AGGRESSION AND INTEREST IN INFANTS IN WOMEN WITH COMPLETE ANDROGEN INSENSITIVITY SYNDROME

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ABSTRACT

The purpose of this study was to examine the role of the Y chromosome on aggression and interest in infants. Self-reports of aggression and interest in infants were obtained from 44 women with Complete Androgen Insensitivity Syndrome (CAIS), who have XY chromosomes but cannot respond to testosterone, and 14 of their unaffected female relatives, who served as controls. As hypothesized, women with CAIS were more significantly more likely than controls to choose physical aggression as a response to a hypothetical conflict situation. However, there was no significant difference between women with CAIS and control women in their interest in infants, possibly due to the small sample size. The difference in aggression has important implications for future research on the effects of the Y chromosome on sex-typed behavior.
ACKNOWLEDGEMENTS

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Introduction

There are sex differences in several aspects of behavior including cognition, activities and interests, and personal and social characteristics (e.g., Blakemore, Berenbaum & Liben, 2009; Else-Quest et al., 2006; Halpern, 2000). Some of these sex differences start at a very young age (e.g., Campell & Eaton, 1999; Goldberg & Lewis, 1969). For example, males have better spatial abilities than females and these differences have been found in adults, children, and even infants (Moore & Johnson, 2008; Quinn & Liben, 2008; Voyer, Voyer & Bryden, 1995). Young boys and girls also differ in their choices when playing with toys (Liss, 1981). Boys are more likely than girls to play with toy trucks and tools, while girls are more likely than boys to play with dolls and kitchen toys. However, girls are more likely than boys to show flexibility in their toy choice, with girls playing with a combination of female-typical and male-typical toys, whereas boys mostly play with masculine toys (O’Brien & Huston, 1985). Interestingly, juvenile rhesus monkeys show sex differences in toy play that are similar to the ones found in human children (Alexander & Hines, 2002; Hassett, Siebert & Wallen, 2008), suggesting a biological basis for these early differences in play behavior.

Gender differences have also been found in other aspects of play and behavior. These differences emerge early, with preschool-aged boys engaging in more rough and tumble play than girls (DiPietro, 1981). Gender differences continue through childhood and adolescence, a time when boys are also more likely than girls to engage in risk taking behaviors, (Byrnes, Miller & Schafer, 1999). Boys are also more likely than girls to use physical aggression, particularly in adolescence and young adulthood (Maccoby &
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Jacklin, 1980). In addition, there are gender differences in the incidence rates of psychological disorders: males are more likely than females to be diagnosed with pervasive developmental disorders, such as autism and Asperger syndrome (Hartung & Widiger, 1998; Skuse, 2000; Volkmar, 1993).

Besides these sex differences mentioned above, many more sex differences in behavior have been observed, most of small to medium size (Blakemore et al., 2009). Two important behaviors that show a consistent sex difference are aggression and interest in infants: boys and men are more aggressive and girls and women are more interested in infants.

A meta-analysis of sex differences in aggression, using data from 196 self-report, 66 observational, 51 peer-report and 40 teacher-report studies (Archer, 2004) showed that males were more likely than females to display direct aggression, such as physical aggression. These higher levels of aggression in males when compared to females may be linked to men’s higher levels of prenatal and postnatal testosterone. Supporting evidence for effects of prenatal hormone exposure comes from studies of the effects of artificial progestin (a masculinizing hormone) given to pregnant women to prevent miscarriage. Males and females who were exposed to higher levels of progestins in the womb were more likely than their unaffected siblings to choose physical aggression as a response to a hypothetical situation (Reinisch, 1981). This is consistent with evidence in other species, e.g., prenatal androgen exposure leads to increased aggressive behavior in mice (vom Saal, 1979). Supporting evidence for effects of postnatal hormones, high levels of circulating testosterone have been found to be associated with self-ratings of aggression in teenage boys and men (Christiansen & Knussman, 1987; Olweus et al., 1980).
Circulating levels of testosterone have also been linked to increased aggression in mice (Beeman, 1947; Nelson & Chiaveggato, 2001).

