Effects of Chorion Type on Genetic and Environmental Influences on Height, Weight, and Body Mass Index in South Korean Young Twins

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The present study examined the effects of chorionicity of twins on variations of height, weight, and body mass index (BMI) during childhood in the classical twin design. Mothers of 81 pairs of monochorionic monozygotic (MCMZ), 47 pairs of dichorionic monozygotic (DCMZ), and 457 pairs of dizygotic (DZ) twins drawn from the South Korean Twin Registry reported their children's height and weight. Twins' age ranged from 1.9 to 8.7 yrs, with a mean of 4.0 yrs and SD of 1.7 yrs. We computed maximum likelihood twin correlations and performed model-fitting analyses. In correlational and model-fitting analyses, we treated age and sex as covariates to control their main effects. Maximum likelihood MCMZ, DCMZ, and DZ twin correlations were, respectively, .96, .92, and .74, for height, .88, .91, and .57 for weight, and .93, .92, and .61 for BMI. The pattern of these twin correlations suggested very modest chorion effects on body measures. Model-fitting analyses confirmed the observations from twin correlations. Whereas genetic and shared environmental influences were significant for all three body measures, chorion effects attained statistical significance only for height (4%), and those for weight and BMI were zero. These findings indicate that genetic and environmental estimates for height, weight, and BMI during childhood are biased little by the chorion type of MZ twins, supporting the validity of the equal prenatal environment assumption in the classical twin design.

The classical twin method compares similarities between monozygotic (MZ) and dizygotic (DZ) twins. One of the crucial assumptions of the classical twin design is that MZ and DZ twins experience similar degrees of prenatal environment. Due to the variation in placental anatomy, however, MZ and DZ twins experience different environments during the prenatal period, and if these substantially influence the trait under study, the classical twin study will yield biased estimates of genetic and environmental factors.

As the zygotes of DZ twins implant individually in the uterus, each embryo develops its own placenta and chorion. Unlike DZ twins, MZ twins vary in their placentation, according to the timing of division of the inner cell mass. If MZ twins are divided at, or before, the morula stage, that is, around the fourth day of gestation, then each twin will develop an individual chorion and amnion like DZ twins. These twins are known as dichorionic MZ (DCMZ) twins. If the division occurs between the fourth and the seventh day of the gestation, then these twins will share a common chorion, known as monochorionic MZ (MCMZ) twins. Finally, if the division takes place after the eighth day, then the two fetuses will share a common amnion as well as a common chorion. These twins are called monochorionic monoamnionic (MCMA) MZ twins.

Approximately a third of MZ twins are DCMZ and two thirds are MCMZ. Only 2% to 3% of the MZ twins are MCMA twins (Bulmer, 1970). The sharing of a chorion and a placenta, and the presence of vascular anastomoses between the circulations of the two fetuses allow exchange of blood, hormones, oxygen, and other substances like alcohol and viruses between both members of the twin pair (Machin et al., 1996). For this reason, MCMZ twins may resemble each other more than DCMZ twins in postnatal development. Critics of twin studies argue that MCMZ twins should be removed from twin analyses to minimize biases in estimation of heritability (Phillips, 1993).

In twin studies of chorion effect, so far, more attention has been given to personality and cognitive abilities than to other traits, perhaps because some of personality traits and cognitive abilities have been shown to be related to hormonal influences

Received 19 November, 2007; accepted 30 November, 2007.

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https://doi.org/10.1375/twin.11.1.63 Published online by Cambridge University Press

(Davis et al., 2007; Falter et al., 2006). Unfortunately, however, twin studies of cognitive abilities and personality that have investigated chorion effects have produced mixed results. For example, whereas Melnick et al. (1978) and Jacobs et al. (2001) found greater similarities for MCMZ than DCMZ twins on measures of cognitive abilities, Sokol et al. (1995) found no significant differences between the two types of MZ twins. Similarly, in a study of neonatal temperaments using MZ twins of known chorion type, Riese (1999) found that chorion type was not related to co-twin similarity on any of the temperament ratings. In contrast, Sokol et al. (1995) reported that MCMZ twins resembled significantly more than DCMZ twins on several personality traits. Using relatively large samples, two recent studies investigated chorion effects on childhood problem behaviors (Wichers et al., 2002) and prosocial behavior (Hur, 2007). Both studies reported null effects, however. These discrepant results on the effects of chorion on psychological traits, especially cognitive abilities and personality traits may be in part because prior studies often suffered from small samples and used twins of different ages. Also, differences in measures of personality and cognitive abilities, and inaccuracy in diagnosis of twins' chorionicity may be responsible for inconsistent findings. Further studies using large samples are necessary to determine whether and how much chorionicity influences postnatal psychological development.

