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Genetic and Environmental Influences on Obesity-Related Phenotypes in Chinese Twins Reared Apart and Together

**Bin Zhou · Wenjing Gao · Jun Lv · Canqing Yu · Shengfeng Wang ·
Chunxiao Liao · Zengchang Pang · Liming Cong · Zhong Dong · Fan Wu ·
Hua Wang · Xianping Wu · Guohong Jiang · Xiaojie Wang · Binyou Wang ·
Weihua Cao · Liming Li**

Abstract The relative importance of genetic and environmental influences on obesity-related phenotypes remains unclear, and few studies have targeted the Chinese population. Here, we used Chinese twins reared apart and together to explore genetic and environmental influences on body mass index (BMI), waist circumference (WC) and waist–height ratio (WHtR), further to differentiate phenotype heritability between different age groups and genders separately and to differentiate influences of rearing environment and correlated environment. Phenotype heritability was calculated using the structural equation model in 11,401 twin pairs aged 25–85 years. BMI (0.70, 95 % confidence interval (CI) 0.66–0.74) of the total population was highly heritable, while WC (0.53, 95 %CI 0.50–0.57) and WHtR (0.48, 95 %CI 0.45–0.51) were moderately heritable. Age and gender stratified analyses found higher heritability in the younger group and males than the older group and females. The correlated environment had a greater influence on the phenotypes than the rearing environment, especially on WC and WHtR, indicating that more correlated environment actions should be taken to prevent the rising trend of abdominal obesity.

Keywords Twins · Obesity · Heritability · Environment · Adult

B. Zhou (✉) · W. Gao · J. Lv · C. Yu · S. Wang · C. Liao ·
W. Cao (✉) · L. Li (✉)
Department of Epidemiology and Biostatistics, School of Public
Health, Peking University, Beijing 100191, China
e-mail: zhoubin19881988@sina.com

W. Cao
e-mail: caoweihua60@163.com

L. Li
e-mail: lmlee@vip.163.com

Z. Pang
Qingdao Center for Diseases Control and Prevention,
Qingdao 266033, China

L. Cong
Zhejiang Center for Disease Control and Prevention,
Hangzhou 310051, China

Z. Dong
Beijing Center for Disease Control and Prevention,
Beijing 100013, China

F. Wu
Shanghai Center for Disease Control and Prevention,
Shanghai 200336, China

H. Wang
Jiangsu Center for Disease Control and Prevention,
Nanjing 210009, China

X. Wu
Sichuan Center for Disease Control and Prevention,
Chengdu 610041, China

G. Jiang
Tianjin Center for Disease Control and Prevention,
Tianjin 300011, China

X. Wang
Qinghai Center for Disease Control and Prevention,
Xining 810007, China

B. Wang
Harbin Medical University, Harbin 150081, China

Introduction

Obesity is an important risk factor of noncommunicable diseases (NCDs). With increases in body mass index (BMI), the risk of cardiovascular diseases, type 2 diabetes, and certain cancers rises significantly (Apovian et al. 2012; Poirier et al. 2006). According to a report on global NCDs published by the World Health Organization, the obesity rate of men and women (aged $\geq$ 20 years) was 10 and 14 %, respectively, worldwide, and 4.7 and 6.7 %, respectively, in China in 2008 (World Health Organization 2010). Although the obesity rate in China was slightly lower than that of the world, the growth of its obese population has increased at an annual rate of 12.4 % from 1981 to 2012, which was much higher than that of developed countries such as the United States, whose annual obese growth rate was only 3.8 % in the same period (Yu et al. 2012). BMI and waist circumference (WC) have been widely used as indicators of obesity (Ning et al. 2013). However, in recent years waist–height ratio (WHtR) has been suggested as a new indicator because it better evaluates the risk of developing cardiovascular diseases (Browning et al. 2010; Hsieh et al. 2005).

Obesity is considered to be the result of both genetic and environmental factors, although the relative importance of these factors is uncertain. A recently published meta-analysis of heritability of BMI showed it to range from 0.47 to 0.90 from twin studies (Elks et al. 2012), while heritability of WC was reported to range from 0.19 to 0.83 (Jermendy et al. 2011; Ji et al. 2014; Mustelin et al. 2009; Nelson et al. 2002; Ning et al. 2013; Rose et al. 1998; Schousboe et al. 2004; Selby et al. 1990; Wardle et al. 2008), and no studies have yet investigated heritability of WHtR. These heritability data derived from twins reared together (TRT) study designs which make the important assumption of equal environment assumption (EEA), meaning that the phenotype-related environments of monozygotic twins (MZ) and those of dizygotic twins (DZ) are similar. If this assumption is violated, however, the heritability will be overestimated (Verweij et al. 2012; Zhang et al. 2012). Moreover, common environmental influences and nonadditive genetic influences cannot be estimated simultaneously when using the TRT design for model fitting analysis (van Dongen et al. 2012). To overcome this, investigations of heritability could instead be based on twins reared apart (TRA) study designs in which four groups of twins can be obtained: (1) monozygotic twins reared apart (MZA); (2) monozygotic twins reared together (MZT); (3) dizygotic twins reared apart (DZA); and (4) dizygotic twins reared together (DZT) (Rushton et al. 2007). Although fewer TRA studies have been performed compared with TRT studies because of the difficulty in collecting TRA samples, they demonstrated heritability estimates ranged from 0.49–0.85 to 0.46–0.78 for BMI and WC, respectively (Allison et al. 1996;