There may also be social factors that contribute to men having higher levels of aggression compared to women. Boys experience less disapproval than girls from their parents over their aggressive actions (Perry, Perry & Weiss, 1989). Over time, this social influence may lead boys to become more aggressive. These examples show that many factors, such as prenatal androgen exposure, circulating testosterone levels, and social influences, are potential causes of increased aggression in males.

Another major sex difference that trends in the opposite direction is that girls and women are more interested than boys and men in caring for and engaging with infants (Melson & Fogel, 1982). This tendency towards infant nurturing may be present throughout from childhood through adulthood in females (Maestripieri & Pelka, 2002). When faced with an unfamiliar baby, adolescent girls are more likely than adolescent boys to respond to the infant (Feldman, Nash, & Cutrona, 1977). At multiple ages (preschool, childhood, and adulthood), females interact with infants more than males do (Blakemore, 1981).

In rodents, there are also sex differences in parental care. Although the specific behaviors vary across species, females exhibit a higher number of nurturing behaviors than do males (Lonstein & De Vries, 2000). In primates, changes in responsiveness to young members of the species seem to be linked to hormonal changes throughout the lifetime, with an increase in pregnancy-related hormones linked to an increase in nurturing behaviors towards young primates (Maestripieri & Wallen, 1995). In humans, nurturing may also be related to gender-role socialization, because girls are socialized to
be more nurturing than boys (Best & Williams, 1997). Thus, it is very likely that nurturing behaviors are caused by a combination of hormonal and social factors.

It is challenging to isolate the specific factors that lead to sex differences, because typical males and females differ in their hormone levels, sex chromosomes and socialization. One way to test biological explanations of sex differences is by manipulating hormones or sex chromosomes in animals. In rodents, when sex hormone levels were manipulated through methods such as a prenatal or postnatal hormone injection, or through castration or ovariectomy, hormone levels were found to correlate with measures of sexually dimorphic behaviors, such as activity level, maze learning ability and avoidance responses (Beatty, 1979). For example, female rats exposed to neonatal androgens exhibit more masculine play behavior, such as play fighting, than unexposed females (Meaney & Stewart, 1981). Female macaques also show behavioral changes with increased prenatal testosterone, though the effects depend on when during the gestation period mothers were injected with testosterone (Goy, Bercovitch & McBrair, 1988). Females exposed to testosterone early in gestation were more likely than unexposed females to show the male-typed behaviors of mother-mounting and peer-mounting and less likely to show the female-typed behavior of mother-grooming. Females exposed to testosterone late in gestation were more likely than unexposed females to engage in rough play and peer-mounting. Thus, hormones present during critical phases of development play a role in development of sex-typed behavior in nonhuman animals.

It is not feasible or ethical to manipulate hormones in people, so studies of their effects take advantage of experiments of nature. These studies can help isolate the social
causes from the biological causes because there are several human conditions where sex chromosomes or sex hormones can be studied independently of each other. One of these is Congenital Adrenal Hyperplasia (CAH), a condition that stems from a defect in the \textit{CYP21} gene on chromosome 6. The mutation leads to a deficiency in 21-hydroxylase, which then leads to an excessive accumulation of androgen (e.g., Speiser & White, 2003). This excess androgen is similar to the testosterone produced by the testes. Females with CAH have higher levels of prenatal androgen exposure than typical girls, but they have sex-typical chromosomes and rearing. Males with CAH have similar androgen levels as typical males, possibly due to a feedback loop involving the testes that allows males to regulate their testosterone levels so that their levels remain within a certain range. Girls and women with CAH are behaviorally masculinized in some ways compared to girls and women without CAH (e.g., Speiser & White, 2003). Reports from parents of girls with CAH, as well as self-reports from girls with CAH, indicate that they are more likely than their unaffected sisters to play with boys’ toys and to be interested in male-typed activities and careers (Berenbaum & Hines, 1992; Berenbaum, 1999). Parents also reported that, compared to their unaffected sisters, girls with CAH were less likely to show interest in infants (Leveroni & Berenbaum, 1998) and to be physical aggressive in conflict situations (Pasterski et al., 2007). Adolescent and adult women with CAH were also more likely than unaffected siblings to report using aggression in conflict situations (Berenbaum & Resnick, 1997). Girls with CAH also had higher spatial ability than their unaffected sisters (Berenbaum, 2001; Puts, et al., 2008).