In the physical domain, significant effects of chorionicity have been reported in dermatoglyphic patterns (Reed et al., 1997), brain morphology (Reed et al., 2002), and tooth size (Burris & Harris, 2002; Race et al., 2006), but not in blood pressure (Fagard et al., 2003) or handedness (Derom et al., 1996). Because studies of chorion effects on physical traits are generally lacking, the results of these studies need to be replicated in future to draw firm conclusions.

Although the effect of chorion in various physical and psychological traits is still controversial, several twin studies of birthweight have consistently shown MCMZ twin correlations to be lower than DCMZ twin correlations (Race et al., 2006; Vlietinck et al., 1989). These results suggest that sharing a chorion may result in competition for nutrients, leading to lower MCMZ twin correlations for birthweight. An extreme form of vascular competition is twin to twin transfusion syndrome, where arterial flow from one twin empties into the vascular system of the co-twin, and the balance is not re-established due to the absence or the small size of the large anastomoses (Blickstein, 1990).

While an effect of chorionicity on birthweight has been well established, to our knowledge, only two studies have so far examined the effects of chorion on postnatal body size. Gutknecht et al. (1999) examined height, weight, and BMI among adolescent MZ twins (10 to 16 years), and found that MCMZ twin correlations for three body measures were lower than DCMZ twin correlations. From these results, the authors concluded that chorion effects on fetal growth might continue to adolescence. On the contrary, in a sample of adult MZ and DZ twins (18 to 34 years), Loos et al. (2001) found the MZMC and DCMZ correlations for height, BMI, and body fat measures to be nearly identical, although lower MCMZ than DCMZ twin correlations for birthweight were replicated in their sample. The Loos et al. (2001) study suggests that the chorion effect on body size diminishes with age. One could reconcile the contradictory findings of the Gutknecht et al. and Loos et al. studies such that, although the chorion effect on body size prevails during adolescence it disappears in adulthood. However, while the Loos et al. study examined 113 DCMZ and 138 MCMZ twin pairs, the Gutknecht et al. study was based only on 16 pairs of MCMZ and 22 pairs of DCMZ twins. Accordingly the Gutknecht et al. study had very limited statistical power, so the results should be viewed with skepticism, and need to be replicated in a larger sample.

In summary, a review of previous studies suggests that prenatal chorion effects may be largely trait specific, pointing to a need for further studies using large samples. The goal of the present study was to assess the impact of chorion type on twin resemblance for height, weight, and BMI in childhood in a relatively large sample of South Korean young twins.

Materials and Methods

Sample and Measures

Our sample was drawn from the South Korean Twin Registry (SKTR), a nationwide volunteer twin registry that includes twins from infants to adults (Hur et al., 2006). The SKTR contained the chorion type information and contact addresses of twins born in two large maternity hospitals between 1998 and 2004. As part of an SKTR telephone interview conducted in 2006 and 2007, mothers of twins born in the maternity hospitals were asked to report their twin children's current height and weight. BMI was calculated as weight in kg divided by the square of height in meters (kg/m^2). Mothers of the twins were predominantly from middle class families. In general, mothers were more confident about their twins' weight than their twins' height. Consequently, the sample size varied across measures (see Table 1).

