AMERICAN JOURNAL OF HUMAN BIOLOGY 22:418–420 (2010)

*Short Report*

# Does Second-to-Fourth Digit Length Ratio (2D:4D) Predict Age at Menarche in Women?

SAMULI HELLE*
*Department of Biology, Section of Ecology, University of Turku, FI-20014 Turku, Finland*

*ABSTRACT* Prenatal steroid levels, estimated as the ratio of second-to-fourth digit length (2D:4D), have been related to reproductive success in women, but direct associations between 2D:4D and physiological measures of fertility remain rare. A recent study reported that lower, masculinized right hand 2D:4D was correlated with delayed age at menarche in women. We addressed this question by investigating whether 2D:4D was associated with recalled age at menarche in 282 post-reproductive Finnish women, using Cox regression model that controlled for a woman's sibling composition, urban or rural residence and temporal trend in menarcheal age. We found no evidence that neither the 2D:4D of the right nor the left hand were related to a woman's age at menarche among these Finnish women. Am. J. Hum. Biol. 22:418–420, 2010. 

Recent decades have witnessed a growing understanding of the importance of prenatal programming on individual's reproductive success during adulthood (Gluckman and Hanson, 2005; Lummaa and Clutton-Brock, 2002). Prenatal steroid levels (mainly androgens) have also been related to reproductive competence, as suggested by the associations found between second-to-fourth digit length ratio (2D:4D) and offspring count in humans (Manning, 2002; Manning and Fink, 2008). During the last 10 years, 2D:4D has thus been strongly highlighted as a potentially useful retrospective marker of steroid exposure in utero (Manning, 2002; McIntyre, 2006). This theory holds that the lower the 2D:4D, the higher testosterone but the lower estrogen levels during the fetal life of an individual.

Studies investigating directly whether the 2D:4D of women relates to the physiological measures of fertility are much fewer than those investigating the measures of mating and reproductive success. It has recently been suggested that 2D:4D could predict age at menarche in women (Matchock, 2008)—an important life-history trait that has a genetic basis (Rowe, 2000) and might be under natural selection even in modern day populations (Kirk et al., 2000). This study reported using Pearson correlations that among 206 college students, the 2D:4D of the right hand but not the left hand negatively correlated with the age at menarche of these women. To our knowledge, this finding has not yet been replicated in any other populations.

Here, we investigated whether 2D:4D was related to age at menarche in 282 contemporary Finnish women. Our current analysis advances this question by using Cox regression model to simultaneously examine the relative effects of both the right and the left hand 2D:4D and by controlling for several factors that have been suggested to affect women's age at menarche.

## METHODS

### *Participants*

In 2006, data on age at menarche (in years) and the right and the left hand 2D:4D was collected from 282 women who were born during the years 1946–1958 in Finland (Helle, 2008; Helle and Lilley, 2008). The data on women's age at menarche (mean ± SD = 13.2 ± 1.5) and all the covariates included in the analysis (see below) were collected by questionnaires and their both hands were scanned (Canon Canoscan D66OU) for 2D:4D measurements. These women consist of a random, racially homogeneous and geographically diverse sample of 50 to 60-year-old women who participated voluntarily in a Finnish national screening program for cervical cancer. The digits were measured from the tip of the finger to the crease proximal to the palm with program Image-J (http://rsb.info.nih.gov/ij/) by one person. Sixty randomly selected hands were measured twice by the same person in order to estimate the repeatability (i.e. intraclass correlation coefficient) of 2D:4D measurements using one-way ANOVA (Lessells and Boag, 1987). The 2D:4D measurements showed a repeatability of 0.79 ($F_{1.59} = 8.44$, $P = 0.0052$).

### *Statistical analysis*

The simultaneous effects of both the right and the left hand 2D:4D on women's age at menarche was examined using Cox proportional hazards regression model (Allison, 1995), as the response variable was years to menarche. This model controlled for the potential confounding effects of the number of brothers and sisters a woman had (Matchock and Susman, 2006; Roberts et al., 1975) and temporal variation with birth cohort (1946–47, 1951–52, or 1956–58) (Okasha et al., 2001) on age at menarche. Because urban residence has been suggested to be associated with an earlier age at menarche (Marrodan et al., 2000; Padez, 2003), women were categorized having either a rural or urban growth environment based on their birth town (born in major cities or habitation centers vs. rural areas). The resulting variable was included in the model

Contract grant sponsor: The Academy of Finland; Contract grant number: 207270

*Correspondence to: Samuli Helle, Department of Biology, Section of Ecology, University of Turku, FI-20014 Turku, Finland.
E-mail: sayrhe@utu.fi

Received 4 May 2009; Revision received 12 July 2009; Accepted 21 August 2009

DOI 10.1002/ajhb.21000

Published online 20 October 2009 in Wiley InterScience (www.interscience.wiley.com).