It is possible that these differences are due to effects of the disease besides prenatal androgen levels or because of differences in the way that parents treat their
daughters with CAH. However, since males with CAH are behaviorally similar to unaffected males (Hines, Brook, & Conway, 2004), it is unlikely that the disease itself causes a difference in gender development. Also, parents actually encourage their daughters with CAH to play with girls’ toys more than their unaffected daughters (Pasterski et al., 2005), which should lead girls with CAH to be more feminized, not more masculinized in their toy play. So while studying individuals with CAH is an imperfect method for studying prenatal hormone levels alone, it is likely that the main reason for differences between girls with CAH and their sisters is the difference in their prenatal androgen levels.

Apart from hormones, sex chromosomes had also been found to play a role in sex-typed behavior in rodents. Among mice with no testes, those with XY chromosomes had more masculinized vasopressin-immunoreactive fibers in the lateral septum of the brain than those with XX chromosomes (De Vries et al., 2002). Also in mice, sex chromosome complement had an effect separate from the influence of the gonads on social behavior, including response to intruders, a sex-typed behavior (McPhie-Lalmansingh, et al., 2008).

Other studies have been done that involve manipulation of the Y chromosome. On the Y chromosome, the Sry gene is responsible for testis development. Transgenic mice have been constructed so that the Sry region is separated from the rest of the Y chromosome. This leads to mice that have Y-chromosomes without male-typical gonads or hormone levels. Findings that these mice have female-typical scores on some traits, such as interest in female-soiled bedding, means that these characteristics are probably controlled by their gonadal sex (sex hormones). Interestingly, however, these XY females
that lack *Sry* chromosomes are more similar to XY males on some behaviors, suggesting that they are at least partially controlled by chromosomal sex (Gatewood, 2006). XY females were more likely than XX females to be physically aggressive and to display lower pup retrieval, an indicator of parental behavior. This suggests that genes on the Y chromosome outside of the testis-determining region, influence sex-typed behavior.

Another group of mice were sex reversed so that they had XX chromosomes, but one of their X chromosomes contained a portion of the Y chromosome. These XX males had levels of infanticide and pup retrieval that were in between those of XY males and XX females (Reisert et al., 2001). This suggests that a region of the Y chromosome may contribute to the sex differences in behavior towards pups, but there are other factors involved because XX males did not behave exactly like XY males. This study is complicated by the fact that the levels of prenatal hormones for this group of XX males were estimated to be about the same as XY males. This means that the change in behavior may be due to hormones rather than sex chromosomes. This experiment illustrates why not much is known about the behavioral effects of sex chromosomes; it is difficult to manipulate chromosomes without also affecting hormone levels.

In another study where the genetic control of gonad development was manipulated, there was no difference between XY females and XX females in levels of aggression (Canaster, Maxson, & Bishop 2008). Differences between this study and the others previously mentioned could be due to the way that the Y chromosome was manipulated, or to the types of measures used.

Chromosomes cannot be manipulated in humans the same way that they are manipulated in mice, but there is a naturally occurring human condition in humans in
which sex chromosomes are dissociated from sex hormones: Complete Androgen Insensitivity Syndrome (CAIS). Individuals with CAIS have male-typical (XY) sex chromosomes but do not respond to androgen because they have defective or non-functional receptors (Cheikhelard et al., 2009). Due to their Y chromosome, individuals with CAIS develop testes that produce testosterone and anti-mullerian hormones, leading to suppression of the development of the uterus and the upper part of the vagina (Nichols, Bieber, & Gell, 2008). Because of the lack of response to androgen, individuals with CAIS develop female-typical external genitals, including labia, a shallow vagina, and a clitoris (Ahmed et al., 2000; Muller, 1984). Individuals with CAIS are therefore raised as girls and most develop a core female gender identity and are satisfied with their female sex of rearing (Wisniewski et al., 2004). At puberty, they develop secondary sexual characteristics, such as breasts, because their testosterone is converted to estrogen (Papadimitriou, Linglart, & Chaussain, 2006). However, menstruation does not occur because of the lack of uterus and ovaries; lack of menarche is often the reason that girls are diagnosed with CAIS (Oakes et al., 2008; Rutgers & Scully, 1991).