Chorion type was diagnosed in the pathology labs of the maternity hospitals according to their routine procedures. A section of the membranous septum of the placenta of the same-sex twins at delivery was submitted for histologic examination. The section was processed with a routine Hemtoxylin-Eosin stain and examined for the number of amnia and choria present under a light microscope. If microscopic examination revealed two layers of amnion and one chorionic layer, then it was diagnosed as a monochorionic placenta. If there were two layers of amnion and chorion, it was diagnosed as a dichorionic placenta. Opposite-sex twins were classified as dichorionic without an examination.

https://doi.org/10.1375/twin.11.1.63 Published online by Cambridge University Press

Table 1
Means and Variances for Height, Weight, and BMI for MCMZ, DCMZ, and DZ Twins by Birth Order

Measure		MCMZ[1]		DCMZ		DZ	
		1st-born	2nd -born	1st -born	2nd -born	1st -born	2nd-born
Height (cm)	*N*	65	65	41	41	379	379
	Mean	102.8	102.9	103.2	103.5	102.5	102.2
	Variance	115.6	118.3	171.1	170.1	114.4	119.9
Weight (kg)	*N*	81	81	47	47	459	459
	Mean	16.2	15.9	16.8	16.7	16.5	16.3
	Variance	11.5	15.6	24.9	24.8	16.3	20.3
BMI (kg/m2)	*N*	64	64	41	41	374	374
	Mean	15.4	15.2	15.6	15.4	15.5	15.5
	Variance	4.1	4.1	2.5	2.6	2.5	2.6

Note: [1] Includes two pairs of monoamnionic twins. MCMZ = monochorionic monozygotic twins, DCMZ = dichorionic monozygotic twins. DZ = dizygotic twins.

Zygosity was determined from chorionicity of the twins and from mothers' responses to a questionnaire about physical similarities and frequency of confusion by family members. In order to minimize misclassification of zygosity in the present sample, 14 pairs were excluded from data analyses because their zygosity was ambiguous. The final sample comprised 81 pairs of MCMZ twins (30 male and 51 female pairs),[1] 47 pairs of DCMZ twins (25 male and 22 female pairs), and 459 pairs of DZ twins (115 male, 117 female, and 227 opposite-sex pairs). The twins ranged in age from 1.9 to 8.7 years, with a mean of 4.0 years, and a *SD* of 1.7 years. The ratio of MCMZ to DCMZ twins in the present sample was generally consistent with the expected ratio (i.e, approximately 66% vs. 32%) in the MZ twin population. However, females were somewhat over represented in the MCMZ twin group. The higher number of DZ than MZ pairs in the present sample is due to the number of assisted pregnancies (Hur & Kwon, 2005).

Statistical Analyses

To examine effects of the chorion on height, weight, and BMI in twins, maximum likelihood estimates of correlations for the three body measures were computed for the three types of twins, and a structural equation model incorporating chorion effects (Figure 1) was fitted to the twin data. We used the raw data option in Mx (Neale et al., 2003) to perform correlational and model-fitting analyses. Prior to correlational and model-fitting analyses, means and variances for height, weight, and BMI were compared across three types of twins, and across the first-born and the second-born twins. We used Mx for these comparisons. Main effects of age and sex were also examined.

The full model employed in the present study includes additive genetic (A), shared environmental (C), and nonshared environmental (E) factors, and a chorion effect. Measurement error is confounded with the E factors. The A factors, the sum of the average effect of all genes that influence a trait, correlate at 1.0 for both types of MZ twins, and at .5 for DZ twins. The C factors correlate at 1.0 for both MZ and DZ twins, because the twins in the present sample were raised together in the same home. The chorion effect correlates at 1.0 for MC twins, and at 0 for DC twins. Finally, the E factors, environmental factors that are unique to each member of a twin pair, and measurement error, do not contribute to twin similarity and are therefore depicted in the path diagram as residual arrows for each twin. The parameterization of this model is explained in detail in Prescott et al. (1999).

The raw data option in Mx calculates twice the negative log-likelihood (–2LL) of the data. If the models are nested, the difference in –2LL between the nested models is chi-square distributed, which permits evaluation of alternative models. To select the best-fitting model, the fit of the full model in Figure 1 was first compared to that of a saturated model. Next, the fit of the full model was compared to the fit of a series of reduced models, where the parameters of the chorion effects, additive genetic factors, and shared environment factors were respectively constrained to be zero. A significant difference in chi-square between the full and reduced model indicates a significant influence from the constrained parameter, indicating that the reduction of the model is not acceptable. In contrast, a nonsignificant change in chi-square between the full and reduced model suggests a nonsignificant influence from the constrained parameter, suggesting that the parameter needs to be eliminated from the full model to achieve parsimony of the model.