Elder et al. 2009; Hong et al. 1997; Nelson et al. 1999, 2000; Price et al. 1991; Stunkard et al. 1990). These ranges are narrower than those derived from TRT studies, which is likely to be because of the limited number of studies and because four of the existing seven papers came from the Swedish Adoption/Twin Study of Aging (SATSA).

Sex and age differences in heritability of the three obesity-related phenotypes remain imprecise. However, evidence has shown that different genomic mechanisms underlying obesity susceptibility in men and women might lead to differences in heritability (Lewis et al. 2005; Liu et al. 2014). A large multinational comparative study evaluating gender differences in heritability of BMI found significant differences between men and women (Schousboe et al. 2003). The main assumption for age differences in heritability is that different genes are active at different stages of life (Rankinen et al. 2006). Indeed, some longitudinal studies evaluating age differences in BMI have reported altered heritability of BMI with aging (Hjelmborg et al. 2008; Ortega-Alonso et al. 2009).

Few studies have investigated heritability of BMI, WC and WHtR in Chinese populations, particularly involving TRA. Therefore, the present study used MZA, MZT, DZA, and DZT data to quantitatively investigate genetic and environmental influences on obesity-related phenotypes and to explore heritability differences between different age groups and genders, separately. We also reported the respective influences of the rearing and correlated environments.

Materials and methods

Participants

The participants of our study were from the Chinese National Twin Registry (CNTR), which is the largest national population-based twin registry in China (Li et al. 2013). Since its establishment in 2001, it has recruited 36,565 twin pairs (as of June 2014) from nine provinces and municipalities.

A total of 11,401 adult twin pairs aged 25–85 (39.0 ± 10.8) years from CNTR were included in the study, of whom 155 pairs were MZA, 6226 pairs were MZT, 124 pairs were DZA, and 4896 were DZT. TRA was defined according to SATSA's definition as twins who had been reared apart for at least 1 year before the age of 11. The average age of TRA at separation was 2.3 ± 2.2 years, and their average time spent reared apart was 24.9 ± 21.4 years. Of all TRA, 62.4 % separated within 1 year after they were born, and 90.3 % by the age of 5. Following separation, 70.3 % of TRA lived within the same city as their brothers or sisters, 15.1 % lived within the same province, and the remainder lived in other provinces of China or abroad.

The height, weight, and WC of the participants were self-reported in questionnaires administered in 2011 and 2012. Height and weight were required to the nearest centimeter (cm) and kilogram (kg), respectively. WC was reported to the nearest cm or 0.1 Chinese "chi" (1 chi = 33.33 cm; Instructions: Measured at the midpoint between the rib cage and iliac crest). Correlation coefficients of measured and reported height, weight, and WC values were high in adults, at >0.90 (Dahl et al. 2010; Dekkers et al. 2008). The phenotypes included in the study were BMI, WC, and WHtR, where BMI was calculated as weight in kilograms divided by squared height in meters and WHtR as WC in cms divided by height in cms.

The zygosity of twins was determined by questionnaires. Twins of different genders were classified as DZ. For twins of the same gender, a model was built according to age, gender, and "whether they were as alike as two peas in a pod". Using this model, we determined the zygosity of 191 pairs of same-gender twins who had undergone genetic analysis. The accuracy of the model was 0.88 (95 % CI 0.82–0.92), which was sufficient to determine twin zygosity in large epidemiological studies.

Statistical analysis

Descriptive statistics and intraclass correlation coefficients (ICC) were calculated using SPSS software (20.0, Chicago, IL). To obtain normal distributions and facilitate model fitting analysis, BMI, WC, and WHtR were natural log transformed and then multiplied by 100 to expand the variance. The ICC of MZA represent a simple estimate of heritability (Elder et al. 2009), and the ICC of MZT and DZT could be a reference for selecting the parameters of model fitting analysis. If the ICC of MZT are less than twice that of DZT, the correlated environmental influence is estimated in the model; otherwise, the nonadditive genetic influence is estimated (Kato et al. 2005).