Women with CAIS are similar to typical women in many important ways, including gender role behavior, recalled childhood masculinity and personality characteristics (Hines, Ahmed & Hughes, 2003). The similarities between women with CAIS and typical women indicate that androgen levels and/or sex of rearing (which is female-typical for both groups of women) play a large role in gender development. However, women with CAIS have not been studied very much because CAIS is a very rare condition. Studying women with CAIS may help to understand whether genes on the
Y chromosome play a role in sex-typed behavior, independent of the influence of sex hormones and socialization.

Hypothesis: On the basis of animal studies, I hypothesize that genes on the Y chromosome will have an effect on aggression and interest in infants. Thus, I hypothesize that women with CAIS will have higher scores on aggression and lower scores on interest in infants than typical women.
Methods

Participants

Women with AIS were recruited through the Androgen Insensitivity Syndrome Support Group of the United States (AISSG). Members of the group who were 18 years of age and older and who also had AIS or a related condition were invited to participate in the study. Unaffected female relatives (sisters and mothers) served as control subjects. They were also recruited through the AISSG and by contacting family members of participants with CAIS. Relatives were studied as a control for general genetic and environmental background. We studied 44 women with CAIS and 14 unaffected female relatives. Women with CAIS were 18-75 years old (Mean: 47.67 years, Median: 49.11 years); unaffected relatives were 35-74 years old (Mean: 52.37 years, Median: 50.02 years). The difference in mean age was not significant. Details of the study and consent procedures were provided to participants over the telephone. Implied consent was used; participants signified their consent by returning completed test booklets. The test booklets contained a variety of self-report questionnaires, including measures of aggression and interest in infants.

Measures

Aggression was measured with a modified version of Reinisch’s Aggression Inventory (Reinsich and Sanders, 1986) used in other studies (Berenbaum & Resnick, 1997). The participant reads about interpersonal situations and then chooses how she would have responded when she was 8 years old; this age is chosen to minimize socially desirable responses. The measure is scored for how often the participant would respond
with physical aggression, verbal aggression, withdrawal, or non-aggressive coping. There is a significant sex difference in physical aggression, with males scoring higher than females (Reinisch & Sanders, 1986). The difference is influenced by hormones: Women with CAH score higher than their unaffected sisters on physical aggression (Berenbaum & Resnick, 1997); males and females prenatally exposed to androgenizing progestins also score higher than their unexposed siblings (Reinisch, 1981).

Interest in infants was measured with a modified version of Melson’s Questionnaire (Melson, 1987) Instead of parents reporting on their children’s behavior, women were asked about their own behavior towards babies and pets when they were eight years old. The responses were scored for interest in infants and interest in pets. The parent-report measure showed a significant sex difference in interest in infants (girls more interested than boys), but not in interest in pets (Melson & Fogel, 1996); girls with CAH were also reported to have less interest in infants than their unaffected sisters and to have slightly more interest in pets (Leveroni & Berenbaum, 1998).

Data Analysis

Data were available for all 58 participants for interest in infants, but only 53 participants had complete data on aggression. Scores from both questionnaires were compared between women with CAIS and control women using a two sided t-test, because women with CAIS could have scores that are more or less female-typical than their unaffected female relatives, depending on their biological influences, as detailed below. Type I error was set to.05.
There were several possible outcomes that could be explained by the chromosomal, hormonal and social influences on women with CAIS. If genes on the Y chromosome have an effect on aggression and interest in babies, then women with CAIS will have more male-typical scores than control women. If, instead, aggression and interest in infants are affected by prenatal androgen, then women with CAIS will have more female-typical scores than control women. This is because unlike typical women who have low levels of androgen (Davison, 2005; Reinisch, J. M., 1974), women with CAIS have no effective androgen. If there is no difference in the scores of women with CAIS and control women, this could be because chromosomes and hormones have the opposite effects and the effects cancel each other out. In Further, individuals with CAIS are raised as girls and probably have similar socialization as typical girls (Wisniewski et al., 2004). This feminine socialization would lead women with CAIS to have similar scores to typical women. Finally, a lack of a difference could also result from the relatively low power in our sample. We had power to detect large effect sizes.
Results