Results

Descriptive Statistics

Table 1 presents means and variances for height, weight, and BMI for MCMZ, DCMZ, and DZ twins by birth order. Means and variances were not

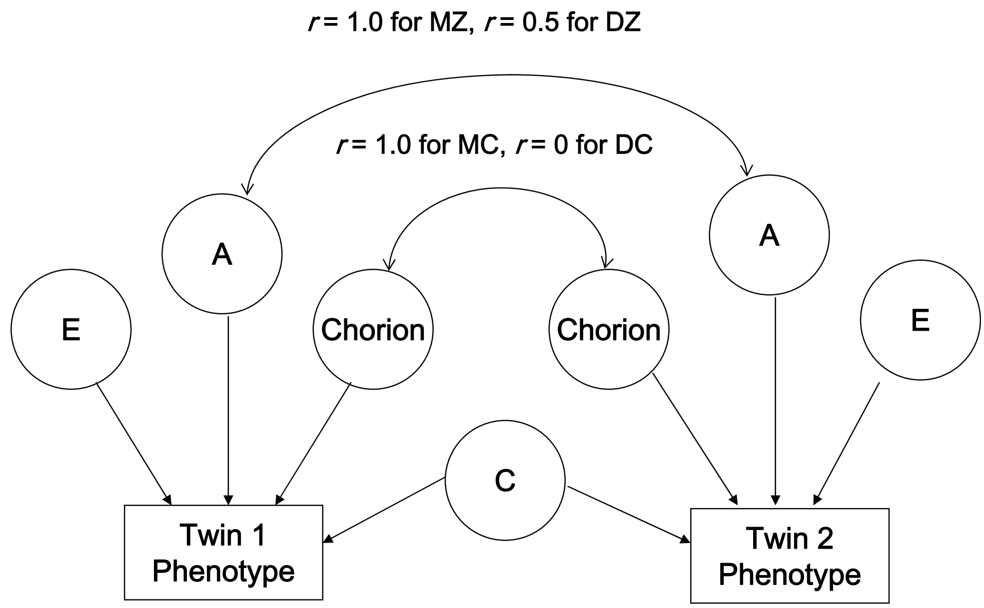

Figure 1

Twin model incorporating chorion effects.

Note: A = additive genetic factors, C = shared environmental factors, E = nonshared environmental factors including measurement error. MZ = monozygotic twins, DZ = dizygotic twins. MC = monochorionic twins, DC = dichorionic twins.

significantly different across the three types of twins for any of the three body measures. The first-born twins were not significantly different from the second-born twins for the mean levels of height, weight, and BMI, indicating no birth order effects on means. Variances were not significantly different between the first- and the second-born twins in all three types of twins for height and BMI. For weight, although the variances between the first- and the second-born twins were not significantly different in MCMZ or in DCMZ twins, the variance of the second-born twins was significantly higher than that of the first-born twins in DZ twins.

In the present sample of children, age was significantly associated with height (r = .88), and weight (r = .80), but not with BMI (r = –.01). Males were slightly, but significantly taller and weighed more than females (103.1 vs. 102.0 for height and 16.6 vs. 16.2 for weight). BMI was also slightly, but significantly higher in males than in females (15.6 vs. 15.3). In correlational and model-fitting analyses, therefore, sex and age were treated as covariates to control their main effects.

Among the three body measures, the distribution of weight was significantly skewed (skewness = 1.7), and kurtotic (kurtosis = 4.8). Weight was therefore log-transformed to obtain approximate normality.

Twin Correlations

Table 2 provides maximum likelihood correlations for height, weight, and BMI for MCMZ, DCMZ, and DZ twins. For weight and BMI, MCMZ twin correlations were not significantly different from DCMZ twin correlations. For height, however, the difference between the two types of MZ twin correlations was statistically significant.

