Multivariate Genetic Analyses of the 2D:4D Ratio: Examining the Effects of Hand and Measurement Technique in Data from 757 Twin Families

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The ratio of the lengths of the second to fourth digits of the hand (2D:4D) is a sexually dimorphic trait that has been proposed as a measure of prenatal testosterone exposure and a putative correlate of a variety of later behavioral and physiological outcomes including personality, fitness and sexual orientation. We present analyses of 2D:4D ratios collected from twins (1413 individuals) and their nontwin siblings (328 individuals) from 757 families. In this sample 2D:4D was measured from photocopies using digital calipers, and for a subset of participants, computer-aided measurement. Multivariate modeling of the left- and right-hand measurements revealed significant genetic and environmental covariation between hands. The two methods yielded very similar results, and the majority of variance was explained by factors shared by both measurement methods. Neither common environmental nor dominant genetic effects were found, and the covariation between siblings could be accounted for by additive genetic effects accounting for 80% and 71% of the variance for the left and right hands, respectively. There was no evidence of sex differences in the total variance, nor in the magnitude or source of genetic and environmental influences, suggesting that X-linked effects (such as the previously identified association with the Androgen receptor) are likely to be small. However, there were also nonshared environmental effects specific to each hand, which, in addition to measurement error, may in part explain why some studies within in the literature find effects for the 2D:4D ratio of one hand but not the other.

The ratio of the lengths of the second to fourth digits (2D:4D) is a sexually dimorphic trait that has been hypothesized to reflect the levels of prenatal androgens to which an individual was exposed prenatally. Since Manning and his colleagues first proposed that the 2D:4D ratio might serve as a noninvasive window into prenatal hormonal conditions (Manning et al., 1998), there have been over 100 studies reporting associations between 2D:4D and a variety of later behavioral and physiological outcomes (McIntyre, 2006). However, the evidence supporting this theory is mixed. Manning directly examined the relationship between the level of testosterone in the amniotic fluid and 2D:4D and found no significant correlation (Manning, 2002). In a follow-up study, Lutchmaya et al. (2004) reported a correlation between the ratio of fetal testosterone to fetal estradiol from amniocentesis and the 2D:4D ratio of the right hand at age 2 (Spearman rank correlation -.47). No such correlation was found for the left hand and no significant relationships were found between the 2D:4D ratios of either hand and the levels of fetal testosterone or estradiol. While much attention has been focused on the 2D:4D ratio, ratios involving other fingers have been found to differ between clinical and control groups even when no 2D:4D differences were found (McFadden et al., 2005).

The heritability of 2D:4D has been examined in three twin samples: Paul et al. (2006), Voracek and Dressler (2007), and Gobrogge et al. (2008). The sample sizes and results of these studies are summarized in Table 1 below. The point estimates from these studies indicate substantial additive genetic effects. However, it is also obvious, from the wide confidence intervals, that the power of previous studies to detect significant common environmental effects, or sex differences in the variance components, was limited. The present study addresses these issues by examining the evidence for sex differences in the both sources and magnitude of genetic influences on 2D:4D, and common environmental or nonadditive genetic effects, in a larger twin sample (N = 1741 individuals from 757 families).

Since the initial popularization of 2D:4D as a noninvasive measure of fetal testosterone exposure, the

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Table 1

ACE Model Parameter Estimates From Previous Twin Studies of 2D:4D (With 95% Confidence Intervals)

	Additive genetic effects	Common environmental effects	Unique environmental effects	*N* MZ pairs	*N* DZ pairs
Right hand					
Paul et al.	.61 (0.28,0.95)	.03 (–0.2,0.28)	.36 (.27, 43)*	148	308
Gobrogge et al.	.43 (0,0.70)	.15 (0,.52)	.42 (.30–.59)	146	154
Left hand					
Paul et al.	.70 (0.35,1.05)	.01 (–0.23,0.25)	.29 (.23, 36)*	148	308
Gobrogge et al.	.50 (.03,0.70)	.08 (0,.45)	.42 (.30–.60)	146	154
Mean 2D:4D					
Voracek and Dressler	.62 (.09, 1)*	.17 (0, .79)*	.21 (.13, 35)*	34	20

Note: *Confidence intervals/point estimates were not provided in the original paper and have been computed from the MZ and DZ twin correlations using Mx.