Scores of control subjects were compared to scores of women with CAIS using a two-sided t-test that assumed equal population variances. They were first compared on the four scores from Reinisch’s Aggression Inventory: physical aggression, withdrawal from aggression/conflict, verbal aggression, and non-aggressive coping. As seen in Table 1, women with CAIS were significantly more likely than control women to choose physical aggression as a response to the hypothetical conflict situations ($M = 3.39, SD = 3.02$ vs. $M = 1.08, SD = 1.17$, $t(51) = 2.57, p < .02$). Women with CAIS were also significantly less likely than control women to withdraw from aggression/conflict ($M = 11.90, SD = 3.37$ vs. $M = 14.92, SD = 1.78$, $t(51) = 2.97, p < 0.005$). Differences for verbal aggression and non-aggressive coping were not significantly different.

Using data from Melson’s Questionnaire, scores of women with CAIS were compared to scores of unaffected women for interest in infants and infants in pets. As shown in Table 2, women with CAIS were less likely than control women to report childhood interest in infants ($M = 28.93, SD = 8.68$ vs. $M = 32.26, SD = 9.29$), the difference was not significant, $t(56) = 1.23, p > 0.2$. The groups were not significantly different on self-reported interest in pets: women with CAIS, $M = 16.11, SD = 4.50$) vs. control women, $M = 15.70, SD = 4.37, t(56) = -0.30, p > 0.7$).
The purpose of this study was to examine the role of the Y chromosome on aggression and interest in infants. Studies in mice suggest that genes on the Y chromosome affect these behaviors, but parallel effect have not previously been tested in people. Women with CAIS provide a unique opportunity to compare relative effects of the Y chromosome vs. androgens because they have XY chromosomes and female-typical hormone (low or no androgen) levels.

As hypothesized based on studies in mice, women with CAIS did report that they were significantly more likely than control women to use physical aggression in a hypothetical conflict situation (Table 1). Women with CAIS were also significantly less likely than control women to report that they would withdraw from the conflict (Table 1). Because Reinisch’s Aggression Inventory is a forced choice measure, statistically significant results for one choice can lead to statistically significant results for another choice. This means that the difference between women with CAIS and control women could be due to women with CAIS having a preference for physical aggression, a dislike of withdrawal compared to the control women, or a combination of both. Future studies could investigate aggression separately, possibly by using a measure like the aggression subscale of the Multidimensional Personality Questionnaire (Tellegen, 1982).

There were no significant differences between women with CAIS and control women in interest in infants or pets (Table 2). This may have been due to the small sample size and limited statistical power. It is interesting that the overall trend suggests
that women with CAIS might be less likely than control women to have had a childhood interest in infants. This means that in a future study with a larger sample size and more power it is possible that we might find a significant difference.

There are several potential explanations for the significant difference between women with and without CAIS in aggression, but not interest in infants. First, the measure of aggression might be more sensitive than the measure of interest in infants. Second, women with CAIS may differ from control women more on aggression than on interest in infants, and our relatively small sample prevented detection of small effects. Third, the Y chromosome may be important for some human behaviors but not others, thus affecting physical aggression, but not for interest in infants.