As expected, both types of MZ correlations were significantly greater than DZ twin correlations for all three measures, suggesting significant genetic influences on body measures in childhood. The importance of shared environmental influences was also evident, as DZ twin correlations were generally higher than half the MZ twin correlations for all three body measures. Taken together, these results suggest that genetic and shared environmental influences on height, weight, and BMI are significant, while the effects of chorion are negligible except for height.

Model-Fitting

Table 3 summarizes the results of model-fitting analyses. The differences in chi-square between the saturated and full models were not significant for height or BMI, and marginally significant for weight, suggesting that the full model incorporating

Table 2

Maximum Likelihood Correlations for Height, Weight, and BMI and their 95% Confidence Intervals for MCMZ, DCMZ, and DZ Twins

	MCMZ	DCMZ	DZ
Height	.96 (.94–.98)	.92 (.86–.96)	.74 (.69–.78)
Weight	.88 (.83–.92)	.91 (.85–.95)	.57 (.51–.63)
BMI	.93 (.89–.96)	.92 (.85–.95)	.61 (.54–.67)

Note: MCMZ = monochorionic monozygotic twins, DCMZ = dichorionic monozygotic twins.
DZ = dizygotic twins. Age and sex were treated as covariates in correlational analyses.

Table 3

Model-Fitting Results for Height, Weight, and BMI[a]

Model Description	Height					Weight					BMI				
	–2LL	*df*	$\varnothing\chi^2$	$\varnothing$ *df*	*p*	–2LL	*df*	$\varnothing\chi^2$	$\varnothing$ *df*	*p*	–2LL	*df*	$\varnothing\chi^2$	$\varnothing$ *df*	*p*
Saturated	5382.2	953				7053.7	1157				3298.0	941			
Full	**5389.3**	**963**	**7.1**	**10**	**.95**	7072.2	1167	18.5	10	.05	3312.7	951	14.7	10	.15
Drop A	5404.5	964	15.2	1	.00	7103.6	1168	31.4	1	.00	3340.3	952	27.6	1	.00
Drop C	5472.8	964	83.5	1	.00	7087.5	1168	15.3	1	.00	3335.8	952	23.1	1	.00
Drop chorion	5395.5	964	6.2	1	.01	**7072.2**	**1168**	**0**	**1**	**.99**	**3312.8**	**952**	**0.1**	**1**	**.99**

Note: [a] Sex and age were treated as covariates in the model. A = additive genetic factors, C = shared environmental factors, E = nonshared environmental factors including measurement error. LL = log-likelihood.
Goodness-of-fit statistics for the best-fitting models are in bold .

the chorion parameter is acceptable for all three body measures.

When the additive genetic (A) or shared environment parameter (C) was removed from the full model, significant changes in chi-square occurred for all three body measures. These results indicate that both genetic and shared environmental influences are important for variations of height, weight, and BMI in childhood. Finally, we eliminated the chorion parameter from the full model. A significant difference in chi-square occurred for height. In contrast, the differences in chi-square were not significant for weight and BMI. From these results, we chose the full model as the best-fitting one for height, and the model without a chorion effect as the best-fit for weight and BMI. These model-fitting results were consistent with the observations made from twin correlations.

The genetic and shared and nonshared environmental parameter estimates and their 95% confidence intervals are presented in Table 4. Additive genetic influences were 32% for height, 61% for weight, and 55% for BMI, and shared environmental influences for the corresponding body measures were 59%, 27%, and 35%, respectively. Nonshared environmental influences including measurement error were small: 5% for height, 12% for weight, and 10% for BMI. The chorion effect was significant only for height, which was 4%. Taken together, the model-fitting results suggested that chorion effects on variations of height, weight, and BMI during childhood were either nonsignificant or very modest when the effects attained statistical significance.