measurement and reliability of the ratio has attracted considerable attention. Although Manning (2002) initially advocated measuring 2D:4D using photocopies of the hand, he and his associates have since reported that measures from photocopies yield lower average 2D:4D ratios than direct measures from the hand (Manning et al., 2005). However 2D:4D studies using multiple forms of measurement typically find a general consistency of results among them. Perhaps more concerning are the recent findings from Voracek et al. (2007) that showed that while the interrater reliability (measured by intraclass correlation) for measurements of the fingers from the same set of photocopies measured by 17 experts ranged between .94 and .96, the reliability of the 2D:4D ratio was lower: ICC .72 and .76, for the left and right hands, respectively. To address measurement issues in the present study, 2D:4D was measured using both the standard digital caliper technique and with the assistance of computer imaging software. Multivariate genetic analyses, combining the two methods of measurement and the data from left and right hands, were used to assess (1) whether the measurement method influenced the heritability of 2D:4D and (2) whether a single common gene effect is sufficient to explain the genetic influences on this trait or whether the magnitude and sources of gene action differ between the hands, possibly contributing to the conflicting findings in the literature.

Method

Sample

Adolescent twins and their nontwin siblings were recruited from the general population, in the context of ongoing studies of melanoma risk factors and studies of cognition. The clinical protocols have been described in detail elsewhere (Aitken et al., 1996; McGregor et al., 1999; Wright et al., 2001; Wright & Martin, 2004). Participants were enlisted by contacting the principals of primary schools in the greater Brisbane area, media appeals and by word of mouth. It is estimated that approximately 50% of the eligible birth cohort were recruited into the study, which began in 1992. The sample is predominantly Caucasian, with over 95% of participants reporting the ancestry of at least three of their four grandparents as being English, Irish, or Scottish. The sample appears representative with respect to mole count (Zhu et al., 1999) and IQ (Wright et al., 2001).

This article concerns data collected from twins between July 2002 and January 2007. Photocopies of the participants' hands were taken when the participants attended clinical sessions at the Queensland Institute of Medical Research (QIMR, Brisbane, Australia). Participants were asked to place their hands flat on the glass with their fingers slightly apart, and were instructed not to press down on the glass. Given the number of twins who had participated in the study prior to the introduction of digit ratio protocol, twins and their siblings who had participated in the study before July 2002 were sent a letter asking them to send in photocopies of their hands. Of the 1335 individuals who were approached, 323 sent in photocopies, yielding a response rate of 24%.

Informed consent was obtained from all participants and parents prior to testing. The protocol used was approved by the QIMR Human Research Ethics Committee. Initial zygosity diagnoses were determined by typing eight highly polymorphic DNA microsatellite markers and three blood groups (ABO, MNS, Rh). This has subsequently been confirmed by microsatellite and/or whole genome single nucleotide polymorphism scans for this sample.

Procedure

Two procedures were used to measure finger length. First, for all photocopies, finger length was ascertained from the photocopied hands by measuring the distance from the most basal crease of the finger to the tip using calipers that recorded to 0.01 mm. All measurements were made by a trained research nurse. These measurements are referred to as the QIMR measurements.

In addition, for photocopies obtained between July 2002 and October 2003 (n = 680) the photocopies

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were scanned and computer-assisted measurements were obtained using the imaging software program Canvas, as described by McFadden and Shubel (2002). These measurements were performed at the University of Texas by researchers blind to the twin and zygosity status of the participants. To make the measurements researchers used the tools of Canvas to draw a line segment that appeared to best fit the proximal crease at the base of the digit. The length of this line was approximately equal to the width of the digit. A second line was drawn from the midpoint of the first line to the tip of the digit. These points are identified using a greatly magnified image, so that these landmarks can be identified with one-pixel accuracy resulting in high inter-rater and test–retest reliabilities (McFadden & Shubel, 2002). A measuring tool in Canvas was then used to obtain the length of all four fingers of each hand. Those for the second and fourth fingers, used in this article, are referred to as the UT measurements.

In both cases, the 2D:4D ratio was calculated as the length of the second digit divided by the length of the fourth digit. Given the very low variance of the 2D:4D ratio, the left- (LH) and right- (RH) hand ratios measurements were multiplied by 100 to avoid computational difficulties. The correlations between the UT and the QIMR finger length measurements were .97, .97, .97, and .96 for L4, L2, R4, and R2, respectively, and .79 and .77 for the left and right 2D:4D ratios.

