Original Research Article

Maternal 2nd to 4th Digit Ratio Does Not Predict Lifetime Offspring Sex Ratio at Birth

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ABSTRACT The low ratio of second-to-fourth digit length (2D:4D) of parents, a putative indicator of high prenatal and even adult testosterone levels, has been suggested to predict a male-biased secondary offspring sex ratio. We investigated this question in 244 contemporary postreproductive Finnish women. Information on the lifetime offspring birth sex ratio of women was collected by questionnaires and the 2D:4D of both their hands were measured from scanned photographs. We found no evidence that the right hand 2D:4D, the left hand 2D:4D, the mean of the right and the left hand 2D:4D, or the difference between the right and the left hand 2D:4D was related to offspring sex ratio at birth among these women. Our results thus do not support the suggestion that offspring birth sex ratio is related to 2D:4D in women. Am. J. Hum. Biol. 20:700–703, 2008.

The ratio of second-to-fourth digit length (2D:4D) has been suggested to reflect prenatal exposure to sex steroids (Manning, 2002; McIntyre, 2006). The lower the 2D:4D, the higher and lower the testosterone and estrogen levels during fetal life, respectively. This hypothesis rests on findings showing that 2D:4D is sexually dimorphic with lower ratios among males from the end of the first trimester of fetal development (Malas et al., 2006; Manning et al., 1998; Peters et al., 2002) and that 2D:4D does not markedly change from childhood to adulthood (McIntyre et al., 2005; Trivers et al., 2006). Furthermore, congenital adrenal hyperplasia (CAH), resulting in high prenatal testosterone levels, has been shown to be related to low 2D:4D in children (Brown et al., 2002; Ökten et al., 2002). Most importantly, 2D:4D has been found to negatively relate to the ratio of fetal testosterone to estrogen levels measured by amniocentesis (Lutchmaya et al., 2004). Therefore, 2D:4D has been highlighted as a useful marker of steroid exposure in utero, which has enduring effects on individual physiology and behavior throughout their adult life (Lummaa and Clutton-Brock, 2002; Metcalfe and Monaghan, 2001).

Apart from prenatal testosterone levels, in adult men low 2D:4D and small difference between the right and the left hand 2D:4D (D_{r-l}) have also been suggested to covary with high circulating testosterone levels (Manning et al., 1998, 2004). However, associations between 2D:4D and testosterone levels in adulthood have not been generally supported by other studies, and particularly among women (Hönekopp et al., 2007). On the other hand, in women 2D:4D has been suggested to correlate with high adulthood estradiol levels (McIntyre et al., 2007). The potential link between 2D:4D and circulating steroid levels in adults is unclear at present. Such a link may be established, if steroid levels experienced in utero, that arguably affect the formation of 2D:4D, have carry-over effects on the adulthood steroid levels.

Moreover, in mammals high parental testosterone levels around conception have been proposed to skew secondary offspring sex ratio toward sons (Grant, 2007; James, 2004). These findings led Manning et al. (2002) to propose that if parental 2D:4D relates to adulthood testosterone levels, which in turn correlates with offspring sex ratio, parental 2D:4D should be negatively associated with secondary offspring sex ratio. These authors provided support for their hypothesis by showing that men and women from England, Spain, and Jamaica with low 2D:4D in both the right and the left hand gave birth to proportionally more male descendants. To the best of our knowledge, the study of Manning et al. (2002) has not yet been replicated in any other data set. In addition to circulating testosterone, high maternal estrogen levels have been reported to correlate with a female-biased offspring sex ratio in the gray mouse lemur (Perret, 2005), but with a male-biased offspring sex ratio in African wild dogs (Creel et al., 1998).

We investigated whether contemporary, postreproductive Finnish mothers with low 2D:4D delivered proportionally more sons during their lifetime. We thus examined the effect of both the right and the left hand 2D:4D, as well as the mean of the right and the left hand 2D:4D and the difference between the right and the left hand 2D:4D (D_{r-l}) on offspring sex ratio at birth.

MATERIALS AND METHODS

Data

We collected data on lifetime offspring sex ratio at birth (proportion of sons born) and the right and the left hand 2D:4D of 244 women born during the years 1946–1958 in Finland (Helle, 2008). The data on offspring sex ratio was collected by questionnaires in 2006, while both their hands were scanned for 2D:4D measurements. These women consist of a random and geographically diverse sample of 50- to 60-year-old women who participated voluntarily in a Finnish national screening program for cervical cancer. The digit ratios were measured from the tip

Contract grant sponsor: The Academy of Finland; Contract grant number: 207270; Contract grant sponsor: Nessling Foundation; Contract grant number: 2008172.