For genetic analyses, the present study could estimate one more component than the TRT design for the inclusion of TRA. The total phenotypic variance can be decomposed into additive genetic variance (A), nonadditive genetic variance (D), shared rearing environment variance (S), correlated environmental variance (C), and unique environment variance (E). The correlation coefficient of A and D is 1.0 and 0.5 for MZ, and 0.5 and 0.25 for DZ, respectively (Hasselbalch et al. 2008). TRT, but not TRA, share factors of the rearing environment such as parents, family economic conditions, and dietary habits. The correlated environment refers to the factors that lead to twin similarities but cannot be accounted for by either A or S, such as similar rearing environments resulting from selective placement, cultural habits of the same district, province or country, and communication between the twins

after separation (Kato et al. 2005). Unique environmental influences differ between both TRT and TRA. In the ASCE model of the present study, the covariances of MZA, MZT, DZA, and DZT were A + C, A + S + C, 0.5A + C, and 0.5A + S + C, respectively. The relationships between variables are depicted in a path diagram (Fig. 1).

To obtain heritability of BMI, WC, and WHtR for the total population, we performed the ASCE model with age and gender included as covariates. Because of the inclusion of TRA, the ASDE model was also performed to detect the effect of S and D simultaneously. To better understand the influences of age and gender on heritability, we performed the ASCE model separately for younger and older subgroups using gender as a covariate, and for men and women with age as a covariate (That is sex-limitation model including opposite-sex DZ twins) (Dubois et al. 2012). To maximize the sample size of each subgroup, the median age of 37 years was used as the demarcation point when stratified by age. Participants ≤37 years of age belonged to the younger group, while those >37 years belonged to the older group.

For stratified analyses, firstly, we estimated all parameters separately by age and by gender (full model). Secondly, the parameters were constrained to be equal in the younger/older group or male/female (equated model), then the equated model was compared with the full model to determine whether the difference between the two models was statistically significant. Finally, we sequentially removed corresponding parameters based on either the full model or equated model according to the Akaike information criterion (AIC), to obtain the model of best fit. OpenMx (Version 1.4) was used for model fitting analysis, where parameters were estimated from the maximum likelihood. The smallest AIC indicated the most parsimonious and best-fit model (Verweij et al. 2012).

Results

The distribution of the four groups of twins is listed by age and gender in Table 1. When stratified by age, the average age of the younger and older groups was 30.4 ± 3.7 years and 47.8 ± 8.3 years, respectively. 60.9 % of all twins were male, and 51.1 % of all twin pairs were male–male (MM) twins.

The mean levels and standard deviations (SD) of BMI, WC, and WHtR stratified by age and gender are listed in Table 2. When stratified by age, the mean values of all phenotypes were statistically significantly lower in the younger group than in the older group (P < 0.001). Differences were also statistically significant when stratified by gender, with higher mean phenotype values in men than in women (P < 0.001).

Fig. 1 Path diagram of the ASCE Twin Model. *A* additive genetic variance, *S* shared rearing environment variance, *C* correlated environmental variance, *E* unique environment variance, P_1 phenotype in twin 1, P_2 phenotype in twin 2, *MZ* monozygotic twins, *DZ* dizygotic twins, *TRA* twins reared apart, *TRT* twins reared together, *a*, *s*, *c*, *e* are path coefficients; *Circles* represent latent variables. *Squares* represent observed variables. *Single-headed arrows* represent hypothesized casual relationship between variables. *Double-headed arrows* represent correlation or covariance between variables
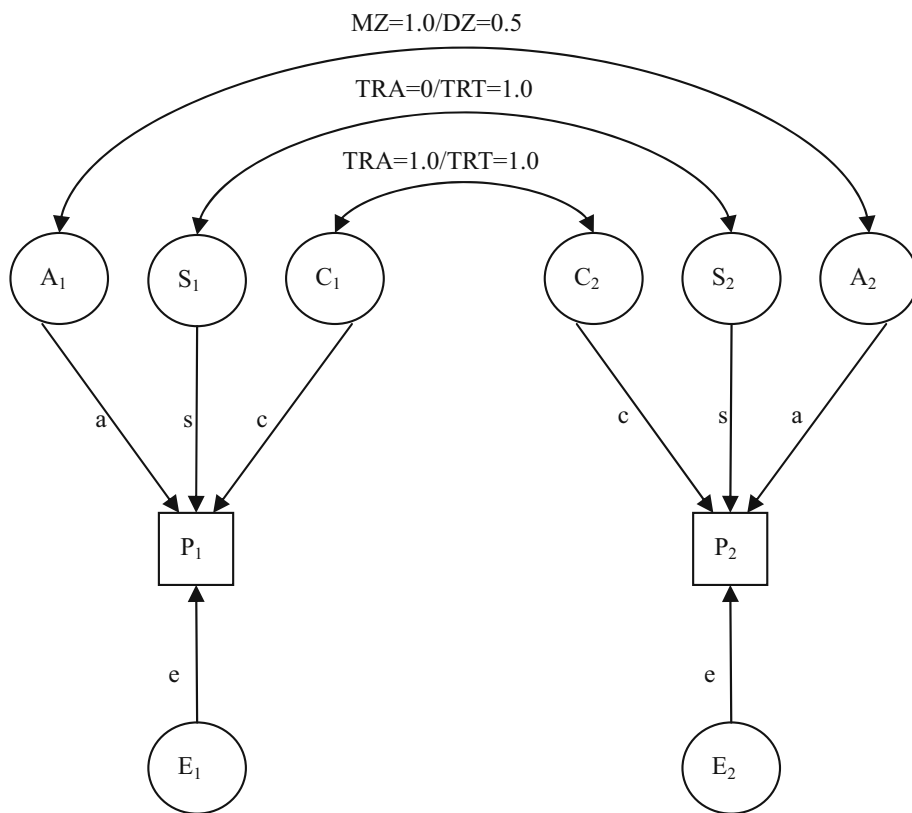
Table 1 Distribution of twins reared apart and together by age and gender