Seventy individuals who had attended a clinical visit also sent in photocopies, allowing us to assess the reliably of the photocopies received by mail. Interclass correlations for individual finger measurements made using the digital calipers ranged between .95 and .93; those for the left and right 2D:4D ratios were .72 and .69, respectively. In addition, 372 individuals attended a second clinical session and had their hands photocopied again 2 years after the first photocopy was made. For these photocopies made during the clinical sessions 2 years apart, the correlations for individual finger measurements made using the digital calipers ranged between .67 and .65. However, the ICC for the left and right 2D:4D ratios were .74 and .68 respectively, indicating that while the measurement of the individual fingers was greatly influenced by the growth of the fingers during adolescence, the ratio remained relatively stable. These 2-year test–retest reliabilities for 2D:4D from different photocopies are quite similar to the interrater reliabilities reported by Voracek et al. (2007) for single photocopies, suggesting the actual intrarater reliability would be higher and that there was a relatively small amount of measurement error. In cases where two measurements were available for a participant we used the clinical photocopy rather than the one supplied by the participant, and when two clinical measures were available, the later of the two measures was used. Thus for a small number of individuals the UT measurements were taken from a photocopy supplied by the participant while the QIMR measurements were taken from a clinical photocopy.

Measurements of the second and fourth digits were available for 1759 individuals. The data of 18 individuals were excluded due to outlying 2D:4D values more than 3 standard deviations from the mean. One participant did not return a photocopy of his left hand, so only the right hand data were included in the analyses. After excluding outliers, data were available for 1741 individuals from 757 families. In the present article we consider the data of twin pairs (1413 individuals) and, when available, one of their nontwin siblings (328 individuals). Participation by zygosity and family structure is summarized in Table 2.

Statistical Analyses

Maximum likelihood analyses of individual observations (as implemented in Mx 1.66, Neale et al., 2006) were used for all analyses. Mx is a structural equation modeling program which has been specifically designed for use with twin and family data. The program is flexible in its approach, allowing tests of specific hypotheses and is suitable for use with incomplete data sets (where partial missingness has arisen). Within these analyses missingness was assumed to be unlinked to an individuals' trait value and to have occurred at random.

Results

Descriptive Statistics and Assumption Testing

Previous analyses of the means, variances and covariances showed no differences between female dizygotic (DZ) twins from same versus opposite-sex pairs, nor between male DZ twins from same versus opposite-sex pairs (Medland et al., 2008). In the current study, no differences were observed between the means and variances of monozygotic (MZ) and DZ twins, nor between the twins and their singleton siblings. Nor did the covariance of DZ twins differ from that observed between the twins and their singleton siblings. As expected the MZ correlations differed significantly from those of the siblings/DZ twins (χ^2_1 : 45.02 QIMR-

Table 2

Number of Families Participating by Zygosity and Family Structure

Family structure	MZF	MZM	DZF	DZM	DZ OS
••	47	33	71	69	124
••♀	35	35	27	23	46
••♂	35	33	23	21	34
•○	6	2	22	14	41
•○♀	3		2	3	5
•○♂		2		1	
Number of families	126	105	145	131	250
Number of individuals	316	276	318	292	539

Note: Closed circles (•) represent members of the twin pair for whom data are available, with open circles (○) indicating missing data. For twin pairs where sibling data were available the sex of the sibling is indicated (e.g., ••♂ represents a twin pair with a male sibling).

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Table 3

Means and Variances of Digit Ratio and MZ and DZ/Twin–Sibling Correlations

	QIMR Measurements		UT Measurements	
	Left hand	Right hand	Left hand	Right hand
Means				
Female	98.29	97.85	98.00	98.82
Male	96.94	96.32	96.95	96.97
Variance	10.78	9.80	8.85	9.14
Correlations (95% CI)				
MZ	.69 (.59, .76)	.52 (.37, .63)	.70 (.63, .84)	.66 (.40, .73)
DZ/twin–sibling	.30 (.24, 36)	.22 (.16, .29)	.31 (.20, .42)	.40 (.30, .49)

Note: The digit ratios were multiplied by 100 prior to analysis to avoid computational difficulties.

Left; 27.76 QIMR-Right; 23.79 UT-Left; 10.27 UT-Right). The means, variances and co-twin correlations are summarized in Table 3.

