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2D:4D finger-length ratios in children and adults with gender identity disorder

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ABSTRACT

Previous research suggests that prenatal testosterone affects the 2D:4D finger ratio in humans, and it has been speculated that prenatal testosterone also affects gender identity differentiation. If both things are true, then one would expect to find an association between the 2D:4D ratio and gender identity. We measured 2D:4D in two samples of patients with gender identity disorder (GID). In Study 1, we compared the 2D:4D ratios of 96 adult male and 51 female patients with GID to that of 90 heterosexual male and 112 heterosexual female controls. In Study 2, we compared the 2D:4D ratios of 67 boys and 34 girls with GID to that of 74 control boys and 72 control girls. In the sample of adults with GID, we classified their sexual orientation as either homosexual or non-homosexual (in relation to their birth sex) to examine whether or not there were any within-group differences as a function of sexual orientation. In the sample of adult men with GID (both homosexual and non-homosexual) and children with GID, we found no evidence of an altered 2D:4D ratio relative to same-sex controls. However, women with GID had a significantly more masculinized ratio compared to the control women. This last finding was consistent with the prediction that a variance in prenatal hormone exposure contributes to a departure from a sex-typical gender identity in women.

Introduction

Biological influences on the development of gender identity disorder (GID) have long been the subject of intense theoretical conjecture (Baum, 2006; Gooren, 2006; Meyer-Bahlburg, 1984). Genetic factors may play a role (see, e.g., Coolidge et al., 2002); however, because there are well-documented cases of identical twins discordant for GID (e.g., Segal, 2006), it is clear that other factors are also involved. In this regard, the most prominent biological model about GID development concerns the role of prenatal sex hormones (Meyer-Bahlburg, 1984): as a direct main effect (Reiner and Gearhart, 2004), in relation to the genes involved in the sexual differentiation of the gonads and, possibly, of the brain (Arnold, 2004; Fleming and Vilain, 2005), or, perhaps, in interaction with postnatal psychosocial factors.

The empirical evaluation of prenatal hormone theory, as applied to sex-dimorphic behavioral differentiation in humans, has often focused on within-sex variations in sex steroid exposure. Numerous studies of children born with disorders of sex development (physical intersex conditions) have shown sex-dimorphic behavioral effects; for example, research on genetic females with congenital adrenal hyperplasia (CAH), a condition characterized by high prenatal androgen levels, has consistently identified evidence for postnatal behavioral masculinization, particularly with regard to gender role behavior and sexual orientation (for review, see Cohen-Bendahan et al., 2005).

Children and adults with GID have strong cross-gender identification, display an array of cross-gender behaviors, and express the desire to become a member of the opposite sex. Many children with GID, but not all, differentiate a homoerotic sexual orientation in adolescence (Drummond et al., 2008; Green, 1987; Zucker and Bradley, 1995). Adults with GID who have a childhood history of pervasive cross-gender behavior ("early-onset" cases) also have a homoerotic sexual orientation. In contrast, "late-onset" adults with GID, i.e., those without a childhood history of pervasive cross-gender behavior, are much more likely to have a non-homosexual sexual orientation (see, e.g., Blanchard, 1989). For children and adults (particularly the "early-onset" cases) with GID, it has long been speculated that a variance in prenatal testosterone exposure contributes to their departure from a sex-typical gender identity, gender role, and sexual orientation. However, at present, there is no clear clinical evidence of atypical prenatal sex steroid levels in children or adults with GID (even at levels that might allow the configuration of the external genitalia to remain intact, which is almost always the case) or variation in androgen metabolism (Bentz et al., 2007).

In the present study, we used an indirect method for investigating the putative effects of prenatal exposure to testosterone on gender identity differentiation by assessment of the 2D:4D finger ratio — the relative lengths of the 2nd ("index") finger and the 4th ("ring") finger. Use of 2D:4D measurement as a "window" (Manning, 2002) into prenatal development has become extremely popular over the past 10 years and several lines of evidence have accumulated suggesting that 2D:4D variation might be related to variation in prenatal exposure to testosterone and to variation in postnatal sex-dimorphic behavior.

