Behavior Genetics, Vol. 27, No. 4, 1997

Genetic and Environmental Factors in Relative Body Weight and Human Adiposity

Hermine H. M. Maes,[1,2] Michael C. Neale,[1] and Lindon J. Eaves[1]

We review the literature on the familial resemblance of body mass index (BMI) and other adiposity measures and find strikingly convergent results for a variety of relationships. Results from twin studies suggest that genetic factors explain 50 to 90% of the variance in BMI. Family studies generally report estimates of parent–offspring and sibling correlations in agreement with heritabilities of 20 to 80%. Data from adoption studies are consistent with genetic factors accounting for 20 to 60% of the variation in BMI. Based on data from more than 25,000 twin pairs and 50,000 biological and adoptive family members, the weighted mean correlations are .74 for MZ twins, .32 for DZ twins, .25 for siblings, .19 for parent–offspring pairs, .06 for adoptive relatives, and .12 for spouses. Advantages and disadvantages of twin, family, and adoption studies are reviewed. Data from the Virginia 30,000, including twins and their parents, siblings, spouses, and children, were analyzed using a structural equation model (Stealth) which estimates additive and dominance genetic variance, cultural transmission, assortative mating, nonparental shared environment, and special twin and MZ twin environmental variance. Genetic factors explained 67% of the variance in males and females, of which half is due to dominance. A small proportion of the genetic variance was attributed to the consequences of assortative mating. The remainder of the variance is accounted for by unique environmental factors, of which 7% is correlated across twins. No evidence was found for a special MZ twin environment, thereby supporting the equal environment assumption. These results are consistent with other studies in suggesting that genetic factors play a significant role in the causes of individual differences in relative body weight and human adiposity.

KEY WORDS: Human adiposity; body mass index; body weight; genetic factors; environmental factors; heritability; twin studies; family studies; adoption studies; review.

INTRODUCTION

The genetics of obesity has been the topic of at least eleven reviews in the last decade (Price, 1987; Bouchard and Pérusse, 1988, 1993, 1994; Stunkard, 1991; Grilo and Pogue-Geile, 1991; Meyer and Stunkard, 1993, 1994; Sorensen and Stunkard, 1994; Sorensen, 1995; Meyer, 1995). The focus of these reviews was usually on a particular type of study, be it adoption, twin, or family study. In recent years the growing body of work on the search for obesity genes has lead to reviewing findings from linkage and association studies (Bouchard, 1995). The shift of the focus of research in obesity is based in part on the increasingly widespread understanding that genetic factors play a significant role in the variation of body fatness. However, the agreement on "just how much of the variation is explained by genetic factors" is not great. The agreement within type of study is larger than between study type, and, results from twin studies

[1] Virginia Institute for Psychiatric and Behavioral Genetics, Box 980003, Richmond, Virginia 23298.
[2] To whom correspondence should be addressed. Fax: (804) 828 8801. E-mail: hmaes@gems.vcu.edu.

0001-8244/97/0700-0325$12.50

tend to indicate a higher heritability for body fatness than do adoption and family studies. Few reports have incorporated relatives of different types in an attempt to integrate results from different studies. In this paper we

(i) summarize findings from different types of studies on the genetics of obesity,
(ii) evaluate these findings in light of the assumptions of various designs,
(iii) test with results from an extended pedigree design, and
(iv) highlight special issues.

The most widely used measure for obesity is the body mass index (BMI), measured as weight (kg) divided by height^2 (m). Skinfold measurements have been used in selected studies. Only one study has obtained more direct estimates of body fatness with underwater weighing on a large sample of family members (Bouchard and Pérusse, 1988). The focus of this review is on BMI.

REVIEW OF STUDIES

Twin Studies

The twin design has been extensively used to study the genetics of obesity. Most twin studies have found evidence for the genetic factors on obesity. Reported heritabilities vary mostly between .50 and .90 (see Table I for review). Estimates from twin samples from adolescents tend to be higher than those from adults.

BMI in Adolescent Twin Samples

Relatively few studies have focused on adolescent twins (Allison *et al.*, 1994; Bodurtha *et al.*, 1990; Wang *et al.*, 1990; Maes, 1992; Beunen *et al.*, 1996; Meyer *et al.*, 1996, 1997). The largest study is the MCV Twin Study (Bodurtha *et al.*, 1990; Meyer *et al.*, 1996). In this longitudinal project, approximately 500 white and black twin pairs were ascertained through the schools in Virginia and invited to participate in a range of cardiovascular evaluations, including an anthropometric assessment. Twins were first measured either at 11, and followed up every 18 months through the age of 17, or at 9.5, and followed up through age 14. Genetic model fitting of BMI at age 11 (Bodurtha *et al.*, 1990) and later ages (Meyer *et al.*, 1997) showed high heritabilities (.87) for Caucasian pairs. Similar estimates for heritability of BMI were reported by Allison *et al.* (1994) for 112 white and 126 black twin pairs between 12 and 18 years of age from Georgia, Kentucky, and Indiana, although both genetic and environmental influences exerted a greater influence on BMI of black than white adolescents. The Leuven Longitudinal Twin Study (LLTS) (Maes, 1992; Beunen *et al.*, 1996) is a similar project in which 105 twin pairs were ascertained from the East Flanders Prospective Twin Study. Twins first participated at age 10 and were followed up every 6 months through the age of 16. The estimated heritability was between .89 and .92 at age 10 (Maes, 1992) up to age 14 (Beunen *et al.*, 1996). A study (Wang *et al.*, 1990) on 7- to 12-year-old Chinese twins reported correlations consistent with a heritability of .90. Height and weight were also measured for 1412 twin pairs from the Virginia Twin Study of Adolescent Behavioral Development (VTSABD) (Meyer *et al.*, 1996). Heritability estimates increased from .67 for 8- to 10-year-old twins, to .88 for 11- to 13-year-old twins, to .93 for 14- to 16-year-old twins.

Skinfolds in Adolescent Twin Samples

Two adolescent twin studies have obtained skinfold measurements as adiposity indicators (Brook *et al.*, 1975; Borjeson, 1976). Triceps and subscapular skinfolds were obtained from 222 like-sex twins aged 3 to 15 (Brook *et al.*, 1975). Classical heritability estimates [$2(r_{MZ} - r_{DZ})$] obtained from MZ and DZ correlations were .98 for trunk fat and .46 for limb fat. Borjeson (1976) selected 101 7-year-old Swedish twin pairs on the basis of their height and weight and calculated intrapair mean differences for triceps, subscapular, and abdominal skinfolds. For all measures, greater similarity was found for MZ than for DZ twins, supporting a genetic variability in adiposity. Skinfold measures were also obtained in the MCV and LLTS twin samples (Bodurtha *et al.*, 1990; Maes, 1992; Beunen *et al.*, 1996). Results from these studies provided more evidence for a strong genetic component to fatness in adolescence.

BMI in Adult Twin Samples

Data from adult samples are abundant. Height and weight data have been collected on over 20,000 twin pairs, aged 18 or older. Regardless of sample, age and sex of the twins MZ twin pairs are consis-

Table I. Review of Twin Studies on Obesity[a]

Author	Year	Sample	Size[b]	Method		Age (yr)	mz	dz	h^2	
Feinlieb *et al.*	77	NAS–NRC	514	Falconer	T	Induction	.71	.39	.64	
Fabsitz *et al.*	80	NAS–NRC	1,028	Falconer	T	Induction	.83	.43	.80	$r_g = .60$
						25	.62	.29	.67	$r_g = .71$
						40–50	.66	.41	.51	
						42–56	.71	.42	.57	
Stunkard *et al.*	86	NAS–NRC	4,071	Falconer	T	Induction	.81	.42	.77	$r_g = .69$
						25	.66	.24	.84	
Bouchard *et al.*	87	Quebec	156	Beta model		0+	.88	.34	.10	
Austin *et al.*	87	Kaiser Permanente California	434	Falconer	T	Ad F			.89	
						Envir vars			.63	
Hunt *et al.*	89	Utah	154	Falconer	T	26+	.68	.41	.54	$c^2 = .14$
						Envir vars	.68	.43	.51	$c^2 = .18$
Bodurtha *et al.*	90	Virginia	259	LISREL	T	11	.84	.44	.87	
Wang *et al.*	90	China	110	Christian	T	7–12	.90	.51		
Stunkard *et al.*	90	SATSA	311	LISREL	A	M	.70	.15	.70[c]	
						F	.66	.25	.66[c]	
			362		T	M	.74	.33	.74	$d^2 = .57$
						F	.66	.27	.69	$d^2 = .37$
Macdonald & Stunkard	90	Britain	45	Corr	A	F	.39	.25		
						M	.64			
			39		T	F	.76			
						M	.68			
Turula *et al.*	90	Finnish TR	7,730	LISREL	T	Ad, −55				
						M			.72	
						F			.66	
Price & Gottesman	91	Britain	34	MZA	A				.61	
			38		T				.75	
Hewitt *et al.*	91	Birmingham, UK	80	LISREL	T	16–24	.85	.54	.87	
Selby *et al.*	91	NAS–NRC	513	Christian Falconer	T	Induction	.91	.52	.68	
						25	.87	.47	.58	
						40–50	.83	.50	.81	
			267			42–56	.80	.47	.63	
Tambs *et al.*	91	Norway	169 + rel	SAS NLIN	T	19+	.58	.20	.39	d^2
									$s^2 = .08$	
									$c^2 = .02$	
									$r^2 = .03$	
Korkeila *et al.*	91	Finland	7,245	LISREL		18–24				
						M	.77	.41	.72	
						F	.72	.33	.71	
						25–34				
						M	.70	.39	.74	
						F	.70	.39	.69	
						35–44				
						M	.64	.33	.67	
						F	.73	.30	.68	
						45–54				
						M	.59	.29	.67	
						F	.56	.20	.53	
						Total				
						M	.70	.38	.72	
						F	.68	.31	.68	
Fabsitz *et al.*	92	NAS–NRC	243	LISREL	T	Induction	.80	.42	.82	2G's
						25	.73	.44	.78	
						40–50	.72	.35	.73	
						42–56	.69	.35	.73	
Martin; In Neale & Cardon	92	Australia NH&MRC	3,569	LISREL	T	18–30				
						M	.77	.32	.80	$d^2 = .44$
						F	.78	.30	.78	$d^2 = .38$
						MF		.23		
						31 +		.37		
						M	.70	.32	.70	
						F	.69	.24	.69	
						MF				