As expected mean 2D:4D ratios were higher for females than males for both left and right hands (χ^2_1: 72.94 QIMR-Left; 92.20 QIMR-Right; 18.03 UT-Left; 52.24 UT-Right). No sex differences were observed in the variance. Male and female means were allowed to differ in all further analyses.

Univariate genetic analyses

In order to investigate whether the sources or magnitudes of genetic and environmental effects on 2D:4D differed between males and females, a series of structural equation models was fit to the data. As summarized in Table 4 we began by fitting a general sex limitation ACE model (row 1). This model allows the magnitude of genetic and environmental effects to differ between males and females and specifies an additional set of genetic factors specific to one sex (in this case males). For all four variables (left and right hand 2D:4D for QIMR and UT) we were able to drop this sex-specific effect (row 2) and were able to equate the magnitude of the male and female genetic and environmental effects (row 3). Furthermore, we were able to drop all common environmental effects from the model (row 5 vs. row 3). As the common environmental path coefficients were estimated at zero we re-ran the model fitting analyses allowing for nonadditive genetic effects instead of common environmental ones (row 7). However, there was no evidence for dominance or epistasis in these data (row 9 vs. row 8). The estimates of additive genetic and unique environmental effects for each of the measures from the best fitting model (AE) are given in rows 10 and 11 of Table 4.

Table 4

Results of the Univariate Genetic Analyses

	df	QIMR Measurements				UT Measurements			
		Left Hand		Right Hand		Left Hand		Right Hand	
		Δ–2LL	*p*	Δ–2LL	*p*	Δ–2LL	*p*	Δ–2LL	*p*
1 General sex-limitation ACE (–2LL)		8997.21		8801.18		3194.65		3190.38	
2 Sex limitation	1	0.00	.00	0.00	1.00	0.00	1.00	0.00	1.00
3 ACE	3	4.55	.21	0.72	.87	2.62	.45	3.47	.32
4CE	1	44.46	1.00	26.78	.00	23.38	.00	10.27	.00
5 AE	**1**	**0.00**	**1.00**	**0.00**	**1.00**	**0.00**	**1.00**	**1.39**	**.24**
6 E	2	189.376	.00	116.16	.00	85.14	.00	93.21	.00
7 Sex-limitation ADE(-2LL)		8996.674		8798.59		3194.26		3192.24	
8 ADE	3	4.57	.21	1.73	.63	2.59	.46	3.01	.39
9 AE	**1**	**0.51**	**.47**	**1.58**	**.21**	**0.42**	**.52**	**0.00**	**1.00**
Variance Components from the AE model (95% CI)									
10 A		.64 (.57, .70)		.51 (.42, .59)		.69 (.58, .77)		.68 (.58, .76)	
11 E		.36 (.30, .43)		.49 (.41, .58)		.31 (.23, .42)		.32 (.24, .42)	

Note: Best fitting model is indicated in bold

–2LL = –2 log-likelihood. *df* = corresponding difference in degrees of freedom. Best fitting model = most parsimonious, based on Akaike's information criterion. The –2LL of the general sex limitation ACE is given in line 1, the Δ–2LL in line 2 refers to the change in fit between the model in line 1 and that in line 2. The –2LL of the Sex limitation ADE is given in line 7, the Δ–2LL in line 8 refers to the change in fit between the model in line 7 and that in line 8.

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Multivariate Genetic Analyses

High correlations were observed between the QIMR and UT 2D:4D ratios for each hand: left hand .79 (95% confidence intervals .76, .82); right hand .77 (.73, .79). Similarly, substantial correlations were observed between the left- and right-hand digit ratios for the QIMR and UT measurements: QIMR .54 (.50, .58); UT .64 (.59, .68). These correlations are comparable to the test–rest correlations from the QIMR measurements.

A structural equation model, summarized in Figure 1, was used to simultaneously model the QIMR and UT data of the left and right hands. Neither common environmental nor nonadditive genetic effects were found. Initially, covariation was allowed between the two QIMR measurements at the level of the observed variable (via the paths from A1 and E1 to the right QIMR 2D:4D ratio). However this covariation could be dropped without affecting the fit of the model. Similarly, the covariation between the unique environmental effects of the two UT measures (i.e., the path from E2 to the right UT 2D:4D ratio) could also be dropped ($\chi^2_2 = 4.8$, $p = .09$). In addition, all variable specific additive genetic effects on the QIMR measures (A1 and A3) could be dropped ($\chi^2_3 = 1.2$, $p = .56$). While the covariation between the additive genetics effects of the two UT measures could not be dropped without a highly significant decrease in fit ($\chi^2_1 = 23.6$, $p = .000001$), the additional specific additive genetic factor influencing the right UT 2D:4D (A4) could be dropped ($\chi^2_1 = .01$, $p = .96$) and the loadings of A2 on the right and left hands could be equated ($\chi^2_1 = 1.8$, $p = .18$).