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Received 31 March 2008; Accepted 7 April 2008

DOI 10.1002/ajhb.20796

Published online 16 June 2008 in Wiley InterScience (www.interscience.wiley.com).

of the finger to the crease proximal to the palm with program Image-J (http://rsb.info.nih.gov/ij/). All the measurements were made by one person (T. Lilley). Sixty hands were measured twice to estimate the repeatability of 2D:4D measurements (Lessells and Boag, 1987). The 2D:4D measurements showed acceptable repeatability ($r = 0.79$, $F_{1,\ 59} = 8.44$, $P = 0.0052$). The mean ($\pm$ S.D.) of the right and the left hand 2D:4D was 0.977 ($\pm$ 0.031) and 0.971 ($\pm$ 0.033), respectively. The mean ($\pm$ S.D.) offspring sex ratio at birth was 0.53 ($\pm$ 0.39), which is significantly higher (an exact binomial test, $z = -7.58$, $P < 0.0001$) than the national birth sex ratio of 0.512 in Finland during the study period 1964–2000. The reason for this increased male-bias among the women studied is unknown. Data on the 2D:4D of fathers was not available, but with regard to the hypothesis of birth sex ratio variation in relation to parental testosterone levels, maternal circulating testosterone is likely to play a more important role in vertebrates (Helle et al., 2008).

TABLE 1. The effects of the right and the left hand 2D:4D on offspring sex ratio at birth

Explanatory variable	Odds ratio (95% CIs)	$df_{num,den}$	F	P
Right hand 2D:4D	0.95 (0.75–1.21)	1,233	0.17	0.68
Left hand 2D:4D	1.01 (0.79–1.29)	1,233	0.01	0.92
Total number of births	0.98 (0.78–1.23)	1,233	0.03	0.87
Educational level		2,233	0.48	0.62
Elementary school	0.94 (0.48–1.87)			
Secondary school	0.79 (0.41–1.51)			
University degree	0			
Birth cohort		2,233	2.27	0.11
1946–47	1.64 (1.04–2.60)			
1951–52	1.22 (0.76–1.95)			
1956–58	0			
Birth area		3,233	0.08	0.97
South-Finland	0.74 (0.16–3.54)			
West-Finland	0.84 (0.20–3.51)			
North-Finland	0.89 (0.19–4.13)			
Non-Finnish	0			

Statistical analysis

The simultaneous effects of both the right and the left hand 2D:4D on offspring sex ratio at birth was examined with multiple logistic regression model, fitted with binomial errors and logit link function (Wilson and Hardy, 2002). We used events/trials syntax (i.e., grouped binary) to enter offspring sex ratio at birth in our model, where the number of sons born was the numerator (events) and the total number of offspring born to a mother was the denominator (trials). Because of obvious collinearity problems, the mean and the difference between the right and the left hand 2D:4D were not included into the same model. Therefore, their effect on offspring birth sex ratio was investigated with separate models. Since the socioeconomic status of a woman (e.g. Almond and Edlund, 2007) and parity (e.g. Biggar et al., 1999) have been suggested to be related to secondary offspring sex ratio, we included a woman's educational level (elementary school, secondary school, or university/college degree) and the total number of offspring born into the analyses. Furthermore, a woman's birth cohort (1946–47, 1951–52, or 1956–58) and birth area (South-Finland, West-Finland, North-Finland, or non-Finnish) were included into the models to control for spatial and temporal variation in sex ratio at birth. To obtain more interpretable parameter estimates, all the 2D:4D variables were standardized to a zero mean and 1 standard deviation prior to analyses. The effect size of explanatory variables is given as odds ratio and its 95% confidence intervals (CIs). Because of standardization, the odds ratios represent how the change of 1 standard deviation in the measures of 2D:4D affect birth sex ratio. Pearson's χ^2 was used to rescale the parameter covariance matrix to accommodate any overdispersion, and thus two-tailed F-tests were used to asses the statistical significance of explanatory variables (Wilson and Hardy, 2002). Multicollinearity among continuous independent variables was assessed with variance inflation factors and tolerance values. The largest variance inflation factor was 1.57 and the lowest tolerance value 0.64, suggesting no severe bias in the CIs of odds ratios. After fitting the models, the standardized Pearson and deviance residuals showed no values exceeding 3, indicating a good fit of the models (Allison, 1999). All analyses were conducted with SAS statistical software version 9.1 (SAS Institute, Cary, NC).