Table 1. Continued

Author	Year	Sample	Size[b]	Method		Age (yr)	mz	dz	h^2	
Meyer; in Neale & Cardon	92	VA 30,000 Virginia TR AARP	5,588	LISREL	T	Ad				
						M	.70	.31	.72	d^2 = .37
						F	.74	.35	.75	
						MF		.25		
Maes	92	Belgium	105	Mx	T	10				
						M	.87	.60	.89	
						F	.90	.26		
						MF		.49		
Allison *et al.*	94	Georgia, Kentucky, Indiana	496	LISREL, Mx	T	b				
						M	.85	.79	.93	
						F	.93	.54		
						MF		−.19		
						w				
						M	.89	.67	.91	
						F	.87	.31		
						MF		.11		
Korkeila *et al.*	95	Finland	5,967	LISREL	T	18–54				
						M	.65	.34	.67	r_g = .97
						F	.65	.27	.64	r_g = .98
						24–60				
						M	.62	.31	.61	d^2
						F	.68	.28	.67	
Harris *et al.*	95	Norway	2,570	LISREL	T	8–25	.70	.36	.71	r_g = .62
							79	.36	.79	
								.23		
Carmichael & McGue	95	Minneosta	610	LISREL	T	18–38	.83	.29	.82	
		MTR	282			39–59	.60	.33	.70	
		MTSADA	141			60–81	.63	.22	.63	
Herskind *et al.*	96	Denmark	1,233	Mx	T	46–59				
						M	.53	.20	.46	
						F	.78	.34	.77	
						60–76				
						M	.51	.33	.61	
						F	.74	.41	.75	
Allison *et al.*	96	Finland	17	Regression	A	Ad			r_p = .50	
		Japan	10		A	47–87			r_{sp} = .70	
		Archival	26		A	Ad				
Beunen *et al.*	96	Belgium LLTS	105	Mx	T	10	.90	.52	.89	
						11	.90	.55	.92	
						12	.88	.52	.91	
						13	.91	.55	.92	
						14	.88	.51	.90	
Meyer *et al.*	96	Virginia MCV Twin Study	311w 81b	Mx	T	11			M F	M r_g = .83–.97
						12.5			.89 .89	F r_g = .85–.97
						14			.91 .89	
						15.5			.88 .91	
						17			.93 .90	
									.90 .91	
Meyer *et al.*	96	Virginia ABD	1,412	Mx	T	8–10	.71	.36	.67	r_g = .91
						11–13	.88	.51	.88	r_g = .89
						14–16	.93	.46	.93	

[a] mz, MZ correlation; dz, DZ correlation; h^2, heritability; r_g, genetic correlation; d^2, dominance; T, reared together; A, reared apart; Ad, adult; w, white; b, black; M, male; F, female; Envir vars, environmental variables; Rel, relatives; s^2, sibling environment; c^2, cultural transmission; r^2, GE covariance; r_p, partial correlation; r_{sp}, semipartial correlation.

[b] Number of twin pairs.

[c] Direct estimate from MZAs.

tently more similar in BMI than are DZ twin pairs. One of the largest and most published data sets is the National Academy of Sciences–National Research Council (NAS-NRC) sample. Twin pairs for this registry were ascertained through the Veterans Administration and all had prior military service. Height and weight measurements were available from induction (mean age, 20) to the military service (N = 13,376) and from three follow-up examinations with mean ages of 48 (N = 514), 59 (N = 362), and 65 (N = 267). BMI was also calculated from 25-year follow-up questionnaire data on 4071 pairs. Heritability estimates of BMI at induction vary between .64 and .82 based on various subsets of the sample (Feinlieb *et al.*, 1977; Fabsitz *et al.*, 1980, 1992; Stunkard *et al.*, 1986; Selby *et al.*, 1991). MZ twin correlations gradually decrease with age; the trend is less clear for the DZ correlations, leading to more variable heritability estimates (.51 to .84).

Scandinavian Samples

Among the larger twin studies with data on BMI are the Scandinavian. Results from the Finnish Twin Registry on approximately 7000 twin pairs showed that 53–74% of the total variance is explained by genetic factors (Turula *et al.*, 1990; Korkeila *et al.*, 1991, 1995). Heritability decreased with age in both genders and was significantly higher in males versus females. Higher heritabilities for males (.74) than females (.69) were also reported on 362 Swedish twins reared together from SATSA (Stunkard *et al.*, 1990). Different heritability estimates were obtained for males (.46–.61) and females (.75–.77) with data on 1233 twins from the Danish Twin Registry (Herskind *et al.*, 1996). Lower estimates of the genetic variance in males (.71) versus females (.79) were also found for 2570 18- to 25-year-old twins from the Norwegian Twin Panel, with a male–female correlation of .62 (Harris *et al.*, 1995). The study on BMI in first-degree relatives in Norway, which included 196 twin pairs (Tambs *et al.*, 1991), estimated the broad heritability at .39, the lower limit of estimates from twin studies.

The Australian and Virginian Samples

Data from two other large twin samples are discussed by Neale and Cardon (1992). The first is the Australian NH and Medical Research Council (NH&MRC) twin sample, which contains 3569 adult twin pairs. Heritability was estimated separately for a younger (age 18–30) and an older (30+) cohort. Consistent with results from the NAS–NRC sample, heritability was higher for the younger (.78–.80) than the older (.69–.70) twins. The second consists of 5580 twin pairs from the "Virginia 30,000" (Eaves *et al.*, 1996), which combines data from the Virginia Twin Registry and twins from the American Association for Retired Persons (AARP). According to the best-fitting model, genetic factors explained 72 and 75% of the variation in BMI in males and females, respectively.

Other Twin Samples

Several other twin studies have reported similar heritabilities. Consistent with other results on different age groups, estimates from 1033 Minnesota twin pairs (from the Minnesota Twin Study and MTSADA) decreased with increasing age from .82 to .63 (Carmichael and McGue, 1995). Data from Utah pedigrees including 154 twin pairs showed evidence for genetic factors contributing 51 to 54% of the variance (Hunt *et al.*, 1989). Overcorrection of the heritability estimate for environmental variables reduced the heritability from .89 to .73 for data on 434 adult female twins from the Kaiser Permanente Twin Registry in California (Austin *et al.*, 1987). Heritability was estimated at .87 from 80 British 16- to 24-year-old twins (Hewitt *et al.*, 1991).

Nonadditive Genetic Factors

Based on most large-scale Scandinavian twin studies (Stunkard *et al.*, 1990; Tambs *et al.*, 1991; Korkeila *et al.*, 1995) and the Australian and Virginian twin studies (Neale and Cardon, 1992), a significant proportion of the genetic variance is explained by nonadditive factors. Given that sample sizes of at least 1000 twin pairs are needed to detect dominance genetic variance accounting for 20% of the total variance in many circumstances (Martin *et al.*, 1978; Maes, unpublished data), the fact that only samples of this size or more showed evidence for dominance is expected. Shared environmental factors do not appear to contribute to the variation in BMI, except in one study in which they explain 14–18% of the variance (Hunt *et al.*, 1989). Since the sample sizes of several studies were large

enough to detect such effects, it is unlikely that environmental factors shared with family members contribute substantially to variance in BMI.