Zygosity	Age		Gender			Total (%)
	Younger group (%)	Older group (%)	MM (%)	FF (%)	MF (%)	
MZA	67 (43.2)	88 (56.8)	82 (52.9)	73 (47.1)	–	155 (100.0)
MZT	3090 (49.6)	3136 (50.4)	3853 (61.9)	2373 (38.1)	–	6226 (100.0)
DZA	59 (47.6)	65 (52.4)	46 (37.1)	21 (16.9)	57 (46.0)	124 (100.0)
DZT	2550 (52.1)	2346 (47.9)	1849 (37.8)	875 (17.9)	2172 (44.4)	4896 (100.0)
Total	5766 (50.6)	5635 (49.4)	5830 (51.1)	3342 (29.3)	2229 (19.6)	11401 (100.0)

Pairs of twins; younger group, 25–37 years; older group, 38–85 years

MM male–male twins, *FF* female–female twins, *MF* male–female twins, *MZA* monozygotic twins reared apart, *MZT* monozygotic twins reared together, *DZA* dizygotic twins reared apart, *DZT* dizygotic twins reared together

The ICC of the four groups of twins are listed in Table 3. Because MZ share 100 % genes while DZ share only 50 % genes, the ICC of MZ should be higher than those of DZ. However, because the common rearing environment makes TRT more similar to each other than TRA, the ICC of TRT should be higher than those of TRA (Kendler et al. 2000; van Dongen et al. 2012). When stratified by age, the ICC of MZA were higher in the younger group than in the older group. When stratified by gender, the ICC of MZA were higher in most MM twins than in female–female (FF) twins (with the exception of BMI). Whether stratified by age or by gender, the ICC of

most MZT were less than twice those of DZT, indicating that C should be included in the ASCE model.

The heritability of BMI, WC, and WHtR for the total population with age and gender included as covariates is listed in Table 4 (ASCE model and ASDE model). Comparing the ASCE model with the saturated model, all the AIC of full models and best-fit models were smaller and the *P* values were nonsignificant, indicating that the reduced sub-model fitted the data more parsimoniously. The heritability of the best-fit model for BMI, WC, and WHtR was 0.70, 0.53, and 0.48, respectively. In the case of the ASDE model, although D was included, the values of the

Table 2 Mean levels (±SD) of BMI, WC and WHtR in 11,401 twin pairs by age and gender

Phenotype	Total	Age		Gender	
		Younger group	Older group	Male	Female
N[a]	22,802	11,532	11,270	13,889	8913
BMI (kg/m^2)	22.9 ± 2.9	22.4 ± 3.0[b]	23.5 ± 2.8	23.4 ± 2.8[c]	22.1 ± 2.9
WC (cm)	80.3 ± 10.2	78.6 ± 10.3[b]	82.1 ± 9.7	84.1 ± 9.3[c]	74.5 ± 8.6
WHtR	0.484 ± 0.055	0.471 ± 0.054[b]	0.497 ± 0.054	0.495 ± 0.053[c]	0.466 ± 0.054

[a] N number of twins

[b] $P < 0.001$, the difference between the younger and older twins was statistically significant

[c] $P < 0.001$, the difference between male and female twins was statistically significant; younger group, 25–37 years; older group, 38–85 years; *BMI* body mass index, *WC* waist circumference, *WHtR* waist-height ratio

Table 3 Intra-class MZA, MZT, DZA and DZT correlations and 95 % CI by age and gender