In the model the QIMR and UT 2D:4D ratios were considered independent measures of the underlying latent traits 'Left 2D:4D' and 'Right 2D:4D' and the loadings of the QIMR and UT measures on these latent traits were estimated. However, the standardized factor loadings could be equated across hands and measure ($\chi^2_1 = 5.98$, $p = .20$). This indicated that both the QIMR and UT measures provided an accurate proxy for the latent phenotype which explained ~77% of the variance across measures. The simplified model fitted the data well (Cholesky decomposition: –2LL 22078.6, *df* 4716; Simplified model: –2LL 22096.74, *df* 4737; $\chi^2_{21} = 18.12$, $p = .64$)

The latent traits were modeled as being influenced by both shared and latent specific additive genetic and unique environmental variance. Following Loehlin (1996), to identify the decomposition of the latent traits the paths from each latent trait to the shared variance components were set to be equal. The majority of variance at the latent trait level (64%) was due to genetic influences and unique (within-individual) environment factors (6.6%) shared equally between the two hands, with small specific genetic (8%–17%) and unique environmental effects (13%–21%). The vast majority of the covariation between the hands was due to additive genetic effects (91%).

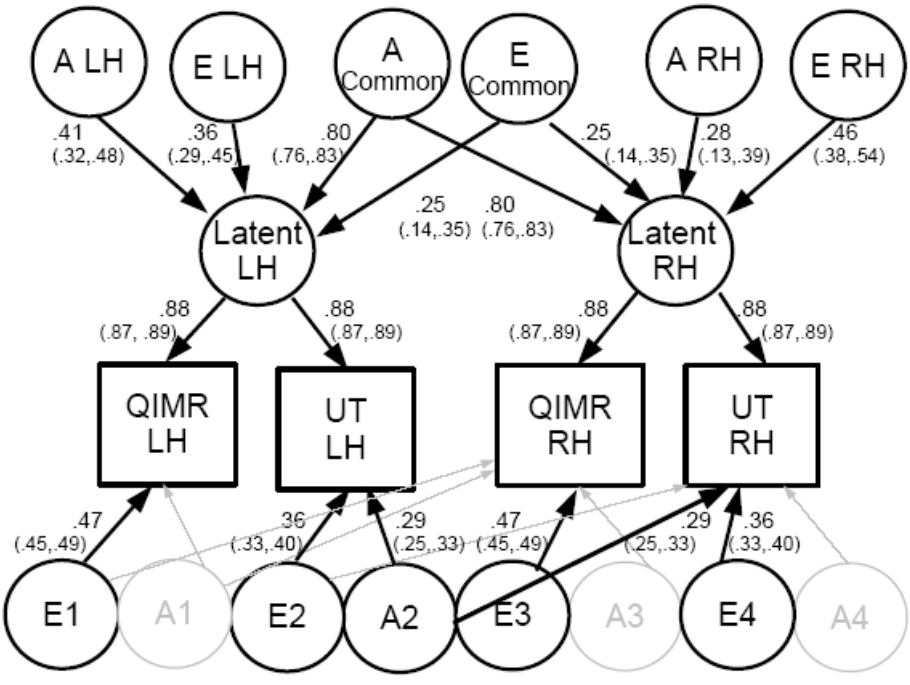

Figure 1

Measurement model used for the multivariate analysis. Latent factors and paths shown grey were not significant and were dropped from the simplified model. The paths are labeled with standardized path coefficients (and 95% confidence intervals).

Note: A = additive genetic, E = unique environment, LH = left hand, RH = right hand, QIMR = the digital caliper measurements, UT = the computer-assisted measurements. A paths and E paths from the common factors to the Latent LH and Latent RH factors were set to be equal across both hands. The E common factor refers to a unique (within individual) environmental effect that influenced both hands. The factor loadings were equated, as were the paths from A2 to the left- and right-UT measurements.