Twins Reared Apart

These findings of significant evidence for genetic factors on BMI were corroborated by the results of studies of twins reared apart (Stunkard *et al.*, 1990; Price and Gottesman, 1991; Allison *et al.*, 1996a) which report heritability estimates in the same range as those of twins reared together. The MZA correlation serves as a direct estimate of the heritability. MZA pairs (N = 311) from the SATSA sample correlate .66–.70 (Stunkard *et al.*, 1990). The MZA correlation for females (.39) was much lower than that for males (.64) for a small sample of 45 British twins (Macdonald and Stunkard, 1990). Another sample of 34 British twins reared apart showed a correlation of .61 (Price and Gottesman, 1991). The partial correlation—taking into account environmental covariates—between 53 MZAs combined from Finnish, Japanese, and archival data was .50 (Allison *et al.*, 1996a).

Longitudinal Studies

All but five studies to date have been cross sectional in nature and therefore do not allow us to test whether the same genetic factors account for heritability at different ages. Two longitudinal studies on adults have included estimates of the genetic correlation between different ages. In the NAS–NRC twin panel the estimates between young (age at induction) and middle adulthood (25-year follow-up) ranged from .60 to .71 (Fabsitz *et al.*, 1980; Stunkard *et al.*, 1986), and those between middle and late adulthood, from .93 to .96 (Fabsitz *et al.*, 1992). From a developmental analysis of the same sample, Fabsitz *et al.* (1992) found two independent genetic contributions to the variability in BMI: one at induction and one between age 20 and age 48. A much higher genetic correlation (.97–.98) was reported for a shorter time interval (6 years between two measurements) for the Finnish Twin Cohort (Korkeila *et al.*, 1995). Repeated measures were collected on three juvenile samples, the MCV Twin Study, the VTSABD, and the LLTS. Meyer *et al.* (1996) reported genetic correlations (r_g) between .83 and .97 for males and between .79 and .97 for females in the MCV Twin Study, indicating that, for the most part, the same genetic factors influence BMI from age 11 to age 17. Similar results were found for the VTSABD (r_g, between .86 and .88) (Meyer *et al.*, 1996) and the LLTS (r_g, between .78 and .98) (Maes, unpublished data).

Family Studies

Family studies have been very popular in the field of obesity. Any type of relationship between family members fall under this category. The most commonly studied are parent–offspring and sibling relationships (see Table II). Most studies report correlations; few estimate heritability. The majority of the family studies concluded that genetic factors contribute to variation in BMI.

The Quebec Family Study

One of the larger, and certainly most published, bodies of results of family studies are those of the Quebec Family Study (Bouchard *et al.*, 1987; Bouchard and Pérusse, 1994). Data were obtained from 1698 members of 409 families of French descent in Quebec. They comprised biological and adoptive relationships as well as twins. BMI and other fatness indicators were available for 1239 parent–offspring pairs, 370 full sibs, 348 spouse pairs, 322 parent-adopted child pairs, 120 siblings by adoption, 183 second-degree relatives, 69 DZ twins, and 87 MZ twins. The estimated correlations were .23 for parent–offspring, .26 for sibling, and .10 for spouse correlations. The beta model (Rice *et al.*, 1978) was used to analyze the data, which allows a common environment parameter that may differ for sibs, DZ, and MZ twins. The total transmissibility for BMI was .40; biological inheritance accounted for 10% of the variation in BMI. According to Table 3 of Bouchard *et al.* (1987), the nontransmissible variance was correlated .0 in siblings, .16 in DZ twins, and .96 in MZ twins.

The Canada Fitness Survey

A second large Canadian study including several family relationships is the Canada Fitness Survey. Pérusse *et al.* (1988) used the tau model (Rice *et al.*, 1978) to estimate transmissibility for BMI from 4825 spouse pairs, 8881 parent–offspring pairs, 3929 sibling pairs, and 128 second-degree relatives, totaling 18,073 subjects. The correlations for parent–offspring, siblings, and spouses were

Table II. Review of Family Studies on Obesity[a]

Author	Year	Sample	Size[b]	Method	Age (yr)	po	sib	sp	
Bayley	54	Berkeley	43f	Corr	0–21	fs, −.54–23 fd, −.16–32 ms, −.32–51 md, .07–.81			
Tanner & Israelsohn	63	London	117f	Corr	0–7	fs, .00–.15 fd, .30–.44 ms, −.09–.10 md, .03–.16		.17	
Mueller	78	Columbia	111	Corr	20–60 <7Δ >7Δ		 .51 .21		
Byard *et al.*	83	Ohio	523	Corr	0–18 30		bb, .20–.50 ss, .30–.55 bs, .15–.40		
Heller *et al.*	83	Framingham	7,948	Corr	20–49	fs, .27 fd, .23 ms, .23 md, .21	bb, .27–.29 ss, .24–.25 bs, .09–.29	.19	av, .05–.14
Khoury *et al.*	83	Cincinnati	877 125wp 52bp	Corr	w <20 >20 b <20 >20	pc .23–.29 .01–.11 .07–.08 .03–.37	 .35 .16 .39 .48	 .14 .20 	
Longini *et al.*	84	Tecumseh, MI	5,174	Corr model	6–19 20–74	fo, .27 mo, .25	.36 .17	.12	h^2 = .31–.37 co, −.04
Province & Rao	85	Brazil	6,750 1,076f	Tau model	0–30	.25 fo, .25 mo, .25	ss, .30	.15	
Zonta *et al.*	87	Italy	179f		bmi[c]	fo, .31 mo, .37	.36	.13	
Friedlander *et al.*	87	Jerusalem, ethnically diverse	4,203f	Corr	17+	.22 fs, .27 fd, .21 ms, .21 md, .17	.33 bb, .38 ss, .43 bs, .25	.08	
Bouchard *et al.*	87	Quebec	1,698 409f	Beta model	0–	.23	.26	.10	av, .14
Perusse *et al.*	88	Canada	18,073	Tau model	7–69	.20	.31	.12	av, −.11 gpc, .05
Byard *et al.*	89	Ohio	500	Corr	2–18	fs, −.10–.40 fd, .07–.70 ms, .15–.64 md, −.12–34	bb, .31–.49 bs, .24–.44 ss, .43–.61		
Hunt *et al.*	89	Utah	1,102	Corr	17+		bb, .18 ss, .15	.10	h^2 = .24 h^2 = .21
Burns *et al.*	89	Iowa	284f	Corr	5–14	fo, .25–.32 mo, .21–.36	.51	.16	h^2 = .36–.52

Table II. Continued

Author	Year	Sample	Size[b]	Method	Age (yr)	po	sib	sp	
Price *et al.*	90	New York	566o	Relative risk	Ad				RR, 1.84 ch/ad
		Philadelphia Boston Buenos Aires	1,743r						
Garn *et al.*	89	Tecumseh, MI	1,419o	Relative risk					RR, 1.5
Moll *et al.*	91	Iowa	1,580	PAP	12–24	.22	.35	.17	av .08-.09
Ness *et al.*	91	New York?	60bf	Corr	9–74				
			961bf	Pointer	b	.16	.36	.44	
					w	.18	.22	.09	
Tambs *et al.*	91	Norway	74,994	SAS	19+	fo, .19	bb, .21	.12	2nd rel,
				NLIN	h^2 = .39	fs, .21	ss, .26		−.22–.07
					s^2 = .08	fd, .17	bs, 21		
					c^2 = .02	mo, .20			
					r^2 = .03	ms, .20			
						md, .21			
Donahue *et al.*	92	Minnesota	1,767	Corr	13–17	ms, .32			
			712f	quintiles		md, .38			
						fs, .37			
						fo, .39			
Ayatollahi	92	Iran	1,207	Corr	6–12 bmi[c]	ps, .20		.23	
				quintiles		pd, .20			
						fo, .15			
						mo, .17			
Nirmala *et al.*	93	India	1,691	Corr	5+	.24	bb, .55	.37	
			486f				ss, .28		
							bs, .36		
Ramirez	93	Utah	529	Corr	11–20	ms, .18	bb, .46	−.05	
						md, .03	ss, .21		
						fs, .29			
						fd, .12			
Esposito-del Puente *et al.*	94	Italy	110	Corr	10	fo, .38			
						mo, .27			
Sellers *et al.*	94	Iowa	1,166	Corr	Ad F	md, .21	ss, .17–.21		2nd rel, .07–.10
Guillaume *et al.*	95	Belgium	1,028	*p* values	6–12				
Rotimi & Cooper	95	Illinois	534b	Corr	10–40	md, .33	ss, .28	.12	
						ms, .26	bb, .30		
							sb, .27		
Skinfolds									
Twin studies									
Brook *et al.*	75	London	222p	Falconer	3–15	mz, .77	dz, .40		h^2 = .74
Borjeson	76	Sweden	127p	H index	7				