Phenotype	Total	Age		Gender		
		Younger group	Older group	MM	FF	MF
BMI r(95 %CI)						
MZA	0.79 (0.72,0.84)	0.80 (0.70,0.87)	0.75 (0.65,0.83)	0.71 (0.59,0.81)	0.83 (0.75,0.89)	–
MZT	0.83 (0.82,0.84)	0.84 (0.83,0.85)	0.81 (0.80,0.82)	0.83 (0.82,0.84)	0.81 (0.80,0.83)	–
DZA	0.42 (0.26,0.55)	0.32 (0.07,0.53)	0.51 (0.31,0.67)	0.52 (0.27,0.70)	0.50 (0.11,0.76)	0.19 (−0.07,0.43)
DZT	0.47 (0.45,0.49)	0.42 (0.39,0.46)	0.49 (0.46,0.52)	0.53 (0.50,0.56)	0.63 (0.58,0.66)	0.33 (0.29,0.36)
WC r(95 % CI)						
MZA	0.88 (0.83,0.91)	0.92 (0.87,0.95)	0.83 (0.75,0.88)	0.86 (0.79,0.91)	0.80 (0.70,0.87)	–
MZT	0.88 (0.88,0.89)	0.90 (0.89,0.90)	0.86 (0.85,0.87)	0.86 (0.85,0.87)	0.83 (0.82,0.84)	–
DZA	0.43 (0.28,0.56)	0.41 (0.17,0.60)	0.44 (0.22,0.62)	0.64 (0.44,0.79)	0.36 (−0.06,0.68)	0.13 (−0.13,0.37)
DZT	0.51 (0.49,0.54)	0.46 (0.43,0.49)	0.55 (0.52,0.58)	0.64 (0.61,0.66)	0.72 (0.69,0.75)	0.22 (0.18,0.26)
WHtR r(95 % CI)						
MZA	0.85 (0.80,0.89)	0.89 (0.83,0.93)	0.79 (0.69,0.86)	0.85 (0.78,0.90)	0.81 (0.71,0.88)	–
MZT	0.86 (0.85,0.87)	0.87 (0.86,0.87)	0.84 (0.83,0.85)	0.86 (0.85,0.86)	0.84 (0.82,0.85)	–
DZA	0.53 (0.39,0.64)	0.47 (0.24,0.64)	0.55 (0.35,0.70)	0.65 (0.44,0.79)	0.35 (−0.07,0.67)	0.45 (0.22,0.64)
DZT	0.60 (0.58,0.61)	0.55 (0.52,0.58)	0.60 (0.57,0.62)	0.64 (0.62,0.67)	0.76 (0.73,0.78)	0.46 (0.42,0.49)

CI confidence interval, younger group 25–37 years, older group 38–85 years, *MM* male–male twins, *FF* female–female twins, *MF* male–female twins, *MZA* monozygotic twins reared apart, *MZT* monozygotic twins reared together, *DZA* dizygotic twins reared apart, *DZT* dizygotic twins reared together, *BMI* body mass index, *WC* waist circumference, *WHtR* waist-height ratio

three phenotypes approached 0.00 and all the AIC of full models and best-fit models (model with a smaller AIC except for the saturated model) were greater than that of the saturated model, so D was not included in stratified analyses.

The results of stratified analyses are listed in Tables 5 and 6. When stratified by age, heritability was higher in the younger group than in the older group for all full models. We also found that the correlated environment was of key importance for the three phenotypes, as shown by the fact that C accounted for 31 and 37 % of the total variation in the best-fit model of WC and WHtR, respectively. Differences between the equated model and full model of BMI were statistically significant

($P < 0.001$). For the best-fit model of BMI, heritability was 0.76 in the younger group and 0.64 in the older group.

When stratified by gender, heritability was higher in males than in females for all full models. Again, we showed that the correlated environment was of key importance for the three phenotypes, for example, in the case of the best-fit model of WHtR, C accounted for 45 and 62 % of the total variation in males and females, respectively. The differences between equated models and full models of BMI, WC and WHtR were all statistically significant ($P < 0.001$). For the best-fit models of the three phenotypes, heritability in males and females was 0.56 and 0.35, 0.41 and 0.15, and 0.41 and 0.12, respectively. The

Table 4 Variance components from ASCE and ASDE model for obesity-related phenotypes

