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SHORT REPORT

No strong association between second to fourth digit ratio (2D:4D) and adult anthropometric measures with emphasis on adiposity

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***Objectives*: This report aimed to assess whether second to fourth digit ratio (2D:4D) is associated with adult anthropometric measures and, in particular, measurements of adiposity.**
***Methods*: Height, weight, waist circumference, hip circumference and bioelectrical resistance and reactance were measured at baseline attendance of the Melbourne Collaborative Cohort Study. 2D:4D was measured from photocopies of participants' hands that were taken at a recent follow-up of the cohort. Complete anthropometric and 2D:4D data were available for 8840 women and 6076 men. Linear regression models adjusted for age at baseline and country of birth were used to estimate the expected mean increment in anthropometric measures for a standard deviation increment in 2D:4D.**
***Results*: No substantial association was found between any assessed anthropometric measure, including those of adiposity and 2D:4D.**
***Conclusions*: 2D:4D is not strongly associated with adult anthropometric measures, including those of adiposity.**

Keywords: Digit ratio, 2D:4D, anthropometric measures, adiposity, BMI, hormones

INTRODUCTION

The ratio of the lengths of the index (2D) and ring (4D) fingers, expressed as the ratio 2D:4D, has been proposed as a negative marker of pre-natal androgen action and a positive marker of pre-natal oestrogen (Manning 2002). Several lines of evidence indicate that pre-natal testosterone exposure is inversely related to 2D:4D, especially right 2D:4D, as well as being inversely related to the difference between right and left 2D:4D (Δ_{r-l}) (Breedlove 2010). Recent evidence from a mouse model suggests that 2D:4D depends critically on *in utero* exposure to androgens relative to oestrogens, with higher testosterone relative to oestrogen leading to lower right 2D:4D (Zheng and Cohn 2011).

Since 2D:4D measures might afford a window into the pre-natal environment in terms of testosterone exposure, many investigators have used these measures in studies of hormone-related diseases in adulthood, such as cancers of the breast and prostate (Manning and Leinster 2001; Muller et al. 2011a). It has been hypothesized, however, that pre-natal androgen exposure might also be related to adult anthropometric measures, especially abdominal adiposity (Abbott et al. 2002), and that finger fat might be responsible for sex differences in 2D:4D (Wallen 2009). Since adiposity has been shown to be a risk factor for some hormone-related cancers (MacInnis et al. 2003, 2004), it is plausible that any association between pre-natal androgen exposure and cancer could be mediated by adult anthropometric measures with particular regard to adiposity.

Several studies have investigated possible associations between adult anthropometric measures and 2D:4D, with largely inconsistent results. We sought to assess whether right or left 2D:4D or Δ_{r-l} are associated with adult anthropometric measures in a large sample of women and men from the Melbourne Collaborative Cohort Study (MCCS).

MATERIALS AND METHODS

The MCCS is a prospective cohort study of 24 469 women and 17 045 men recruited between 1990–1994, 99.3% of whom were aged 40–69 years. At baseline, physical measurements were made by trained research nurses. Height, weight, waist circumference, hip circumference and bioelectrical resistance and reactance were measured following established protocols that have been described

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previously (MacInnis et al. 2004). Body mass index (BMI) was calculated as mass in kilograms divided by the square of height in metres. Fat-free mass and fat mass were estimated using an empirically derived formula that was developed using participants whose characteristics were similar to those of the MCCS participants (Roubenoff et al. 1997).

A face-to-face follow-up of the MCCS was conducted between 2003–2009. At this visit participants had their hands photocopied for the purpose of measuring 2D:4D. The lengths of the index and ring fingers were measured from photocopies of the surface of the hand using digital Vernier calipers. The length of the index finger was divided by the length of the ring finger to obtain 2D:4D and Δ_{r-l} was defined as the difference between right and left 2D:4D. Measurement was undertaken by a team of trained research assistants at Cancer Council Victoria. Detailed information on the measurement protocol and inter-observer reliability has been published previously (Muller et al. 2011b). A total of 8840 women and 6076 men who had available digit measurements were included in this study.

Statistical analysis

Linear regression models were used to estimate anthropometric measures as a function of sex-specific standardized 2D:4D. Coefficients from these models, therefore, represent the expected increment in the measure for a standard deviation increase in 2D:4D. To assess potential non-linear relationships between 2D:4D and anthropometric measures, we fit restricted cubic spline functions of the standardized 2D:4D measures. Separate models were fit for women and men and all models included age at baseline in years. Since 2D:4D is related to country of birth in this sample (Muller et al. 2011b), we also included country of birth in all models. The likelihood ratio test was used to calculate p-values. Statistical analyses were conducted using Stata 12.1 for Linux (Stata Corporation, College Station, TX).