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The formation of both digits and genitals are controlled by the same genes: Homeobox or Hox genes (Kondo et al., 1997). In humans (see Manning et al., 1998) and in mice (Kondo et al., 1997), a mutation of a single Hox gene leads to deregulation of both digits and genitalia. Since sex steroids influence the development of the genitalia, it has been surmised that this might also hold true for the fingers. Indeed, in humans, the 2D:4D ratio has been shown, on average, to differ between males and females. In females, the two fingers are approximately equally long, but in males the fourth digit is usually longer than the second (Manning et al., 1998; McFadden and Shubel, 2002). This sex-dimorphism in 2D:4D has been documented in aborted fetuses at weeks 9–40 of gestation (Malas et al., 2006) and deceased fetuses at a mean gestation of 28 weeks (range, 14–42) (Galis et al., submitted for publication), in children as young as 2 years of age (Manning et al., 1998), and appears to remain relatively stable throughout the life course (e.g., Trivers et al., 2006).

Manning (2002) advanced the hypothesis that variation in prenatal androgen exposure was at least partially responsible for the sex-dimorphism in 2D:4D. Evidence in support of this hypothesis comes from experimental manipulation of prenatal androgen exposure in pheasants (Romano et al., 2005) and from two studies of women with CAH, who had more masculinized finger ratios than unaffected female controls (Brown et al., 2002b; Ökten et al., 2002; for a null finding, see Buck et al., 2003). van Anders et al. (2006) also found that females with a male co-twin had a more masculinized 2D:4D than females with a same-sex twin, which was inferred to be the result of a prenatal androgen transfer effect.

To date, only two studies have examined 2D:4D in adult patients with GID. Schneider et al. (2006) compared the finger ratios of 43 female-to-male transsexuals to a control group of 65 (presumably heterosexual) women and Kraemer et al. (2007) conducted a similar study of 17 female-to-male transsexuals with a control group of 190 women (188 were classified as heterosexual). In both studies, there was no evidence for an altered 2D:4D ratio in the female patients with GID. Thus, these two studies provided no support for the hypothesis of a masculinized prenatal hormonal milieu.

Schneider et al. (2006) also compared the finger ratios of 63 male-to-female transsexuals to a control group of 58 (presumably heterosexual) men. They found some evidence for a feminized 2D:4D ratio in their male-to-female transsexuals, an effect that was even stronger when restricted to right-handed participants, but this was limited only to the right hand. Because Schneider et al. did not have information on the sexual orientation of their patients, it was not possible to determine if the feminized 2D:4D pattern was specific to male-to-female patients with a homosexual sexual orientation or was characteristic of both homosexual and non-homosexual patients (H. J. Schneider, personal communication, November 13, 2007). In the other study, Kraemer et al. (2007) compared the finger ratios of 39 male-to-female transsexuals with a control group of 176 men (163 were classified as heterosexual). Kraemer et al. found a more feminized 2D:4D ratio on the right hand, but not the left hand, in their male patients with GID. The same pattern was reported in an analysis restricted to right-handed participants. Kraemer et al. also compared their homosexual and non-homosexual male patients with GID and found no significant difference in 2D:4D. Thus, for men with GID, these two studies appeared to provide support for the hypothesis of a feminized 2D:4D pattern, which would be consistent with prediction derived from prenatal sex hormone theory.

The purpose of the present study was to compare 2D:4D in two new samples of patients with GID. In Study 1, we compared the 2D:4D ratios of adult male and female patients with GID to that of heterosexual male and female controls. In Study 2, we compared the 2D:4D ratios of boys and girls with GID to that of control boys and girls. In the sample of adults with GID, we classified their sexual orientation as either homosexual or non-homosexual (in relation to their birth sex) in order to examine whether or not there were any within-group differences as a function of sexual orientation.

Study 1

Methods

Participants

Participants were 96 male-to-female and 51 female-to-male adults with GID who were patients at the Gender Identity Clinic, VU Medical Center in Amsterdam. They were recruited for the study at the time of a routine endocrine assessment, but this was not necessarily the patients' first appointment at the clinic. An attending clinic psychologist or psychiatrist diagnosed all patients as meeting *DSM* criteria for GID (American Psychiatric Association, 1994). Control participants (90 men, 112 women) were all self-identified heterosexual students at the VU University, who were recruited via advertisement, and adults who were recruited in a supermarket.