Phenotype	Variance components					−2LL	Compared with saturated model		
	A	S	C	D	E		ΔAIC	Δdf	P
BMI									
Saturated model						170733.8			
Full model	0.70 (0.66,0.74)	0.06 (0.02,0.12)	0.06 (0.00,0.12)	–	0.18 (0.17,0.19)	170747.0	−3.2	15	0.137
Best-fit model	**0.70 (0.66,0.74)**	**0.06 (0.02,0.12)**	**0.06 (0.00,0.12)**	**–**	**0.18 (0.17,0.19)**	**170747.0**	**−3.2**	**15**	**0.137**
Saturated model						170733.8			
Full model	0.72 (0.62,0.75)	0.10 (0.07,0.14)	–	0.00 (0.00,0.07)	0.18 (0.17,0.18)	170749.9	6.1	15	0.002
Best-fit model	**0.72 (0.68,0.75)**	**0.10 (0.07,0.14)**	**–**	**–**	**0.18 (0.17,0.18)**	**170749.9**	**4.1**	**16**	**0.003**
WC									
Saturated model						165264.5			
Full model	0.53 (0.50,0.57)	0.01 (0.00,0.05)	0.31 (0.26,0.35)	–	0.15 (0.15,0.15)	165292.1	−2.4	15	0.246
Best-fit model	**0.53 (0.50,0.57)**	**–**	**0.32 (0.29,0.35)**	**–**	**0.15 (0.14,0.15)**	**165292.7**	**−4.5**	**16**	**0.304**
Saturated model						165264.5			
Full model	0.58 (0.53,0.61)	0.28 (0.24,0.31)	–	0.00 (0.00,0.02)	0.15 (0.14,0.15)	165367.8	73.3	15	<0.001
Best-fit model	**0.58 (0.54,0.61)**	**0.28 (0.24,0.31)**	**–**	**–**	**0.15 (0.14,0.15)**	**165367.8**	**71.3**	**16**	**<0.001**
WHtR									
Saturated model						163837.6			
Full model	0.48 (0.45,0.51)	0.02 (0.00,0.06)	0.35 (0.30,0.40)	–	0.15 (0.14,0.16)	163855.2	−12.4	15	0.280
Best-fit model	**0.48 (0.45,0.51)**	**–**	**0.37 (0.34,0.40)**	**–**	**0.15 (0.15,0.16)**	**163856.8**	**−12.8**	**16**	**0.255**
Saturated model						163837.6			
Full model	0.51 (0.47,0.55)	0.33 (0.30,0.37)	–	0.00 (0.02,0.30)	0.15 (0.14,0.16)	163939.4	71.8	15	<0.001
Best-fit model	**0.51 (0.48,0.55)**	**0.33 (0.30,0.37)**	**–**	**–**	**0.15 (0.14,0.16)**	**163939.4**	**69.8**	**16**	**<0.001**

Bold values indicate the best-fit model

A additive genetic variance, *S* shared rearing environment variance, *C* correlated environmental variance, *E* unique environment variance, *−2LL* −2 times the natural log likelihood, *df* degrees of freedom, *AIC* Akaike's information criterion, *BMI* body mass index, *WC* waist circumference, *WHtR* waist–height ratio

Table 5 Variance components from ASCE model for obesity-related phenotypes by age

Phenotype	Younger Group				Older group				−2LL	Compared with full model		
	A	S	C	E	A	S	C	E		ΔAIC	Δdf	P
BMI												
Full model	0.76 (0.71,0.80)	0.07 (0.01,0.12)	0.00 (0.00,0.07)	0.17 (0.16,0.18)	0.64 (0.58,0.70)	0.05 (0.00,0.13)	0.11 (0.02,0.19)	0.19 (0.18,0.20)	170558.1			
Equated model	0.71 (0.67,0.75)	0.07 (0.02,0.12)	0.05 (0.00,0.11)	0.18 (0.17,0.19)					170579.6	13.5	4	<0.001
Best-fit model	**0.76 (0.71,0.80)**	**0.07 (0.01,0.12)**	**0.00 (0.00,0.07)**	**0.17 (0.16,0.18)**	**0.64 (0.58,0.70)**	**0.05 (0.00,0.13)**	**0.11 (0.02,0.19)**	**0.19 (0.18,0.20)**	**170558.1**	**0**	**0**	**1.000**
WC												
Full model	0.57 (0.52,0.62)	0.00 (0.00,0.05)	0.28 (0.22,0.33)	0.15 (0.14,0.16)	0.50 (0.46,0.55)	0.03 (0.00,0.09)	0.32 (0.25,0.38)	0.15 (0.14,0.15)	165192.9			
Equated model	0.54 (0.50,0.57)	0.01 (0.00,0.05)	0.30 (0.25,0.35)	0.15 (0.14,0.15)					165198.2	−2.7	4	0.260
Best-fit model	**0.54 (0.50,0.57)**		**0.31 (0.28,0.35)**	**0.15 (0.14,0.15)**					**165198.8**	**−4.1**	**5**	**0.321**
WHtR												
Full model	0.51 (0.47,0.56)	0.00 (0.00,0.07)	0.33 (0.25,0.38)	0.15 (0.14,0.16)	0.45 (0.40,0.49)	0.03 (0.00,0.10)	0.37 (0.30,0.43)	0.15 (0.14,0.16)	163772.0			
Equated model	0.48 (0.45,0.51)	0.02 (0.00,0.06)	0.35 (0.29,0.39)	0.15 (0.15,0.16)					163777.7	−2.3	4	0.221
Best-fit model	**0.48 (0.45,0.51)**		**0.37 (0.33,0.40)**	**0.15 (0.15,0.16)**					**163779.1**	**−2.9**	**5**	**0.208**

Bold values indicate the best-fit model

A additive genetic variance, S shared rearing environment variance, C correlated environmental variance, E unique environment variance, −2LL −2 times the natural log likelihood, df degrees of freedom, AIC Akaike's information criterion, BMI body mass index, WC waist circumference, WHtR waist-height ratio