Table 4

Parameter Estimates (%) and Their 95% Confidence Intervals in the Best-Fitting Models

Measure	A	C	E	Chorion
Height	32 (20–43)	59 (50–68)	5 (3–7)	4 (1–10)
Weight	61 (49–74)	27 (14–38)	12 (9–16)	—
BMI	55 (43–68)	35 (22–47)	10 (8–13)	—

Note: — was fixed to be zero
A = additive genetic factors, C = shared environmental factors,
E = nonshared environmental factors including measurement error

Discussion

Recently there has been an increasing interest in prenatal influences on postnatal physical and psychological development. The present study demonstrates that prenatal environment associated with chorionicity does not significantly affect height, weight, and BMI during childhood, supporting the validity of the equal prenatal environment assumption of the classical twin design. Except for height, MCMZ and DCMZ twin correlations for body measures were extremely similar to each other. In the model-fitting analyses, the chorion effect explained only 4% of the total variation in height, whereas the effect was near zero for weight and BMI. The best-fitting models indicated that additive genetic influences ranged from 32% to 61% across three body measures, whereas shared environmental influences ranged from 27% to 59%. The estimates of genetic and environmental influences on weight and BMI found from our sample were generally similar to those found in western twin samples. However, the estimate of genetic factors for height was somewhat lower, while the estimate of shared environment was somewhat higher than those estimates reported by others (Dubois et al., 2007; Koeppen-Schomerus, et al., 2001, Silventionen et al., 2007; Wilson, 1976). Consistent with western populations (Spuhler, 1982), assortative mating for height in the South Korean population has been reported to be low (Hur, 2003). Therefore, at least assortative mating does not seem to be responsible for the high estimate of shared environmental influences on height found in the present sample. As mentioned below, to determine whether our findings on height reflect the characteristics of the middle class South Korean population, or a sampling error, a replication of the present results with clinical measures is necessary.

The fetal programming hypothesis suggests that impaired intrauterine growth and development have

https://doi.org/10.1375/twin.11.1.63 Published online by Cambridge University Press

long-lasting impacts on health (Barker, 1998), although whether this hypothesis can be applied to the twin situation is still controversial (Duffy, 1993; Leslie & Pyke, 1993; Phillips, et al., 2001). Consistent with other studies (Minakami et al., 1999), we found that birthweight for MCMZ twins in the present sample was significantly lower than that for DCMZ or DZ twins (MCMZ < DCMZ < DZ; Hur & Shin, ms in preparation). However, the means of current height, weight, and BMI were not significantly different across MCMZ, DCMZ, and DZ twins (Table 1). These results indicate that the adverse prenatal environment of MZ twins, especially that of MCMZ twins, may not have an enduring influence, as long as twins are raised in normal environments. Although whether body size of our MZ twins is lower than that of singletons is not known, the catch up growth in MZ twins, especially in MCMZ twins, must have occurred early in postnatal life. Also, genetic factors in physical growth that emerged in childhood are likely to have reduced the intrapair differences in body measures in the MCMZ twins observed in the present study.

The results of the present study are not compatible with those of the Gutknecht et al. study (1999), but support the findings from the Loos et al. (2001) study mentioned earlier. One could argue that mothers of MCMZ twins in the present sample may have reported their twins' height, weight, and BMI to be more similar than they really were. This bias can result in smaller variances of the body measures in MCMZ twins than in DCMZ or DZ twins. However, the variances of height, weight, and BMI for MCMZ twins were not significantly different from, or uniformly smaller, than those for DCMZ or DZ twins, suggesting that maternal reporting bias may be minimal in the present sample.

Some limitations of the present study need to be addressed. First, twins' height and weight were reported by mothers rather than measured. Although they are more prone to error than clinical measures, maternal reports of height and weight are of great utility for epidemiological studies using children. One should note that measurement error would increase nonshared environmental influences in the present study. However, the estimates of nonshared environmental influences on body measures in the present study fell between 5% and 12%, which were fairly small. Taken together, these results suggest that maternal reports of height and weight in the present sample may be quite reliable. Secondly, the present sample may not be a representative sample of the South Korean population. As mentioned earlier, the present sample was drawn from two large maternity hospitals, in Seoul and in a city near Seoul, and twins were from predominantly middle class families. Thus, caution is necessary when the results of the present study are generalized to other populations.

Acknowledgment

The present study was conducted with the financial support of the Pioneer Fund, United States, which was awarded to the first author. The authors wish to thank the twins and their mothers for their participation in the study.

Endnote

1 Two pairs of MCMA twins were included.

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