Based on information obtained during clinical assessment, the sexual orientation of the probands (in relation to their birth sex) was classified as either homosexual or non-homosexual (bisexual, heterosexual, or asexual). For the male gender patients, 40 (41.7%) were classified as homosexual and 56 (58.3%) were classified as non-homosexual. For the female gender patients, 39 (76.5%) were classified as homosexual and 12 (23.5%) were classified as non-homosexual.

There is evidence in the literature that GID male patients with a homosexual sexual orientation present for assessment at an earlier age than GID male patients with a non-homosexual sexual orientation (Blanchard, 1994; Blanchard et al., 1987; Smith et al., 2005). Unfortunately, for the present study, it was logistically cumbersome to retrieve data on the patients' age at initial assessment. On the assumption, however, that the age at initial evaluation was not related to the patients' attendance for their routine follow-up evaluation, we predicted that the mean age of the homosexual male patients would be lower than the mean age of the non-homosexual male patients. This proved to be correct: the homosexual male patients were, on average, significantly younger than the non-homosexual patients: *M* age, 40.53 (SD=11.46) vs. 46.55 (SD=12.18) years, $t(94)=2.44$, $p=0.016$. Because non-homosexual female patients are relatively few in number, we had no particular prediction about their age at presentation compared to the homosexual female patients. There was no significant difference in age at the time of participation in the present study. The homosexual female patients had a mean age of 38.44 years (SD=9.38) and the non-homosexual female patients had a mean age of 41.25 years (SD=14.51), $t(49)<1$.

The mean age of the control men was 30.01 (SD=11.12) years and the mean age of the control women was 28.47 years (SD=9.93). Because the controls were significantly younger than the probands, age was treated as a covariate.

Measure and procedure

Participants' right and left hand were photocopied using a standard copy machine. Digit length was measured on the copy from the basal crease of the finger to the tip, using vernier calipers measuring to 0.01 cm. The finger ratio was calculated by dividing the length of the second finger by that of the fourth. A total of 100 scans (28.9%) were scored separately by two raters. The coders were masked to the participants' sex and group membership. Pearson correlations showed high inter-scorer reliability: $r=.94$ for right 2D, $r=.95$ for right 4D, $r=.96$ for left 2D, and $r=.97$ for left 4D.

Results

Normative sex differences in the control group. Table 1 shows the mean 2D:4D ratios for the right and left hands in the control group as a function of sex. For both the right and left hands, there was a significant sex difference, with the men having a lower 2D:4D ratio than the women: for the right hand, $t(199)=4.29$, $p<0.001$; for the left hand, $t(199)=4.39$, $p<0.001$. Cohen's *d* was 0.58 for the right hand and 0.60 for the left hand. Thus, for both hands, the predicted normative sex difference in 2D:4D was confirmed.

Proband-control comparisons by sex. Table 1 also shows the mean 2D:4D ratios for the right and left hands in the GID probands whose sexual orientation was classified as homosexual in relation to their birth sex (androphilic for the biological males and gynephilic for the biological females).

Table 1
Study 1: Mean 2D:4D as a Function of Group, Sex, and Hand

	Right Hand			Left Hand			Combined		
Group	M	SD	N	M	SD	N	M	SD	N
GID males	.952	.029	39	.967	.035	38	.959	.024	37
GID females	.969	.050	38	.961	.034	39	.966	.032	38
Control males	.955	.041	89	.960	.039	89	.957	.034	88
Control females	.978	.034	112	.982	.032	112	.981	.029	111

Note. GID = gender identity disorder. The GID males were all classified as androphilic (homosexual in relation to their birth sex) and the GID females were all classified as gynephilic (homosexual in relation to their birth sex). The control males were all classified as gynephilic (heterosexual) and the control females were all classified as androphilic (heterosexual). In the ANOVAs reported in the text, there were 37 GID males, 88 control males, 38 GID females, and 111 control females, due to loss of either a RH or LH measurement because of poor scan quality (see the Combined column).