Table 6 Variance components from ASCE Model for obesity-related phenotypes by gender

Phenotype	Male				Female				−2LL	Compared with full model		
	A	S	C	E	A	S	C	E		ΔAIC	Δdf	P
BMI												
Full model	0.56 (0.50,0.62)	0.10 (0.04,0.19)	0.18 (0.07,0.26)	0.16 (0.16,0.17)	0.35 (0.28,0.43)	0.04 (0.00,0.12)	0.42 (0.32,0.51)	0.19 (0.19,0.20)	170955.0			
Equated model	0.52 (0.50,0.55)	0.07 (0.03,0.12)	0.23 (0.17,0.28)	0.17 (0.17,0.18)					171006.7	51.7	5	<0.001
Best-fit model	**0.56 (0.50,0.62)**	**0.10 (0.04,0.19)**	**0.18 (0.07,0.26)**	**0.16 (0.16,0.17)**	**0.35 (0.28,0.43)**	**0.04 (0.00,0.12)**	**0.42 (0.32,0.51)**	**0.19 (0.19,0.20)**	**170955.0**	**0**	**0**	**1.000**
WC												
Full model	0.41 (0.37,0.45)	0.02 (0.00,0.07)	0.46 (0.40,0.51)	0.11 (0.11,0.12)	0.14 (0.10,0.14)	0.05 (0.00,0.13)	0.65 (0.56,0.72)	0.16 (0.15,0.16)	166925.4			
Equated model	0.59 (0.56,0.62)	0.02 (0.00,0.05)	0.26 (0.22,0.30)	0.13 (0.13,0.14)					167305.7	370.3	5	<0.001
Best-fit model	**0.41 (0.37,0.45)**		**0.48 (0.43,0.52)**	**0.11 (0.11,0.12)**	**0.15 (0.10,0.20)**		**0.69 (0.64,0.73)**	**0.17 (0.16,0.18)**	**166928.4**	**−1.0**	**2**	**0.230**
WHtR												
Full model	0.41 (0.36,0.45)	0.02 (0.00,0.07)	0.45 (0.39,0.51)	0.12 (0.12,0.13)	0.12 (0.07,0.17)	0.08 (0.01,0.18)	0.62 (0.52,0.70)	0.18 (0.17,0.19)	164139.5			
Equated model	0.39 (0.36,0.41)	0.02 (0.00,0.07)	0.44 (0.39,0.44)	0.15 (0.14,0.15)					164322.2	172.7	5	<0.001
Best-fit model	**0.41 (0.36,0.45)**	**0.02 (0.00,0.07)**	**0.45 (0.39,0.51)**	**0.12 (0.12,0.13)**	**0.12 (0.07,0.17)**	**0.08 (0.01,0.18)**	**0.62 (0.52,0.70)**	**0.18 (0.17,0.19)**	**164139.5**	**0**	**0**	**1.000**

Bold values indicate the best-fit model

A additive genetic variance, S shared rearing environment variance, C correlated environmental variance, E unique environment variance, −2LL −2 times the natural log likelihood, df degrees of freedom, AIC Akaike's information criterion, BMI body mass index, WC waist circumference, WHtR waist–height ratio

sex-limitation model allowed the inclusion of opposite-sex DZ in the full model, and provided reasonable heritability estimations although they were smaller than those of the pooled results.

Discussion

Numerous studies have investigated the heritability of BMI and WC, including those based on twins and family pedigrees. However, the reported ranges of heritability are wide, and few studies have focused on Chinese populations. Moreover, most previous study designs were TRT, which limits the estimation of nonadditive genetic influence and correlated environment influence. Our study, including both TRA and TRT, explored the magnitude of genetic and environmental influences on BMI, WC, and WHtR, as well as heritability differences between different age groups and genders. Furthermore, because of the inclusion of TRA, we differentiated the influences of the rearing environment and correlated environment on the three phenotypes in Chinese population.

Heritability of BMI, WC, and WHtR in the total population showed that BMI (0.70) was highly heritable while WC (0.53) and WHtR (0.48) were moderately heritable compared with previous TRA studies mentioned above (0.49–0.85 for BMI and 0.46–0.78 for WC). However, for more than half the existing TRA studies are based on SATSA, it should be noted that twins of this registry were in the older age range, who were born between 1886 and 1958 (Kendler et al. 2000). An international MZA study showed that heritability of BMI was 0.63 for Finnish twins (aged 36.4 ± 11.9 years), 0.73 for Japanese twins (aged 64.7 ± 6.3 years), and 0.85 for other twins (aged 40.0 ± 18.6 years) (Allison et al. 1996). Another TRA study based on Chinese twins reported the heritability of BMI was 0.66 (Gao et al. 2011). These genetic differences could at least in part be explained by the observed different genetic mechanisms underlying obesity, such as the newly found SNPs in or near the *CDKAL1*, *PCSK1*, and *GP2* genes in East Asian populations but not in those of European ancestry (Wen et al. 2012).