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In addition variable specific unique environmental effects (which included measurement error) explained 22% of the variance in the left- and right-hand QIMR measurements and 14% of the variance in the left- and right-hand UT measurements. The additive genetic effects shared between the left- and right-hand UT measurements explained 8.5% of the variance in these measures. Thus, the UT measurements were influenced by an additional, small but significant, genetic effect independent of the latent 2D:4D phenotypes.

Discussion

The present study is the first to examine the 2D:4D ratio in a large sample of MZ and DZ twins and their singleton siblings. No differences were observed in the means, variances or covariances of twins and siblings, and as has been previously shown in this sample, there was no evidence of hormone transfer effects in same versus opposite-sex DZ pairs (Medland et al., 2008). As is typically found, the digit ratio of females was higher than that of males and this was true of both twins and siblings. However, there was no evidence of sex-limitation in either the magnitude or proportions of variance explained by genetic and environmental sources. Thus, whatever is responsible for the well-documented mean effect does not appear to be affecting the variance.

A high degree of additive genetic influence was observed on the 2D:4D ratio at both univariate and multivariate levels. As shown by the multivariate analyses, both measurement techniques provided accurate assessments of the latent 2D:4D phenotypes. Interestingly, the UT measurements shared an additional genetic effect aside from that shared between the latent phenotypes. While it is possible that this may reflect a difference in the accuracy of the measurement, the additional genetic covariation between these measures remained significant even when the factor loadings were not constrained to be equal. It is also interesting that at the latent level the heritability of left hand 2D:4D was higher than the right (.80 vs. .71). This trend is consistent with the results of previous studies (see Table 1).

The 2D:4D ratio owes much of its current popularity to its presumed association with prenatal androgen levels. In male adults and adolescents the regulation of testosterone levels is predominantly controlled by genetic mechanisms (Harris et al., 1998). However, comparatively little is known about the regulation of androgen levels in the developing fetus. The androgen receptor is currently considered a popular candidate gene (Manning et al., 2003). However, the lack of sex differences in the variance and covariance between males and females suggests that this X-linked gene does not play a major role in the development of 2D:4D. Other genes known to play important roles in limb development and differentiation, such as genes within the homeobox family, would also seem promising candidates particularly given the evidence for their expression in the fetus.

Significant unique environmental covariation was also found between the left- and right-hand digit ratios, indicating individual specific influences such as poor placental or perinatal nutrition, accident or illness may influence the 2D:4D of both hands either directly through growth asynchronies across the digits, or indirectly, perhaps through the hypothesized testosterone mechanism. It is also possible that common measurement errors or across- photocopier skewing may be responsible for part of this environmental covariation. However, the high test–retest correlations make this seem a less likely explanation. We have no compelling explanation for the small amount of additional genetic covariance between left and right hands detected in the UT data, unless it is in some way a function of the greater precision of the computer-assisted measurements.

Although a strong correlation was found between left and right 2D:4D, there was also significant nonshared genetic and environmental variation. This finding may account for some of the discrepancies in the literature, where some studies have found associations with the 2D:4D ratio of one hand but not the other. While it is possible that such discrepant results may reflect differential sensitivity of the digits of the left and right hands to the effects of testosterone as is suggested within the literature, it is also possible that some of the reported correlations between 2D:4D and traits such as neuroticism and IQ may in part represent the common effects of an insult or disturbance in early development. Until more is known about the genetic and environmental mechanisms regulating testosterone in the fetus and the mechanisms by which prenatal testosterone may influence the left and right hands differently, presenting the results of associations with both the left- and right-hand digit ratios is recommended. It may also be prudent to measure routinely all four fingers, not just the second and fourth, as not all finger-length ratios are alike (Loehlin et al., in press; McFadden et al., 2005).

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References

Aitken, J. F., Pfitzner, J., Battistutta, D., O'Rourke, P. K., Green, A., & Martin, N. (1996). Reliability of computer image analysis of pigmented skin lesions of Australian adolescents. *Cancer, 78*, 252–257.

Gobrogge, K. L., Breedlove, S. M., & Klump, K. L. (2008). Genetic and environmental influences on 2D:4D finger length ratios: A study of monozygotic and dizygotic male and female twins. *Archives of Sexual Behavior, 37*, 112–118.

Harris, J. A., Vernon, P. A., & Boomsma, D. I. (1998). The heritability of testosterone: A study of Dutch adolescent twins and their parents. *Behavior Genetics, 28*, 165–171.

Loehlin, J. C. (1996). The Cholesky approach: A cautionary note. *Behavior Genetics, 26*, 65–69.