Table II. Continued

Author	Year	Sample	Size[b]	Method	Age (yr)	po	sib	sp	
Family studies									
Hawk & Brook	79	London	1,083	Corr	Ad	fs, .19 fd, .10 ms, .21 md, .20	bb, .30 ss, .05		
Garn *et al.*	79	Tecumseh, MI	6,405p	Corr	5–18	po, .19–.21 apo, .09–.11	si, .23–.29 asi, .12–.29		
Mueller & Malina	80	Philadelphia	114b 101w	Corr	6–12	b	bb, .19–.23 ss, .58–.59 bs, .33–.44		
						w	bb, .26–.36 ss, .19–.37 bs, .33–.46		
Kaur & Singh	81	India	321	Corr	18–39	.15–27	.20–24	.05–.24	
Kapoor *et al.*	85	India	120 300	Corr	New born 18–26	md, .01–.33 ms, .0–.28 md, .27–.35	ss, .47–.68		
Bouchard *et al.*	85	Quebec	971	Corr	8–26	asi, −.06–.15 unr, .05–.17 co, .06–.30	.18–.49 dz, .30–.49 mz, .76–.87		
Pérusse *et al.*	87	Quebec	1,258 304f	Corr Corr	0–	.22	.26	.06	
Bouchard	87	Quebec	1,698 409f	Corr		.18–.34 apo, .19–.28	.18–.42 asi, .06–.18 dz, .30–.49 mz, .76–.87	−.01 −.19	av, .00–30
Commuzzie *et al.*	94	Texas	408		16–84				h^2 = .26–.58 r_g = .37–.95

[a] po, parent–offspring correlation; sib, sibling correlation; sp, spouse correlation; av, avuncular correlation; co, cousin correlation; gpc, grandparent–child correlation; 2nd rel, second-degree relatives correlations; h^2, heritability; s^2, sibling environment; c^2, cultural transmission; r^2, GE covariance; o, obese; RR, relative risk; ch/ad, child/adult; ad, adult; M, male; F, female; f, families; p, pairs; r, relatives; w, white; b, black; pc, parent–child; fo, father–offspring; mo, mother–offspring; fs, father–son; fd, father–daughter; ms, mother–son; md, mother–daughter; bb, brother–brother; ss, sister–sister; sb, brother–sister; a, adoptive; unr, unrelated.

[b] Number of individuals.

[c] BMI–like measure.

.20, .31 and .12, respectively. The model fitted the data well and the transmissibility was estimated at .36. Hypotheses of no assortative mating, no parental transmission, and no shared sibling environmental effect were rejected. This model does not allow the separation of biological and cultural transmission.

The Trøndelag Study in Norway

The study on BMI in a Norwegian sample of first- and second-degree relatives is without a doubt the largest of its type (Tambs *et al.*, 1991). This sample includes 23,936 spouse pairs, 43,586 parent–offspring pairs, 19,157 sibling pairs, and more than 2400 second-degree relatives. The estimated correlation for spouses was .12, which was ascribed to assortative mating. The average parent–offspring correlation was .20 and varied little by the age of the parents or the offspring. Similarly the sibling correlations showed a narrow range by sex, ranging from .21 for brothers to .26 for sisters. Second-degree relatives did not correlate significantly. Using a path model that includes genetic and cultural transmission, assortative mating, and genotype–environment covariance, Tambs estimated the heritability at .39, of which a large proportion was due to dominance. Cultural transmission (.02) and sibling environment (.08) were both significant, introducing genotype–environment covariance (.03).

tability at .39, of which a large proportion was due to dominance. Cultural transmission (.02) and sibling environment (.08) were both significant, introducing genotype–environment covariance (.03). According to this study, the largest proportion of variance is explained by the unique environment.

Parent–Adult Offspring BMI Data

Three American and one ethnically diverse study in Jerusalem presented parent–offspring correlations with offspring aged 18 or older. One of the early large family studies was the Framingham Heart Study, in which 7948 individuals were studied (Heller *et al.*, 1983). In Jerusalem, 4203 families from different ethnic backgrounds participated in a family study (Friedlander *et al.*, 1987). Some 1166 adult women were measured in Iowa (Sellers *et al.*, 1994). The correlations between parents and their adult offspring in these three studies varied between .17 and .27. In the Princeton School District Family Study in Cincinnati (Khoury *et al.*, 1983), separate parent–offspring correlations were reported for black and white probands and their relatives (N = 1928). Correlations varied between .01 and .11 for white and between .03 and .37 for black pairs with offspring aged 20 years or older.

Parent–Adolescent Offspring BMI Data

Twelve studies reported parent–offspring correlations in which children or adolescents between age 5 and age 22 were included. Longini *et al.* (1984) modeled familial correlations based on a sample of 5174 individuals from Tecumseh, Michigan. Province and Rao (1985) used a tau model (Rice *et al.*, 1978) to derive transmissibility estimates from 6750 individuals comprising 1076 families in Brazil. Both studies reported parent–offspring correlations between .25 and .27 for father–offspring and mother–offspring pairs. A obesity score, comparable to BMI, was calculated for 179 Italian families and parent–offspring correlations varied between .31 and .37 (Zonta *et al.*, 1987). A small Italian study (N = 110) presented a correlation of .38 for fathers and .27 for mothers of 10-year-old children (Esposito-del Puente *et al.*, 1994). The correlations between 13- to 17-year-old adolescents and their parents from 712 families in Minnesota ranged from .32 to .39 (Donahue *et al.*, 1992). A BMI-like measure was also obtained from 1207 parents and 6- to 12-year-old offspring in Iran, which correlated between .15 and .20 (Ayatollahi, 1992). The parent–offspring correlation calculated from 1691 individuals from 486 families in India was .24 (Nirmala *et al.*, 1993). The widest range of parent–offspring correlations (.03–.29) was found for 529 individuals from Utah pedigrees (Ramirez, 1993). Burns *et al.* (1989) and Moll *et al.* (1991) reported on 1607 individuals from 284 families in Iowa. From father–offspring (.25–.32), mother–offspring (.21–.36), sibling (.35–.51), and spouse (.16–.17) correlations, heritability was estimated between .36 and .52. Significant associations were found in 1028 6- to 12-year-old Belgian children and their parents (Guillaume *et al.*, 1995). Correlations between 105 Belgian twin pairs and their parents (N = 181) were .21 for father–offspring and .36 for mother–offspring pairs (Maes, 1992). All the previous studies were based on white samples. Only two studies to date have reported correlations from black (N = 60) and white (N = 961) families (Khoury *et al.*, 1983; Ness *et al.*, 1991). Parent–offspring correlations were higher for whites (.23–.29) than blacks (.07) in the first report but similar for blacks (.16) and whites (.18) in the later report. Rotimi and Cooper (1995) found correlations of between .26 and .33 for 534 African American mothers and their 10- to 40-year-old offspring in Illinois. Two early studies reported correlations between parents and their offspring measured annually of from 0 to 21 (Bayley, 1954) and from 0 to 7 (Tanner and Israelsohn, 1963). Because of the small samples, a large variability was observed in the correlations.

No clear trends were observed in the parent–offspring correlations by gender of the parents or the offspring. The range of maternal correlations was .03 to .38, compared to .12–.39 for the paternal correlations. Correlations between parents and their daughters ranged from .01 to .39; those with parents and their sons, between .0 and .37.

Adult Sibling BMI Data

Most studies that include parent–offspring correlations also report sibling correlations. Adult sibling correlations for BMI vary between .09 and .29 for siblings from the Framingham Heart Study (Heller *et al.*, 1983) and from Tecumseh (Longini *et al.*, 1984), between .25 and .43 for ethnically diverse siblings in Jerusalem (Friedlander *et al.*, 1987), between .15 and .18 for sister and brother

pairs from Utah pedigrees (Hunt *et al.*, 1989), and between .17 and .21 for women in Iowa (Sellers *et al.*, 1994). Mueller (1978) estimated sibling correlations separately for siblings who were less than 7 years different in age versus siblings more than 7 years apart. Based on a sample of 111 individuals in Columbia, he found higher correlations between siblings close in age (.51) than between siblings farther apart (.21).

Adolescent Sibling BMI Data

In the Fels Longitudinal Study, approximately 500 participants were measured annually from 0 to 18 years and, again, at age 30 (Byard *et al.*, 1983, 1989). This sample consisted of 523 sibling pairs and correlations were calculated between brothers and sisters at the same age. Brother correlations ranged from .31 to .49, correlations between sisters varied between .43 and .61, and brother–sister correlations varied from .24 to .44. In most other sibling studies pairs were not measured at the same age, but in most cases age-regressed BMI scores were used to calculate correlations. In three studies correlations between brothers (.30–.55) were higher than correlations between sisters (.21–.28) and brother–sister correlations (.27–.36) (Nirmala *et al.*, 1993; Ramirez, 1993; Rotimi and Cooper, 1995). Three other studies reported a sibling correlation of between .30 and .36 (Longini *et al.*, 1984; Province and Rao, 1985; Zonta *et al.*, 1987). Khoury *et al.* (1983) and Ness *et al.* (1991) reported a higher sibling correlation for blacks (.36–.48) than for whites (.16–.35).

The majority of the parent–offspring correlations were between .10 and .40, and most sibling correlations ranged from .15 to .55. These correlations are consistent with heritability estimates of between .20 and .80.