Stratified analysis by age in the present study showed that the heritability of BMI, WC, and WHtR was higher in the younger group than in the older group. Some previous studies have verified a decrease in heritability of BMI with age in adults, which has been supported by specific genetic variants such as *FTO* and *MC4R*, which become less powerful with increasing age (Elks et al. 2012; Hardy et al. 2010). However, some studies revealed the opposite effect; for example, the longitudinal Finnish Twin Study on Aging showed that heritability of BMI increased with age, reporting values of 0.54 in 1975 (aged 42.6 ± 3.4 years) and 0.72 after 29 years (Ortega-Alonso et al. 2009).

Similarly, the National Heart Lung and Blood Institute Veteran Twin Study observed a moderate increase over time in BMI heritability (from 0.48 to 0.57 with mean ages of 48 and 63, respectively) (Goode et al. 2007).

Our stratified analysis by gender found that the heritability of BMI, WC, and WHtR was higher in males than in females. Previous studies have been inconsistent with respect to gender differences (Elks et al. 2012), although strong evidence was provided for differential gene expression between men and women (Schousboe et al. 2003). Additionally, differences in the heritability of WC and WHtR between two genders might reflect differences in fat distribution (Ashwell et al. 2012; Du et al. 2010; Elks et al. 2012). Recently, sex differences in the genetic etiology of obesity have been observed. For example, the gender stratified analyses of the GenSalt study detected significant linkage for obesity at chromosomal region 22q13.31–22q13.33 in women but not in men, while the HyperGEN study observed significant linkage at 15q25.3 for obesity in men but not in women (Chiu et al. 2010; Lewis et al. 2005; Liu et al. 2014).

Another finding of our study was the influence of the correlated environment on the three phenotypes, especially on WC and WHtR, which was found to be more important than the rearing environment. Moreover, according to stratified analyses, the older subgroup and females were more susceptible to correlated environmental factors compared with the younger subgroup and males. This finding is not common to many previous studies. Indeed, Stunkard et al. reported that the nonadditive genetic influence played a more important role than the correlated environment in BMI variation in both men (57 %) and women (37 %) (Stunkard et al. 1990). According to the definition of the correlated environment, component C could be influenced by a number of different factors: (1) The average separation age of our study was 2.3 years, and 62.4 % of twins separated during the first year of life. The time spent living together before separation for TRA might be attributable to an inflated C. (2) Of all TRA, 70.3 % lived in the same city as their brothers or sisters after separation, and could have been reared by relatives (selective placement) which might inflate C. Therefore, more information about foster parents should be obtained. (3) Most TRA studies assumed that TRA do not share any common environment. However, factors, such as the common intrauterine environment, could cause twin pairs to be more concordant for certain phenotypes. The C estimated in our present study made the results meet the actual status better (Elder et al. 2009).

During recent decades, China has experienced rapid economic development and urbanization, leading to changes in lifestyles, nutritional intake, and socioeconomic status, accompanied by changing patterns in obesity.

Recent studies reported that BMI-based obesity is reaching a plateau, while WC-based abdominal obesity is continuing to rise in China (Hou et al. 2013; Lao et al. 2014). According to our present study, the shared rearing, correlated, and unique environments account for around 50 % of the variation in WC and WHtR, with the correlated environment accounting for the most variation. We therefore recommend that environmental policies should be established to prevent the rise of abdominal obesity, including planning for urban environments, and positive health education and promotion.

This study has some limitations. First, for model fitting analysis, we carried out stratifications by age and gender separately rather than simultaneously because of the limited TRA sample size. However, 60.9 % of the participants were male and there were only 21 FF DZA pairs, which could have biased the results. Second, the height, weight, and WC were self-reported so may not be entirely accurate. However, because the correlation coefficients between self-reported and measured values approached 0.90, our results are likely to be reliable.

In conclusion, we estimated the heritability of BMI, WC, and WHtR in Chinese population, and found that the BMI of the total population was highly heritable while WC and WHtR were moderately heritable. Stratified analyses by age and gender revealed higher heritability in the younger subgroup and males. We also observed that the correlated environmental influence had a greater effect on the three phenotypes, especially WC and WHtR, than the rearing environment. Future studies should aim to determine which correlated environmental factors influence obesity and to what extent.

Conflict of interest Bin Zhou, Wenjing Gao, Jun Lv, Canqing Yu, Shengfeng Wang, Chunxiao Liao, Zengchang Pang, Liming Cong, Zhong Dong, Fan Wu, Hua Wang, Xianping Wu, Guohong Jiang, Xiaojie Wang, Binyou Wang, Weihua Cao and Liming Li declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. The study has passed the ethical review of Peking University Biomedical Ethics Committee (IRB00001052-11029). Written informed consent was obtained from all the participants in the study.

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