Loehlin, J. C., Medland, S. E., & Martin, N. G. (in press). Relative finger-lengths, sex differences, and psychological traits., *Archives of Sexual Behavior*.

Lutchmaya, S., Baron-Cohen, S., Raggatt, P., Knickmeyer, R., & Manning, J. T. (2004). 2nd to 4th digit ratios, fetal testosterone and estradiol. *Early Human Development, 77*, 23–28.

Manning, J. T. (2002). *Digit Ratio: A pointer to fertility, behavior, and health*. New Brunswick, NJ: Rutgers University Press.

Manning, J. T., Bundred, P. E., Newton, D. J., & Flanagan, B. F. (2003). The 2nd to 4th digit ratio and variation in the androgen receptor gene. *Evolution and Human Behavior, 24*, 399–405.

Manning, J. T., Fink, B., Neave, N., & Caswell, N. (2005). Photocopies yield lower digit ratios (2D:4D) than direct finger measurements. *Archives of Sexual Behavior, 34*, 329–333.

Manning, J. T., Scutt, D., Wilson, J., & Lewis-Jones, D. I. (1998). The ratio of 2nd to 4th digit length: A predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. *Human Reproduction, 13*, 3000–3004.

McFadden, D., & Shubel, E. (2002). Relative lengths of fingers and toes in human males and females. *Hormones and Behavior, 42*, 492–500.

McFadden, D., Westhafer, J. G., Pasanen, E. G., Carlson, C. L., & Tucker, D. M. (2005). Physiological evidence of hypermasculinization in boys with the inattentive type of attention-deficit/hyperactivity disorder (ADHD). *Clinical Neuroscience Research, 5*, 233–245.

McGregor, B., Pfitzner, J., Zhu, G., Grace, M., Eldridge, A., Pearson, J., Mayne, C., Aitken, J. F., Green, A. C., & Martin, N. G. (1999). Genetic and environmental contributions to size, color, shape, and other characteristics of melanocytic naevi in a sample of adolescent twins. *Genetic Epidemiology, 16*, 40–53.

McIntyre, M. H. (2006). The use of digit ratios as markers for perinatal androgen action. *Reproductive Biology and Endocrinology, 4*, 10.

Medland, S. E., Loehlin, J. C., & Martin, N. (2008). No effects of prenatal hormone-transfer on digit ratio in a large sample of same- and opposite-sex dizygotic twins. *Personality and Individual Differences, 44*, 1225–1234.

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. H. (2006). *Mx: Statistical modeling* (6th ed.). VCU Box 900126, Richmond, VA 23298 http://www.vcu.edu/mx/: Department of Psychiatry.

Paul, S. N., Kato, B. S., Cherkas, L. F., Andrew, T., & Spector, T. D. (2006). Heritability of the second to fourth digit ratio (2D:4D): A twin study. *Twin Research and Human Genetics, 9*, 215–219.

Voracek, M., & Dressler, S. G. (2007). Digit ratio (2D:4D) in twins: Heritability estimates and evidence for a masculinized trait expression in women from opposite-sex pairs. *Psychological Reports, 100*, 115–126.

Voracek, M., Manning, J. T., & Dressler, S. G. (2007). Repeatability and interobserver error of digit ratio (2D:4D) measurements made by experts. *American Journal of Human Biology, 19*, 142–146.

Wright, M. J., De Geus, E., Ando, J., Luciano, M., Posthuma, D., Ono, Y., Hansell, N., Van Baal, C., Hiraishi, K., Hasegawa, T., Smith, G., Geffen, G., Geffen, L., Kanba, S., Miyake, A., Martin, N., & Boomsma, D. (2001). Genetics of cognition: Outline of a collaborative twin study. *Twin Research, 4*, 48–56.

Wright, M. J., & Martin, N. (2004). Brisbane Adolescent Twin Study: Outline of study methods and research projects. *Australian Journal of Psychology, 56*, 65–78.

Zhu, G., Duffy, D. L., Eldridge, A., Grace, M., Mayne, C., O'Gorman, L., Aitken, J. F., Neale, M. C., Hayward, N. K., Green, A. C., & Martin, N. G. (1999). A major quantitative-trait locus for mole density is linked to the familial melanoma gene CDKN2A: A maximum-likelihood combined linkage and association analysis in twins and their sibs. *American Journal of Human Genetics, 65*, 483–492.