as well. In order to obtain more biologically interpretable parameter estimates, both the right (SD = 0.031) and the left hand 2D:4D (SD = 0.033) were standardized to zero mean and 1 standard deviation. Therefore, the parameter estimates represent how the change of 1 SD in the 2D:4D measures affected women's age at menarche. The assumption of proportional hazards was examined by including time-dependent effects of predictor variables in the model. No evidence for nonproportionality was found ($P > 0.15$ in all cases). No stepwise model reduction was applied, because such methods dramatically increase the rate of Type I errors (Mundry and Nunn, 2009) and because our aim here was to obtain accurate point estimates and their confidence intervals (CI) (Harrell, 2001). The model fit to individual observations was checked using martingale and deviance residuals and deemed appropriate. Multicollinearity among continuous independent variables was assessed with variance inflation factors and tolerance values. The largest variance inflation factor was 1.51 and the lowest tolerance value 0.66, suggesting no severe bias in the CIs of hazard ratios. All analyses were conducted with SAS statistical software version 9.2 (SAS Institute Inc, Cary, NC).

## RESULTS

Neither the right nor the left hand 2D:4D was significantly associated with a woman's age at menarche (Table 1). Age at menarche seemed to be related to the number of sisters and brothers a woman had, as one additional sister reduced a woman's hazard of menarche, on average, by 10% while having one additional brother increased it, on average, by 12% (Table 1). This effect of the number of brothers and sister on women's menarcheal age differed statistically from each other ($\chi^2_1 = 4.51$, $P = 0.034$). Birth cohort and whether women were born in rural or urban area were not related to age at menarche in these women (Table 1).

*TABLE 1. The effects of the right and the left hand 2D:4D and the confounding factors considered on women's age at menarche*

| Predictor | Hazard ratio (95% CIs) | *df* | $\chi^2$ | *P* |
|---|---|---|---|---|
| Right hand 2D:4D | 0.86 (0.72, 1.04) | 1 | 2.49 | 0.12 |
| Left hand 2D:4D | 1.09 (0.91, 1.31) | 1 | 0.95 | 0.33 |
| Number of sisters | 0.90 (0.81, 1.01) | 1 | 2.95 | 0.086 |
| Number of brothers | 1.12 (0.98, 1.28) | 1 | 2.91 | 0.088 |
| Birth cohort | – | 2 | 3.99 | 0.14 |
| Urban vs. rural residence | 0.84 (0.61, 1.16) | 1 | 1.11 | 0.29 |

Parameter estimates of categorical variables having more than two categories are omitted for simplicity. CI = confidence interval.

## DISCUSSION

These data on Finnish women provide no evidence to suggest that 2D:4D could be used to predict age at menarche. There are at least three potential explanations for our failure to establish a proposed association between 2D:4D and women's age at menarche. First, 2D:4D may not be a precise enough measure of intrauterine exposure to testosterone in women. At present, there is more convincing evidence from "natural experiments" that women diagnosed for polycystic ovarian syndrome (PCOS) and congenital adrenal hyperplasia (CAH), which are associated with increased exposure to prenatal testosterone, experience delayed menarche (New, 2004; Sadrzadeh et al., 2003) than there is for the causal link between prenatal testosterone and 2D:4D. In other words, prenatal testosterone may well affect menarcheal age, but not 2D:4D to such an extent to produce a detectable association between 2D:4D and menarcheal age. In addition, although some studies have also demonstrated that women with PCOS and CAH have lower 2D:4D (Brown et al., 2002; Cattrall et al., 2005), a correlation between a woman's 2D:4D and her age at menarche does not directly mean a link between prenatal testosterone and menarchael age (Hönekopp et al., 2007).

Second, it is likely that there might have been some errors in women's self-reported age at menarche, as the women were in their 50s and 60s when they completed the questionnaire for their age at menarche. Large-scale studies have suggested that recalled age at menarche even decades later seems to correspond rather well with the true age at menarche, irrespective of actual age at menarche (Cooper et al., 2006; Must et al., 2002). Furthermore, in this study the age at menarche was recorded in years, which, although reducing the variation of recorded menarchael age, likely also reduced the consequences of slight inaccuracies of recalled age at menarche.

Third, the reason for our failure to repeat the findings of Matchock (2008) might be due to the different statistical models applied. Matchock (2008) used Pearson correlation coefficients, whereas our approach was based on a Cox proportional hazards regression, designed for time-to-an-event data, such as women's age at menarche (Allison, 1995). Moreover, our Cox model controlled for several factors suggested to be related to menarchael age in women, such as the number of sister and brothers, urban or rural residence, and temporal variation in age at menarche. However, even Pearson correlation coefficients neither in the right ($r = 0.06$, $P = 0.30$) nor in the left hand 2D:4D ($r = -0.02$, $P = 0.75$) showed a statistically significant correlation with age at menarche in this Finnish sample. This indicates that our failure to replicate previous findings was not due to differences in the statistical approach used.