BMI Data from Spouses

Twenty studies reported spouse correlations on BMI. Most of these vary between .10 and .19 (Allison *et al.*, 1996b; Heller *et al.*, 1983; Longini *et al.*, 1984; Province and Rao, 1985; Zonta *et al.*, 1987; Bouchard *et al.*, 1987; Pérusse *et al.*, 1988; Hunt *et al.*, 1989; Burns *et al.*, 1989; Moll *et al.*, 1991; Tambs *et al.*, 1991; Rotimi and Cooper, 1995; Annest *et al.*, 1983). Lower estimates (−.05, .05, .07, and .08, respectively) were obtained by Ramirez (1993), Rice *et al.* (1995), Maes (1992), and Friedlander *et al.* (1987). Higher estimates (.23 and .37, respectively) were found for spouses in Iran (Ayatollahi, 1992) and in India (Nirmala *et al.*, 1993). A higher correlation was observed for black (.20–.44) versus white (.09–.14) spouses (Khoury *et al.*, 1983; Ness *et al.*, 1991).

Skinfold Family Data

Not all family studies on the genetics of obesity included BMI. Four studies reported parent–offspring correlations for several skinfolds. Parent–offspring correlations ranged from .20 to .21 for 1083 British individuals (Hawk and Brook, 1979), from .15 to .27 for 321 individuals from India (Kaur and Singh, 1981), and between .27 and .35 for 300 mother–daughter pairs in India (Kapoor *et al.*, 1985). The latter study also included correlations between 120 newborn children and their mothers in India, which ranged from .0 to .28 for sons and .01 and .33 for daughters (Kapoor *et al.*, 1985). Adult sibling correlations for skinfolds vary between .05 and .30 for British siblings (Hawk and Brook, 1979) and between .20 and .24 for Indian siblings (Kaur and Singh, 1981). Mueller and Malina (1980) reported correlations separately for 114 black and 101 white adolescent sib pairs from Philadelphia. They found higher sister–sister similarities compared to brother–brother similarities in blacks, but not in whites, and conclude that these could arise from expression of sex-limited genes under less favorable environmental conditions. Newborn sister correlations in India ranged from .47 to .68 (Kapoor *et al.*, 1985). Spouse correlations of between .05 and .25 were reported by Kaur and Singh (1981). Commuzie *et al.* (1994) performed a multivariate genetic analysis on eight skinfolds, measured in 408 subjects in Texas, and reported heritabilities of between .26 and .58. The genetic correlations showed the highest values between skinfolds from the same region.

Reports from the Quebec Family Study also include other measures of obesity besides BMI. Skinfolds were measured on 971 8- to 26-year-old adoptive and biological siblings (Bouchard *et al.*, 1985). Correlations were reported for full siblings (.18–.49), DZ twins (.30–.49), MZ twins (.76–.87), cousins (.06–.30), adoptive siblings (−.06–.15), and unrelated siblings (.05–.17). Two later reports presented parent–offspring, sibling, and spouse correlations of .22, .26, and .06 (Perusse *et al.*, 1987)

and .18–.34, .18–.42, and −.01–.19 (Bouchard, 1987), respectively, for six skinfolds. The latter report also included adoptive relatives; correlations varied between .19 and .28 for adoptive parent–offspring and between .06 and .18 for adoptive siblings.

Adoption Studies

The earliest studies on the genetics of obesity were adoption studies. Comparing the correlations between adoptees and their adoptive parents to those with their biological parents provides a direct estimate of cultural versus genetic transmission of obesity (see Table III). Relatively small sample sizes for which both adoptive and biological parents are available (complete adoption design) have limited the use of adoption studies.

The Danish Adoption Register

One exception is the Danish Adoption Register. This register contains data on every completely nonfamilial adoption granted in Denmark between 1924 and 1947. Height and weight data were available on 3580 adoptees. Four weight groups—namely, thin, medium weight, overweight, and obese, each constituting 4% of the sample—were selected for further study (N = 540). Information on BMI of biological and adoptive parents and siblings was obtained only for the selected sample. Several reports on this sample have concluded that there were strong relationships between the weight class of the adoptees and the BMI of their biological parents (Stunkard *et al.*, 1986) and siblings and half-siblings (Sorensen *et al.*, 1989) but no relation with the BMI of their adoptive parents and siblings. BMI was further calculated from school examinations at ages 7–13 years on 269 adoptees of a selected sample of 840 (Sorensen *et al.*, 1992a, b). Correlations of the BMI of adoptees with that of their adoptive parents (.03–.10) were lower than those with their biological parents (.16–.17) and lower than correlations between biological parents and their non-adopted-away offspring (.16–.36). A similar trend was noted for the sibling correlations (.14 for adoptees with adoptive siblings, .59 with biological siblings, and .77 for biological siblings reared with biological parents) and for half-sibling correlations. Vogler *et al.* (1995) assessed the influences of genes and shared family environment on BMI using a comprehensive path model on a subsample of 660 Danish adoptees and 1486 relatives. Heritability was estimated at .34; neither shared familial environment nor assortative mating was significant.

Other Adoption Studies on BMI

Five other studies included correlations on BMI in adopted children or adolescents and their adoptive and biological parents and siblings. In an early study, Withers (1964) collected data on overweight in 142 adopted 8- to 13-year-old children. Correlations with adoptive parents (.11–.16) were lower than those with biological parents (.14–.24). As part of the Take Off Pounds Sensibly (TOPS) study, data were collected from 254 adoptive and 10337 nonadoptive families with children between 4 and 11 years of age. Based on correlations with adoptive parents (.03–.11) and those with biological parents (.10–.11), the heritability of BMI was estimated at .12 and the contribution of shared environmental factors at .32 (Hartz *et al.*, 1977). Three Canadian adoption studies reported correlations on 374 families and 407 families in Montreal and 409 families in Quebec, respectively (Biron *et al.*, 1977; Annest *et al.*, 1983; Bouchard *et al.*, 1985). Correlations between adopted children and their adoptive parents (−.03–.10) were lower than those with their biological parents (.02 to .18) for the Montreal samples but similar for the Quebec sample (.22 for adoptive and .23 for biological parents). Adoptive children correlated less with adoptive siblings (.00–.08) than with biological siblings (.13–.40) in the three studies.

BMI Data on Adult Adoptees

Only one study reported data on adult adoptees (18–38 years) (Price *et al.*, 1987). Consistent with reports on adopted children, correlations of 357 adoptees in Iowa with their adoptive parents (−.09–.09) were lower than those with their biological parents (.08–.40). Most of the evidence thus points to genetic factors accounting for familial covariation in BMI, given the significant correlations between biological relatives and nonsignificant correlations between adoptive relatives. Only the Canadian studies concluded that the shared environment explained part of the familial resemblance.

Table III. Review of Adoption Studies on Obesity[a]

Author	Year	Sample	Size[b]	Method	Age (yr)	Adop	Biol	sp	
Withers	64	London	142	Corr	8–13	afo., 11	fs, .14		ss, .22
						amo, .16	fd, .24		bb, .29
							ms, .19		bs, .28
							md, .18		
Hartz *et al.*	77	TOPS	254a	Corr	4–11	ao, .03	bfo, .11		h^2 = .12
			10,337b			amo, .11	mfo, .10		c^2 = .32
Biron *et al.*	77	Montreal	374	Corr	wt/ht, 1–21	apo, .00	bpo, .06		
						asi, .00	bsi, .13		
Garn *et al.*	79	Tecumseh, MI	160	Corr		afs, .22	fs, .31		
	76		1,800b			ams, .09	ms, .27		
						afd, .23	fd, .25		
						amd, .19	md, .22		
Annest *et al.*	83	Montreal	407f	Corr	1–10	afo, −.03	bfo, .02	.11	c^2
						amo, .10	bmo, .18		
						asi, .01	bsi, .40		
Bouchard *et al.*	85	Quebec	409	Corr	0–	apo, .22	bpo, .23		
						asi, .08	bsi, .26		
Stunkard *et al.*	86	Denmark	3,651a	4 weight		amo, NS	mo, S		
			540s	classes		afo, NS	md, S		
							fo, S		
Price *et al.*	87	Iowa	357a	Corr	18–38	amd, .06	md, .40	.05–.25	
						ams, .04	ms, .15	sel pl	
						afd, .09	fd, .18	−.07–.18	
						afs, −.09	fs, .08		
Sorensen *et al.*	89	Denmark	3,580a	4 weight			fsi, S		
			540s	classes			mhsi, S		
							phsi, NS		
Sorensen *et al.*	92	Denmark	3,580a	4 weight	7–13	amo, .10	mo, .17	mbo, .36	
			840s	classes		afo, .03		mho, .16	
						asi, .14	fo, .16	fbo, .28	
								fho, .17	
							si, .59	fsi, .77	
							mhsi, .16	mhsi, .44	
							phsi, .03	phsi, .34	
Cardon	92	Colorado	241a	Model fitting	0–9	h^2	h^2		
			245na			.09	.88		
						.01	.43		
						.09	.53		
						.37	.64		
						.52	.52		
						.38	.32		
						.55	.39		
						.38	.58		
						.57	1.00		
Vogler *et al.*	95	Denmark	660a	Path model					h^2 = .34
			1,486r	No c^2, i					

[a] Adop, adoptive relatives; Biol, biological relatives; sp, spouse correlation; sel pl, selective placement; h^2, heritability; c^2, shared environment; i, assortative mating; ad, adult; M, male; F, female; f, families; r, relatives; a, adoptive; na, nonadoptive; b, biological; s, selected; NS, not significant; S, significant; pc, parent–child; si, siblings; hsi, half-siblings; fo, father–offspring; mo, mother–offspring; fs, father–son; fd, father–daughter; ms, mother–son; md, mother–daughter; bb, brother–brother; ss, sister–sister; sb, brother–sister.