These results from women with CAIS are particularly interesting when compared with the results from previous studies of women with CAH. On the physical aggression scale of the Reinisch Inventory, women with CAH had an average score of 7.64, whereas their unaffected female relatives who had an average score of 3.60 (Berenbaum & Resnick, 1997). Both women with CAIS and their unaffected female relatives from our study had lower scores than even the control women in the study of CAH (Table 1). The difference may reflect the populations studied. Females with CAH and their unaffected relatives were younger than the sample of women with CAIS and their unaffected relatives: age range of 12 to 35 (mean age = 19) vs. age range of 18 to 75 (mean age = 49). Further, controls were intentionally selected to be comparable to their relatives with CAH or CAIS. Overall, though, the trends are similar, with women with CAIS and CAH having higher scores than their unaffected female relatives.
On both aggression and interest in infants, women with CAH differed more from their controls than did women with CAIS, suggesting that prenatal androgens have a greater effect than genes located on the Y chromosome. It is very likely that sex-typed traits are influenced by a variety of biological factors, including sex chromosomes and hormones, as well social factors.

This study fits into the larger scientific context by addressing causes of gender differences. This study provides preliminary evidence for the role of the genes on the Y chromosome in one aspect of sex-typed behavior, aggression. Women with CAIS showed increased physical aggression despite having female typical hormone levels and being raised as females. This has implications for future research into the Y chromosome.

Future studies might continue to examine aggression and interest in infants in individuals with CAIS. It would also be interesting to study other behaviors that show a strong sex difference to see if the Y chromosome has an influence on them as well. It is important to study traits that show a strong sex difference because CAIS is a rare condition and sample sizes are typically small in studies involving women with CAIS.

CAIS is usually not diagnosed until adolescence and is rare, so it can be difficult for researchers to get a large sample, or to get a preadolescent sample. Because we used retrospective self-reports of behaviors, it would be interesting to see if the results can be replicated in a sample of younger girls with CAIS reporting on concurrent behavior. It will also be interesting to use multiple measures.
This study is an important step toward further understanding the role of the Y chromosome. Not much is known about the Y chromosome besides its role in promoting testes development, so it is of scientific interest to determine the other ways that it influences development. The evidence from this study indicates that the expression of genes on the Y-chromosome is correlated with increased physical aggression, but the Y chromosome is not linked to interest in infants. The correlation with aggression is an important one and encourages further study.
REFERENCES


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### Table 1

*Reinisch’s Aggression Inventory: Group differences in responses to hypothetical conflict situations*

<table>
<thead>
<tr>
<th></th>
<th>Physical Aggression</th>
<th>Withdrawal from Aggression/Conflict</th>
<th>Verbal Aggression</th>
<th>Non-Aggressive Coping</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control (N=12)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.083*</td>
<td>14.917*</td>
<td>8.917</td>
<td>11.083</td>
</tr>
<tr>
<td>SD</td>
<td>1.165</td>
<td>1.782</td>
<td>0.981</td>
<td>0.793</td>
</tr>
<tr>
<td><strong>CAIS (N= 41)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3.39*</td>
<td>11.902*</td>
<td>10.805</td>
<td>9.902</td>
</tr>
<tr>
<td>SD</td>
<td>3.024</td>
<td>3.368</td>
<td>0.531</td>
<td>0.496</td>
</tr>
</tbody>
</table>


\( d = -1.007* , 1.119* , -2.394 , 1.519 \)

**Note.** Differences between women with CAIS and the control women, tested by separate t-tests for each type of aggression, were significant (*p < 0.05).
Table 2

Melson’s Questionnaire: Group differences in interest in infants and pets

<table>
<thead>
<tr>
<th></th>
<th>Interest in Infants</th>
<th>Interest in Pets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control (N=14)</strong></td>
<td>Mean</td>
<td>32.264</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>9.294</td>
</tr>
<tr>
<td><strong>CAIS (N=44)</strong></td>
<td>Mean</td>
<td>28.928</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>8.685</td>
</tr>
<tr>
<td><em>p</em></td>
<td></td>
<td>.223</td>
</tr>
<tr>
<td><em>d</em></td>
<td>0.371</td>
<td>-0.092</td>
</tr>
</tbody>
</table>

*Note.* Differences between women with CAIS and the control women, tested by separate t-tests for interest in infants and pets, were not significant.
Academic Vitae of Sarah Barcousky

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