rare endocrine disorders such as CAH. Nevertheless, sample size could have limited the ability to detect anything but

large differences between groups. It will be important to determine if research on larger samples produces similar results. This is particularly the case for our assessments of core gender identity in males, where there were no statistically significant differences, despite a moderate to large effect size index in the direction of greater satisfaction with the male gender among those with CAH.

Prior research on males with CAH has not suggested consistent alterations in childhood play behavior, and no information on core gender identity or sexual orientation in these males has been published previously. However, some reports suggest that they may show demasculinization of spatial abilities (Hampson, Rovet, & Altmann, 1998; Hines, Fane, et al., 2003) and hypermasculinization of finger length ratios (Brown, Hines, Fane, & Breedlove, 2002) or hand preferences (Mathews et al., in press). In this regard, it is worth noting that the differences observed in the present study between males with and without CAH were not only statistically insignificant, but also in different directions for sexual orientation versus core gender identity. In regard to sexual orientation, males with CAH were somewhat but not significantly less male-typical than unaffected males, whereas for core gender identity, they were somewhat but not significantly more male-typical. These findings add to prior work suggesting that any prenatal hormonal abnormality experienced by males with CAH has neither a consistently demasculinizing or hypermasculinizing effect on psychosexual development.

Finally, our findings have clinical implications. The association between reduced satisfaction with the female sex of assignment and recollections of male-typical play behavior and interests in childhood suggests that those girls with CAH who show the most cross-gendered behavior in childhood might be at the greatest risk of gender dysphoria, and thus might require increased clinical attention. More generally, it also is important to determine why some women with CAH are less satisfied as females than are others. Although cross-gendered behavior in childhood appears to be associated with adult dissatisfaction as a female as well as with reduced heterosexuality, these relationships cannot be assumed to be causal. Instead, all three outcomes (male-typical interests in childhood, reduced satisfaction with the female gender in adulthood, and reduced heterosexual interest) could result from a number of other causes. Possibilities include the amount or timing of prenatal exposure to androgen, genetic factors other than those causing CAH, the age at diagnosis, the adequacy of postnatal hormone treatment, the age at feminizing genital surgery or its success, the degree of psychological and social support, parental rearing practices, and the broader social and cultural environment (Hines, 2004; Hines et al., 2002a; Meyer-Bahlberg, 2001; Meyer-Bahlberg et al., 1996). Identifying which of these factors influence variability among females with CAH in satisfaction with the female gender as well as other elements of psychosexual differentiation is an important challenge for future research.

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