[b] Number of individuals.

The Colorado Adoption Project

While most adoptive samples date back a number of years, the Colorado Adoption Project (CAP) is an ongoing longitudinal, prospective study in which 241 adoptive and 245 nonadoptive families have been evaluated at annual or semiannual intervals from birth to age 9 (Cardon, 1995). Continuity of BMI, as assessed by correlations over time, resulted entirely from genetic factors, which were transmitted from previous measurements to subsequent occasions. Age-specific environmental effects were substantial at nearly all ages, without a lasting effect. After about age 2 heritability estimates from analyses of siblings (.32–.64) were similar to those from analyses of parents and offspring (.37–.57). Heritability in infancy was high for sibling analyses but low for parent–offspring analyses, indicating that the genetic determinants of BMI in infancy relate to those in later childhood, but not in adulthood. However, the genetic effects that arise later in childhood do continue to determine the BMI in adulthood.

METHODOLOGICAL CONSIDERATIONS

Twin Studies

The Classical Twin Study

The classic twin study includes MZ and DZ twins reared together. It is a powerful design for estimating genetic effects. One thousand twin pairs (500 MZ, 500 DZ) provide 80% power to reject a purely environmental model with a probability of .05 if additive genetic factors explain 10% (only unique environment) and 30% (unique and shared environment) of the variance, respectively. Other advantages are that twins are matched for age. Therefore age-dependent influences of genes or environmental factors are the same for both twins. If age accounts for a significant proportion of the variance, both the MZ and the DZ correlation will be inflated. It is thus important to analyze age-regressed scores or, better, to include age as a measured variable in the model. Including male and female same-sex twin pairs allows testing whether the magnitudes of the effects of genes and environment are the same for both sexes. Adding opposite-sex twins further enables testing of sex-limited effects. A DZ opposite correlation significantly smaller than the DZ same-sex correlations could indicate that different sets of genes or different environmental factors influence males and females.

Twins, Singletons, and Zygosity

Twin studies are often criticized for several reasons. The first is that results from twin studies may not be generalizable because twins may not be representative of the population from which they are drawn. For a large number of characteristics, including BMI, twins have been found not to be significantly different from singletons (Wilson, 1986; Luke *et al.*, 1995). For some variables, differences between twins and singletons were observed at birth and during the first years of life, but twins tend to "catch up" by the age of 8 (Wilson, 1986). Second, most twin studies reviewed here used self-report zygosity measures, which often include questions about difficulty being told apart by parents or teachers. MZ twins who are discrepant in height and weight (at birth or continued later in life, e.g., because of different intrauterine experiences) would be more likely viewed and classified as DZ twins. This bias would lead to increasing heritability estimates.

Equal-Environment Assumption

A third major potential flaw of the twin design is the "equal-environment" assumption (EEA). It is assumed that MZ twins do not share a greater proportion of salient environmental factors than DZ twins. In various reports where this assumption has been tested, it was found to be valid (see, e.g., Scarr and Carter-Saltzman, 1979; Kendler *et al.*, 1993). Similarity between twins may lead to more contact and thus more shared environmental experiences (Lykken *et al.*, 1990; Rose *et al.*, 1990). In the same trend, parents may be responding to, rather than creating, similarities or differences between the twins (Lytton, 1977). Although MZ twins may be closer in a variety of "environmental" factors than DZ twins (Fabsitz *et al.*, 1978; Austin *et al.*, 1987; Heller *et al.*, 1988), these may result from more regular contact. Genetic factors may even control the degree to which "environmental" factors are shared by twins. A related assumption is that there is no special twin environment, which requires that twins are not treated more alike and do not share more salient environmental factors than regular siblings. Viola-

tion of this assumption would cause an increase in the correlation of both MZ and DZ twins, which could lead to overestimation of the shared environmental variance. A special case of twin environment is intrauterine effects on the growth of the fetus. Siblings would share some of this source of variance, being born from the same uterus at different times, whereas both MZ and DZ twins share the same uterus at the same time and would likely be exposed to similar levels of nutrition and teratogens. It is possible that monochorionic twins share such factors to an even greater extent than dichorionic twins, so comparison of BMI correlations from samples where chorionicity has been measured would be one useful way to discern such effects. One observational twin study correlating intrapair differences in birth weight with intrapair differences in adult BMI suggested that the intrauterine period is not a critical period for the development of adiposity (Allison *et al.*, 1995).

GE Correlation and G × E Interaction

Two further potential disadvantages of the twin design are the assumptions of no genotype–environment (GE) correlation and no genotype × environment (G × E) interaction. GE correlation refers to the situation in which genetic and environmental factors are not independent. For example, GE correlation can occur if having a particular genetic background limits ones choice of environments. Another form of GE correlation occurs when both genes and environment have a common source, such as the parent's genotype, if the parent's phenotype affects the offspring's environment. This may result from the combined presence of genetic and cultural transmission and can be estimated in models of twins and their parents. It is possible that different genotypes actively select different environments, which in turn cause phenotypic variation. This "eliciting" is attributed as a genetic effect—even though it has an environmental pathway. G × E interaction may result if the sensitivity to the within-family environment is genotype dependent. If the critical aspect of the environment can be measured, models including twin pairs concordant and discordant for environmental factors allow testing the significance of the G × E interaction. If not explicitly modeled, G × E interaction forms part of the specific environmental variation. One study supporting the concept of G × E interaction for BMI is the overfeeding of identical twins study of Bouchard *et al.* (1990). They concluded that genetic factors were involved in the intrapair similarity in weight gain.

Random Mating

A final assumption often made in twin studies is that of random mating. It is assumed that partners do not choose each other for the characteristic under study. If the marital correlation is significant, however, the heritability will be overestimated when fitting an AE model (additive genetic factors and unique environment) and underestimated when fitting a ACE model (additive genetic factors, shared and unique environment) because shared environmental factors may become significant. Since spouse correlations were significant but low, and shared environmental factors were not significant, heritability for BMI estimated from classical twin studies may have been slightly overestimated. Allison *et al.* (1996b) quantify the magnitude of this bias and obtained a premarital correlation of .13 for BMI.

MZ and DZ Twins Reared Apart

The most powerful genetic epidemiologic design includes reared-apart MZ or DZ twins or both because of the resulting separation of genetic and environmental effects. The correlation of MZ twins reared apart (MZA) is a direct estimate of the heritability. The only sources of familial resemblance between members of a twin pair reared in different environments is their shared genetic background and prenatal environment. One weakness of this design lies in the age of separation of the twins. If twins are not separated close to birth, they may share postnatal environmental factors. Another is that biological parents who put their children up for adoption may not be representative of parents in the population. Likewise, parents who adopt may not be representative of parents generally. Therefore sampling of both genotypes and environments is suspect in an adoption study. Finally, children may not be placed at random with adoptive parents, which may violate the assumption of independence of genetic and cultural transmission.

Advantages and Assumptions

The classical twin study advantages of age matching and sex limitation testing are true of the

MZA DZA study. Similarly, the assumptions are (i) generalizability of twin data, (ii) no G × E interaction, (iii) random mating, and (iv) random placement. Given random placement, there is no GE covariance. However, there is no way to estimate the effects of common environment in this design; such factors would form part of the environmental variance. The equal environments assumption is no longer necessary, as twins are not raised by the same parents if twins are separated early in life.

Family Studies

The Nuclear Family Design

Family studies typically include *parent–offspring* pairs, *sibling* pairs, and *spouse* pairs. The popularity of the design is due partly to the abundance of such relationships in the general population. Unfortunately parent–offspring and sibling correlations do not allow the separation of genetic and environmental transmission. When significant correlations are observed between children and their parents or between siblings, they may result from shared genes or from shared environmental factors. In the case of siblings, the shared environmental factors may be aspects of the environment shared with the parents (cultural transmission) or nonparental shared environment. Adding measured indices of the environment may provide information to sort out the pathways. It is, however, almost impossible to construct an environmental index that is free from any genetic background. A better resolution of genetic versus environmental transmission may be obtained by comparing correlations from biological relatives with relationships which share only genes or only environmental factors, such as adoptive relatives. This design is discussed below.