RESULTS

The distributions of demographic variables, 2D:4D and anthropometric measures are summarized in Table I. As expected, both left and right mean 2D:4D and Δ_{r-l} were higher for women than men. The distribution of age was similar for men and women, as was the distribution of country of birth.

The estimated regression coefficients for a 1 SD increment in 2D:4D measures are presented in Table II for both women and men. There is no evidence of any strong association between left 2D:4D, right 2D:4D or Δ_{r-l} and the anthropometric measures for women. A weak positive association was observed between height and left 2D:4D for women, with a 1 SD increment in left 2D:4D being associated with an expected mean increment of 0.17 cm in height (95% CI = 0.04, 0.29). Similarly, for women there was a weak positive association between fat mass and right 2D:4D, with a 1 SD increment corresponding to an expected mean increment of 0.22 kg in fat mass (95% CI = 0.02, 0.42).

Table I. Demographic and anthropometric characteristics of the study sample by sex.

	Women		Men	
	Mean	SD	Mean	SD
Age (years)	54.0	8.2	54.7	8.4
Country of birth (n)				
Australia/NZ/UK/Other	6582		4275	
Italy	1415		1087	
Greece	843		714	
Left 2D:4D	0.966	0.036	0.953	0.036
Right 2D:4D	0.961	0.037	0.947	0.037
Δ_{r-l}	−0.005	0.034	−0.007	0.034
Height (cm)	160.0	6.6	172.5	7.5
Weight (kg)	68.1	12.0	88.9	11.4
BMI (kg/m^2)	26.6	4.8	27.2	3.5
Waist circumference (cm)	79.4	11.4	93.2	9.6
Hip circumference (cm)	101.4	9.7	101.0	6.8
Waist:hip ratio	0.781	0.067	0.921	0.061
Fat-free mass (kg)	40.4	4.2	57.2	5.7
Fat mass (kg)	27.7	9.3	23.7	7.5
Percentage fat mass	39.8	6.8	28.7	5.8

SD, standard deviation; NZ, New Zealand; UK, United Kingdom.

For men, there was a weak positive association between height and right 2D:4D, with a 1 SD increment in 2D:4D being associated with an expected mean increment of 0.21 cm in height (95% CI = 0.04, 0.38). No other linear associations were observed. Fitting interactions between 2D:4D and country of birth groups did not materially affect the results and models including restricted cubic spline functions of 2D:4D did not reveal any substantial non-linear associations for either men or women (data not shown).

DISCUSSION

In this large sample of men and women aged between 40–69 at baseline we observed no strong associations between 2D:4D measures and height, weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, fat mass, fat-free mass or percentage fat mass.

Wallen (2009) has summarized the evidence that 2D:4D is positively related to adiposity and suggested that the sex difference in 2D:4D reflects differences in finger fat. However, a meta-analysis of sex differences in skeletogenic 2D:4D (i.e. 2D:4D of the phalanges) has shown significant differences between men and women (Hönekopp and Watson 2010). Several small studies have assessed associations between 2D:4D and anthropometric measures. In a study of 386 university students, Barut et al. (2008) found weak inverse associations between both right and left 2D:4D and height and no associations with weight. McIntyre et al. (2003) found a weak inverse association between right 2D:4D and waist circumference in a sample of 42 men between the ages of 31–76 years. Fink et al. (2003) investigated several anthropometric measures in a sample of 50 men and 70 women and found moderately strong inverse associations between waist circumference, hip circumference and waist-to-chest ratio and both right and left 2D:4D for women. This study also found that BMI was strongly positively correlated with left 2D:4D for men. Another study

Table II. Estimated increment in anthropometric measures for a one standard deviation increment in 2D:4D measures.