## ACKNOWLEDGMENTS

Thanks to Thomas Lilley, Tea Amunet, Tuula Salmi and Liisa Lindberg for their help collecting the data.

## LITERATURE CITED

Allison PD. 1995. Survival analysis using the SAS system: a practical guide. Cary, NC: SAS institute Inc.

Brown WM, Hines M, Fane BA, Breedlove SM. 2002. Masculinized finger length patterns in human males and females with congenital adrenal hyperplasia. Horm Behav 42:380–386.

Cattrall FR, Vollenhoven BJ, Weston GC. 2005. Anatomical evidence for in utero androgen exposure in women with polycystic ovary syndrome. Fertil Steril 84:1689–1692.

Cooper R, Blell M, Hardy R, Black S, Pollard TM, Wadsworth MEJ, Pearce MS, Kuh D. 2006. Validity of age at menarche self-reported in adulthood. J Epidemiol Comm Health 60:993–997.

Gluckman PD, Hanson M. 2005. The fetal matrix: evolution, development, and disease. New York: Cambridge University Press.

Harrell FE Jr. 2001. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis. New York: Springer Science+Business Media, Inc.

Helle S. 2008. A trade-off between reproduction and growth in contemporary Finnish women. Evol Hum Behav 29:186–195.
Helle S, Lilley T. 2008. Maternal 2nd to 4th digit ratio does not predict lifetime offspring sex ratio at birth. Am J Hum Biol 20:700–703.
Hönekopp J, Barholdt L, Beier L, Liebert A. 2007. Second to fourth digit length ratio (2D:4D) and adult sex hormone levels: new data and meta-analytic review. Psychoneuroendocrinology 32:313–321.
Kirk KM, Blomberg SP, Duffy DL, Heath AC, Owens IPF, Martin NG. 2001. Natural selection and quantitative genetics of life-history traits in western women: a twin study. Evolution 55:423–435.
Lessells CM, Boag PT. 1987. Unrepeatable repeatabilities: a common mistake. Auk 104:116–121.
Lummaa V, Clutton-Brock T. 2002. Early development, survival and reproduction in humans. Trends Ecol Evol 17:141–147.
Manning JT. 2002. Digit ratio: a pointer to fertility, behaviour, and health. New Jersey: Rutgers University Press.
Manning JT, Fink B. 2008. Digit ratio (2D:4D), dominance, reproductive success, asymmetry, and sociosexuality in the BBC internet study. Am J Hum Biol 20:451–461.
Marrodan MD, Mesa MS, Arechiga J, Perez-Magdaleno A. 2000. Trend in menarcheal age in Spain: rural and urban comparison during a recent period. Ann Hum Biol 27:313–319.
Matchock RL. 2008. Low digit ratio (2D:4D) is associated with delayed menarche. Am J Hum Biol 20:487–489.
Matchock RL, Susman EJ. 2006. Family composition and menarcheal age: anti-inbreeding strategies. Am J Hum Biol 18:481–491.
McIntyre MH. 2006. he use of digit ratios as markers for prenatal androgen action. Reprod Biol Endocrinol 4:10.
Mundry RG, Nunn CL. 2009. Stepwise model fitting and statistical inference: turning noise into signal pollution. Am Nat 173:119–123.
Must A, Phillips SM, Naumova EN, Blum M, Harris S, Dawson-Hughes B, Rand WM. 2002. Recall of early menstrual history and menarcheal body size: after 30 years, how well do women remember? Am J Epidemiol 155:672–679.
New MI. 2004. An update of congenital adrenal hyperplasia. Ann NY Acad Sci 1038:14–43.
Okasha M, McCarron P, McEwen J, Smith GD. 2001. Age at menarche: secular trends and associations with adult anthropometric measures. Ann Hum Biol 28:68–78.
Padez C. 2003. Social background and age of menarche in Portuguese university students: a note on the secular changes in Portugal. Am J Hum Biol 15:672–679.
Roberts DF, Danskin MJ, Chin S. 1975. Menarcheal age in Northhumberland. Act Paediatr Scand 64:845–852.
Rowe R. 2000. Environmental and genetic influences on pubertal development: evolutionary life history traits. In: Rogers J, Rowe D, Miller W, editors. Genetic influences on human fertility and sexuality: theoretical and empirical contributions from the biological and behavioural sciences. Boston: Kluwer. p 147–168.
Sadrzadeh S, Klip WAJ, Broekmans FJM, Schats R, Willemsen WNP, Burger CW, van Leeuwen FE, Lambalk CB;OMEGA Project Group. 2003. Birth weight and age at menarche in patients with polycystic ovary syndrome or diminished ovarian reserve, in a retrospective cohort. Hum Reprod 18:2225–2230.