The Twin Parent Design

Another strategy that allows separation of genetic and environmental transmission is the twin–parent design. Basically this design augments the classical twin design with data from the parents of the twins (Fulker, 1982). Ignoring sex differences, this design includes five unique statistics: MZ twin, DZ twin, parent–offspring and spouse covariances, and total variance. These allow estimating five parameters: genetic variance (heritability), cultural transmission, nonparental shared environment, assortative mating, and unique environmental variance. This model—including sex differences—was applied to data from the Leuven Longitudinal Twin Study (Maes *et al.*, 1996). The sum of skinfolds was calculated for 105 twin pairs and their parents. Shared environmental factors (cultural transmission and nonparental shared environment) did not contribute significantly to the observed variances and covariances. Heritability was estimated at .79 for males and .90 for females. A small percentage of variation (2%) resulted from the genetic effects of assortative mating.

The Extended Family Design

To identify parameters for genetic and cultural transmission, it is not necessary to collect data from the parents of twins, but this design is a relatively straightforward extension of twin studies. Large samples of first- and second-degree relationships (Tambs *et al.*, 1991; Bouchard *et al.*, 1985) tend to include relatively few twin pairs—consistent with the population prevalence of twins—compared to parent–offspring and sibling pairs. The addition of second-degree relatives allows the estimation of additional parameters, such as dominance. As discussed above, Tambs *et al.* (1991) estimated the heritability of BMI at .39 based on a sample of 74994 relatives including 169 twin pairs. Cultural transmission explained 2% and sibling environment 8% of the variance. Bouchard *et al.* (1985) reported a transmissibility of .40 for data from 1698 relatives including 156 twin pairs. The transmissibility is the sum of the genetic and cultural inheritance. This estimate is thus consistent with those of Tambs *et al.* (.39 + .02). The estimate for the biological inheritance is .10 according to Bouchard. The tau model which was used in his analyses, however, allows for a separate parameter for the shared environment for sibs and DZ and MZ twins. This parameter is highly significant for MZ twins, less for DZ pairs, and even less for siblings. It does not appear realistic that the environment of MZ pairs is so much more alike than that of DZ pairs and siblings. A genetic explanation for this difference in the correlations seems more appropriate (Allison, 1995; Neale and Eaves, 1995).

Assortative Mating

Among the advantages of family studies are the fact that an estimate of assortment is often ob-

tained and that separate maternal and paternal effects may be distinguished by comparing the father–offspring and the mother–offspring correlations. The marital correlation usually served as an estimate for assortment. Assortative mating may not be the only reason for spouses to be correlated. It may also result from cohabitation or marital interaction. However, two studies have suggested that assortative mating may be a more likely explanation of the small but significant marital correlations for BMI than cohabitation (Allison *et al.*, 1996b; Knuiman *et al.*, 1996).

Age × Genotype Interaction

One of the major disadvantages of family studies is that children and parents or siblings are measured at different ages. If different genetic and/or environmental factors account for the variation in BMI at different ages, parent–offspring and sibling correlations would be reduced and heritability underestimated. Only two studies to our knowledge have tried to address this problem by comparing correlations of sibs close in age to those of sibs farther apart. Mueller and Malina (1980) found higher correlations between siblings closer in age. Tambs *et al.* (1991) reported a significant effect in the expected direction only for brothers. Differences in these correlations have often been interpreted as evidence for different environmental factors. It has, however, become increasingly clear that genetic factors may also be responsible for such discrepancies. Longitudinal twin studies in which genetic correlations were estimated between twins measured at different ages have all indicated that mostly the same genetic factors account for the variation in BMI in younger and older twins, but the genetic correlations are not unity, suggesting that new genetic factors may switch on at various ages. Some of the discrepancies between results from family and twin studies may be attributed to these effects.

Adoption Studies

The Complete Adoption Design

The adoption design has long been recognized as a powerful tool to resolve to effects from genes and shared environment. In the complete adoption design data are collected from adopted and natural children and their adoptive and biological parents. Adopted children share genes with their biological parents but not with their adoptive parents; they share the environment with their adoptive parents but not with their biological parents. The correlation of adopted children with their biological parents thus provides an estimate of the genetic transmission. The correlation of adopted children with their adoptive parents provides an estimate of the cultural transmission.

Selective Placement

The advantage of an estimate of assortment and the disadvantage of age effects apply equally to adoption and family studies. Two other assumptions are critical to the adoption design. The first is that of no selective placement. This implies that the adopted parents are not selected based on any characteristic of the adopted child or the biological parents of the adopted child. This would induce a correlation between the adoptive parents and the biological parents so that the separation of genetic and environmental pathways no longer holds. If selective placement exists and can be quantified, it should be included in the models (Plomin and DeFries, 1990; Phillips and Fulker, 1989). The second assumption is that of no significant effects of the prenatal environment. If the prenatal environment contributes significantly to the observed variance, the assumption of no genotype–environment covariance is violated. The same problem could arise with respect to early postnatal environmental influences if adoptees were not separated from their biological parents close to birth.

The Partial Adoption Design

It is not always possible to obtain data from the biological parents of adopted children. Data from adopted children and their adoptive parents, the partial adoption design are still useful as they provide an estimate of cultural transmission which is not confounded with genetic transmission. If the adoptive parent–offspring correlations are compared with regular parent–offspring correlations, an estimate of the genetic transmission may be obtained by subtracting and doubling the adoptive parent–offspring correlation from the biological parent–offspring correlation. The other advantages and disadvantages of the complete adoption design are also present for the partial adoption design.

TOWARD AN INTEGRATED APPROACH

From the evaluation of twin, family, and adoption studies, it has become increasingly clear that approaches which integrate the best aspects of these designs will prove useful in better understanding the nature and nurture of quantitative traits. One such approach is the so-called "stealth" model, developed by Eaves *et al.* (1996) within the "Virginia 30,000" study. This study exploits all the collateral two-generational relationships identified in the kinships of twins to estimate the sex-dependent contributions of genes and environment to complex traits in the presence of assortative mating. This design includes the relationships typically studied in twin and family studies. Although adoptive relationships could easily be incorporated in the design, they were not formally specified in the Virginia 30,000 because of the relatively small numbers of these relatives in this sample. The available first- and second-degree relatives (avuncular, cousin, and grandparent–grandchildren) provide statistics to resolve genetic and cultural transmission and both special MZ and special DZ twin environment effects.

Ascertainment and Structure of the Virginia 30,000 Sample

The Virginia 30,000 contains data from 14,763 twins, ascertained from two sources. Details of the ascertainment have been published elsewhere (Truett *et al.*, 1994). Questionnaires were mailed to twins from the Virginia Twin Registry (VTR; twins born in Virginia between 1915 and 1971), with complete returns from 5287 families. The remainder of the twins (N = 9476 individuals) responded to a letter published in the newsletter of the American Association of Retired Persons (AARP).

All pedigrees included a male or female MZ or a male, female, or unlike-sex DZ twin pair and all available parents, siblings, spouses, and children of the twins. This provides a rich combination of 80 sex-specific two-generation relationships (parent–offspring, spouse, twin, siblings, cousins, etc.). BMI data were available on 800 male MZ, 596 male DZ, 1925 female MZ, 1230 female DZ, and 1370 unlike-sex DZ twin pairs. Among the relatives, there were 731 fathers of twins, 1130 mothers of twins, 1031 male twin siblings, 1561 female twin siblings, 1495 wives of twins, 2200 husbands of twins, 1655 sons of twins, and 2495 daughters of twins.

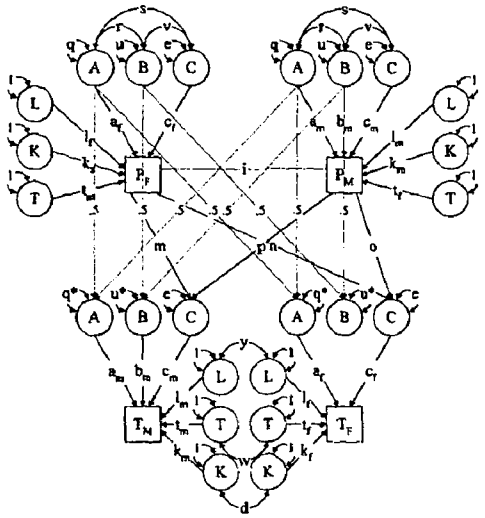

Fig. 1. The extended twin family model for opposite-sex DZ twin pairs and their parents.

All subjects were asked to give their height in feet and inches and their weight in pounds. Twin pairs were asked how frequently they saw their twin on a 6-point scale ranging from (1) we live together, to (2) almost every day, (3) at least once a week, (4) once or twice a month, (5) a few times a year, and (6) once a year or less. Those pairs who reported that they lived apart were asked how frequently they contacted their cotwin, on a 5-point scale similar to the previous scale except for (1). Pairs who reported living together were assigned a value of 0 on the (non-)contact scale.