	Left 2D:4D			Right 2D:4D			Δ_{r-l}		
	β^a	95% CI	p	β^a	95% CI	p	β^a	95% CI	p
Women									
Height (cm)	0.17	(0.04, 0.29)	0.01	0.11	(−0.02, 0.24)	0.09	−0.06	(−0.18, 0.07)	0.38
Weight (kg)	0.16	(−0.09, 0.42)	0.20	0.25	(−0.01, 0.50)	0.06	0.09	(−0.16, 0.35)	0.47
BMI (kg/m^2)	0.02	(−0.08, 0.11)	0.75	0.06	(−0.04, 0.16)	0.24	0.05	(−0.05, 0.14)	0.35
Waist circumference (cm)	0.07	(−0.16, 0.30)	0.53	0.02	(−0.22, 0.25)	0.90	−0.05	(−0.28, 0.18)	0.67
Waist circumference, adjusted for height (cm)	0.06	(−0.17, 0.29)	0.62	0.00	(−0.23, 0.24)	0.97	−0.04	(−0.27, 0.19)	0.71
Hip circumference (cm)	0.09	(−0.12, 0.29)	0.40	0.14	(−0.07, 0.34)	0.19	0.06	(−0.14, 0.27)	0.54
Waist-to-hip ratio × 10	0.00	(−0.02, 0.01)	0.80	−0.01	(−0.02, 0.00)	0.13	−0.01	(−0.02, 0.00)	0.19
Fat-free mass (kg)	−0.05	(−0.13, 0.03)	0.23	0.01	(−0.07, 0.09)	0.75	0.05	(−0.02, 0.13)	0.18
Fat mass (kg)	0.13	(−0.07, 0.32)	0.20	0.19	(−0.00, 0.38)	0.05	0.08	(−0.11, 0.27)	0.42
Percentage fat mass	0.12	(−0.02, 0.26)	0.10	0.10	(−0.04, 0.24)	0.17	0.00	(−0.15, 0.14)	0.95
Men									
Height (cm)	0.12	(−0.05, 0.29)	0.18	0.21	(0.04, 0.38)	0.01	0.09	(−0.08, 0.25)	0.32
Weight (kg)	−0.09	(−0.38, 0.20)	0.54	−0.07	(−0.36, 0.23)	0.65	0.00	(−0.29, 0.29)	0.99
BMI (kg/m^2)	−0.07	(−0.15, 0.02)	0.12	−0.09	(−0.18, −0.00)	0.05	−0.03	(−0.11, 0.06)	0.57
Waist circumference (cm)	−0.15	(−0.40, 0.09)	0.21	−0.07	(−0.31, 0.17)	0.58	0.08	(−0.16, 0.32)	0.52
Waist circumference, adjusted for height (cm)	−0.18	(−0.42, 0.06)	0.14	−0.12	(−0.36, 0.12)	0.33	0.06	(−0.18, 0.30)	0.62
Hip circumference (cm)	−0.05	(−0.22, 0.12)	0.58	−0.07	(−0.24, 0.10)	0.39	−0.02	(−0.19, 0.15)	0.78
Waist-to-hip ratio × 10	−0.01	(−0.03, 0.00)	0.06	0.00	(−0.02, 0.01)	0.54	0.01	(−0.01, 0.02)	0.25
Fat-free mass (kg)	−0.14	(−0.26, −0.02)	0.03	−0.13	(−0.25, −0.01)	0.04	0.02	(−0.10, 0.14)	0.74
Fat mass (kg)	−0.04	(−0.23, 0.14)	0.66	−0.11	(−0.29, 0.08)	0.26	−0.09	(−0.28, 0.09)	0.33
Percentage fat mass	0.00	(−0.14, 0.15)	0.95	−0.03	(−0.18, 0.11)	0.65	−0.06	(−0.21, 0.08)	0.39

[a] Estimated regression coefficients from linear regression models adjusted for age at baseline and country of birth. Coefficients correspond to the expected increment in the mean of the anthropometric measure for a 1 SD increment in the 2D:4D measure.

of 127 men and 117 women found that right 2D:4D was inversely associated with hip circumference and positively correlated with waist-to-hip ratio for men, but found no associations between left or right 2D:4D and any anthropometric measure for women (Fink et al. 2006).

The results of our study, when taken into consideration of the inconsistent results previously reported, provide strong evidence that there are no substantial associations between 2D:4D and the assessed anthropometric measures. Consequently, it is unlikely that adult anthropometrc measures mediate any association between 2D:4D measures and risk of adult diseases and disorders.

The primary advantage of this study is its large sample size, over 15-times larger than all previous studies combined, which affords the opportunity to detect very small associations. Another advantage is that physical measurements were made by trained research nurses, so any attenuation of associations due to measurement error is minimized. A disadvantage of this study is that assessment of 2D:4D and the other anthropometric measures was not contemporaneous. Physical measurements were taken at baseline attendance between 1990–1994, whereas 2D:4D was measured from photocopies of participants' hands collected at a face-to-face follow-up conducted between 2003–2009. Since not all participants attended follow-up, information on 2D:4D was incomplete and the results of this study are, therefore, based on a self-selected sample.

In summary, we found no evidence of substantial associations between 2D:4D measures and adult height, weight, BMI, waist circumference, hip circumference, waist-to-hip ratio, fat-free mass or fat mass for women or men. To the extent that 2D:4D reflects sensitivity to and pre-natal exposure to testosterone, these results suggest that associations between 2D:4D and hormone-related behaviours, diseases and disorders can be interpreted directly, independent of any mediating effects of adult anthropometric measures including adiposity.

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