RESULTS

The right hand 2D:4D was negatively and the left hand 2D:4D was positively related to offspring sex ratio at birth, but neither of these associations reached statistical significance (Table 1). In addition, neither the mean of the right and the left hand 2D:4D (odds ratio (95% CIs) = 0.97 (0.80–1.17), $F_{1,\ 234} = 0.13$, $P = 0.72$) nor the difference between the right and the left hand 2D:4D (odds ratio (95% CIs) = 0.97 (0.80–1.18), $F_{1,\ 234} = 0.08$, $P = 0.78$) were related to offspring birth sex ratio. These results were not changed if model reduction by backward elimination of nonsignificant explanatory variables was applied (results not shown).

DISCUSSION

We could not corroborate the result of Manning et al. (2002) who reported a male-biased offspring sex ratio in parents with low 2D:4D in both the right and the left hand. Among the Finnish women studied, the right hand 2D:4D showed a negative association with offspring birth sex ratio, whereas the left hand 2D:4D showed a positive association with offspring birth sex ratio. However, both of these effects were far from statistical significance. Our data did not allow us to study whether the 2D:4D of fathers was related to offspring birth sex ratio, as suggested by Manning et al. (2002). In fact, they did not statistically test whether the effect of the right and the left hand 2D:4D on offspring sex ratio differed between men and women. However, it is currently unclear how paternal testosterone level might affect offspring sex ratio. Because men are the heterogametic sex, such an effect could be expected if the testosterone levels of men correlate with the sex ratio of sperm in ejaculates. At present, there is no evidence for this (Tiido et al., 2005).

The reasons why we found no evidence for an association between maternal 2D:4D and offspring sex ratio are unclear. It is possible that in women 2D:4D, although potentially related to prenatal steroid levels, does not correlate strongly enough with circulating testosterone levels in adulthood. This possibility is supported by a recent meta-analysis that found no evidence for the association between 2D:4D and adult sex hormone levels in women (Hönekopp et al., 2007). On the other hand, it is also possible that high maternal testosterone levels do not skew offspring sex ratio toward sons. In humans, there is currently no direct evidence for the link between parental testosterone levels and offspring sex ratio; all support for this hypothesis is indirect in nature (James, 1996, 2004, 2006). In mammals, there is increasing but still only correlative evidence that maternal testosterone levels may be related to the excess of male births (Grant and Irwin, 2005; Grant et al., 2008; Helle et al., 2008). Therefore, there is clearly a need for more evidence for both of these underlying hypotheses before we can expect an association between parental 2D:4D and offspring sex ratio.

Some methodological differences may also in part explain the different outcomes between this study and that of Manning et al. (2002). First, the sample of Manning et al. (2002) included individuals over the age of 30, suggesting that some individuals were still potentially reproducing. This may have biased the sex ratio of offspring born used in this study, because parental age and the birth order of offspring have been proposed to affect offspring sex (Chahnazarian, 1988; Lazarus, 2002). We avoided this potential bias by including postreproductive women only. Second, Manning et al. (2002) analyzed their data for the right and the left hands separately, and found that in both hands 2D:4D was negatively related to offspring birth sex ratio. Here, we used a multiple regression model instead, which provided partial regression coefficient for the right and the left hand 2D:4D. We found that the right and the left hand 2D:4D showed negative and positive association with offspring birth sex ratio, respectively. Having excluded the right hand 2D:4D from our model, we would have also found a negative association between the left hand 2D:4D and offspring sex ratio at birth (odds ratio (95% CIs) = 0.98 (0.81–1.19)). Therefore, applying multiple versus univariate regression approach may lead to different biological conclusions. We prefer multiple regression approach, since it enables testing whether the right hand 2D:4D correlates with offspring sex ratio while controlling for the effect of the left hand 2D:4D, and vice versa. Third, to normalize their data on offspring sex ratio, Manning et al. (2002) applied arcsine transformation (whether they succeeded to normalize their data was not stated). By contrast, we used logistic regression models with binomial errors and logit link function, as recommended by Wilson and Hardy (2002) as a default approach to study sex ratios. It is unclear how much of the differences in the study outcome this methodological discrepancy explains, but the use of arcsine transformation may lead to biologically impossible results, since the transformed variable is not bound between 0 and 1 that is the natural range of offspring sex ratio variation (i.e. proportion of sons born) (Wilson and Hardy, 2002).

To conclude, we found no evidence to suggest that the 2D:4D of postreproductive women can be used to predict the sex ratio of their offspring born. We suspect that the main reason for this may be that 2D:4D is not related to the circulating testosterone levels of adult women.

ACKNOWLEDGMENTS

The authors thank Tea Amunet, Tuula Salmi, and Leena Lindberg for their help in collecting the data.

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