The Stealth Model

The model for family resemblance applied to twin pedigrees is referred to as the "stealth" model and is described in detail by Truett *et al.* (1994). We highlight the main features of the model through the path diagram (Fig. 1). Instead of using a numeric counter, we use the path coefficients to enumerate the various aspects of the model. The stealth model includes (a, b) additive genetic effects, (k) genetic dominance, (c) environmental effects, (m, n, p, o) parent-to-offspring vertical cultural transmission, (i) phenotypic correlation between mates modeled as primary phenotypic assortment, (l) residual sibling shared environment

Table IV. Sample, Size, Mean, and Variance of Normalized Residuals of BMI for Relatives of Twins in the Virginia 30,000[a]

	MZM	Mean	Var	DZM	Mean	Var	MZF	Mean	Var	DZF	Mean	Var	DZM F	Mean	Var
T1	806	.03	.69	602	.08	.75	1940	−.06	1.13	1234	.02	1.16	1373	.03	.80
T2	800	.00	.71	598	.07	.79	1921	−.05	1.11	1238	−.00	1.12	1378	−.03	1.12
Fa	113	.09	.60	111	.07	.80	180	−.13	.91	123	.08	.67	205	.04	.69
Mo	168	.07	1.60	147	.09	1.16	319	−.02	1.12	191	.11	1.28	308	.06	1.18
Br	140	−.06	.77	120	.12	.58	289	−.01	.68	196	.11	.71	286	.04	.73
Si	203	−.16	1.18	155	−.01	1.47	479	−.00	1.19	356	.07	1.26	373	−.05	1.30
Sp1	330	−.02	1.02	222	−.19	1.22	639	.04	.72	353	.09	.70	474	−.05	1.21
Sp2	283	−.17	1.11	187	−.13	1.19	556	.09	.72	280	.13	.74	375	.03	.82
S1	113	−.09	.71	61	.00	1.03	349	.01	.82	205	.02	.64	123	.08	.79
D1	188	−.18	1.16	75	−.17	1.05	545	−.04	1.21	299	−.06	1.38	191	−.07	.97
S2	109	−.02	.71	47	.19	.55	340	−.02	.71	149	.15	.66	162	−.09	1.04
D2	157	−.16	1.19	69	−.04	1.05	523	−.11	1.12	246	.05	1.21	211	−.06	1.18

[a] T1, twin 1; T2, twin 2; Fa, father; Mo, mother; Br, brother; Si, sister; Sp1, spouse of twin 1; Sp2, spouse of twin 2; S1, son of twin 1; D1, daughter of twin 1; S2, son of twin 2; D2, daughter of twin 2.

(nonparental shared environment), (t) additional twin shared environment, (x) additional MZ shared environment, (r) the correlation between common and male-specific genetic effects, (s, v) the correlation between genotype and environment, (q, u) residual genetic variance, (e) unique environmental variance, (d, y, w) correlations across sexes of dominance, sibling, and twin shared environmental effects. The subscripts m and f refer to male and female parameters.

Before model fitting,the entire data set was log transformed and corrected for the linear and quadratic effects of age, sex, twin status, source of ascertainment (Virginia vs. AARP), and interactions between these terms. Subsequent analyses were based on the normalized residuals from this regression analysis. Rather than fitting the model to the correlations, we fitted directly to the raw data, using the VL approach in Mx (Neale, 1995), thereby obtaining maximum-likelihood estimates of the parameters and χ^2 goodness-of-fit statistics (from the difference between the sum of the individual pedigree likelihoods of the stealth model and a fully saturated model). The significance of the parameters was tested by likelihood-ratio χ^2 tests. Confidence intervals were calculated for the most parsimonious model.

Sample sizes and summary statistics of the 12 types of relative in the design are shown in Table IV. Disproportionately large MZ and female sample sizes are commonly observed in studies requiring voluntary participation (Lykken *et al.*, 1992) and this pattern is seen here, but it is less than the "rule of two-thirds" reported in many studies. There is no obvious pattern to the means that relates to either the type of relative or the type of twin pair. Variances in females are greater than in males.

The full model includes 93 estimated parameters (of which 60 are parameters for the means) and 12 constraints. Parameter estimates and goodness-of-fit statistics for the full model and a submodel with no special MZ twin environment are shown in Table V. Evidently, the special MZ twin environment parameter x is nonsignificantly different from zero ($\chi^2 = 2.95$, df = 2, $p = .12$). When present, this parameter substantially reduces the estimate of genetic dominance in both males and females, and slightly reduces additive genetic variance. Several further parameters could be dropped from the full model without significantly worsening the fit. These were four parameters relating to nonscalar sex limitation (no male-specific genetic effects, correlations between male and female dominance, shared environment and twin environment equal to 1.0) and the parameters for cultural transmission and nonparental shared environment. Fixing these parameters at zero reduces the number of active constraints to three. The remaining parameters for additive genetic effects, dominance, special twin environment, and unique environment could not be equated across sexes without significantly deteriorating the fit of the model. Assortative mating was also significant.

Parameter estimates, proportions of variance, and confidence intervals for the parsimonious re-

Table V. Statistics, Parameter Estimates, Proportion of Variance, and Confidence Intervals of the Best-Fitting Model for BMI in the Virginia 30,000[a]

Full model with special MZ twin environment		Parameter estimate of Full model without special MZ twin environment		Best-fitting model		Proportion of variance of best-fitting model		Confidence intervals
A^2_m	.28+.16	A^2_m	.19+.20	A_m	.521	A^2_m	.351	.290–.415
(asm)	.01	(asm)	.01	A_f	.637	(asm)	(.020)	
D^2_m	.00	D^2_m	.27	E_m	.474	D^2_m	.307	.211–.395
E^2_m	.23	E^2_m	.27	E_f	.543	E^2_m	.274	.247–.304
CT^2_m	.00	CT^2_m	.00	D_m	.501	T^2_m	.068	.023–.134
S^2_m	−.01	S^2_m	.01	D_f	.532			
C^2_m	.02	C^2_m	.00	T_m	−.236	A^2_f	.394	.350–.437
T^2_m	.03	T^2_m	.03	T_f	.292	(asm)	(.022)	
Tmz^2_m	.24	Tmz^2_m		P_m	1.094	D^2_f	.259	.192–.324
A^2_T	.26	A^2_f	.28	P_f	.819	E^2_f	.269	.252–.288
(asm)	.01	(asm)	.01	I	.159	T^2_f	.078	.033–.128
D^2_f	.00	D^2_f	.32					
E^2_f	.21	E^2_T	.27					
CT^2_f	.00	CT^2_f	.01					
S^2_f	.03	S^2_f	.03					
C^2_f	.10	C^2_f	.01					
T^2_f	.06	T^2_f	.06					
Tmz^2_f	.31	Tmz^2_f						

[a] Goodness-of-fit statistics of best-fitting model: observed statistics, 24,230; estimated parameters, 72; constraints, 12; active constraints, 7; −2 times log-likelihood of data, 64,988.057; degrees of freedom, 24,158. A^2, additive genetic factors; asm, assortment; D^2, dominance factors; E^2, unique environmental factors; CT^2, cultural transmission; S^2, genotype–environment covariance; C^2, nonparental shared environment; T^2, special twin environment; Tmz^2, special twin environment; f and m subscripts, males and females.

duced model are presented in Table V. Additive genetic factors explain 35% of the variance in males and 39% in females, of which 2% result from assortative mating. Dominance accounts for 31 and 26% of the variance for males and females, respectively. These estimates add up to broad heritabilities of .66 and .65 for males and females. Seven to eight percent of the variance is explained by special twin environment. These are aspects of the environment that twin pairs share, but not other family members. The remaining 27% is accounted for by unique environmental factors. Ninety-five percent confidence intervals on these estimates are quite narrow, due to the large sample sizes and the relative simplicity of this model, which accounts for covariation in 88 different familial relationships with only 10 parameters. Correlations for 80 relationships are given in Table VI for reference.

DISCUSSION

The review of the literature of familial resemblance for BMI reveals strikingly convergent results for a wide variety of types of relationship. As expected, studies with smaller sample sizes show greater variability in estimates of correlation between relatives than do studies with larger sample sizes. Pooling across studies, including the new data reported in this article, the weighted mean correlation for MZ twins is .74, for DZ twins .32, for siblings .24, for parents and offspring .19, and for spouses .12 (Fig. 2). More distant and adoptive relatives (.06) typically show smaller correlations, consistent with a substantial role for genetic factors in the etiology of individual differences in BMI. The data reported in this article are in good agreement with those reported in other studies, with correlations close to the weighted means from other studies.

In most reports, data were analyzed using structural equation modeling (i.e., path analysis) and almost always yielded broad heritability estimates from .5 to .9. The "outlier" in this area are the reports by Bouchard and colleagues (1987), who used a model that involved separate special twin environment parameters for MZ and for DZ

Table VI. Observed Correlations of BMI for Biological Relationships in the Virginia 30,000 (Eaves, Unpublished Data)[a]

Family	N	r	Avuncular	N	r	Cousins	N	r	In-laws	N	r		N	r
S	4751	.144	PSib♂♂	92	−.026	Mzm♂♂	39	.094	Sibl♂♀	337	−.075	SPDz♀♂	54	−.223
			PSib♂♀	155	.004	Mzm♀♀	92	.223	Sibl♀♂	728	−.007	SPDz♀♀	80	−.177
Sib♂♂	1493	.234	NSib♀♂	402	.185	Mzm♂♀	107	.185	Sibl♂♂	422	.077	SNDz♂♂	126	.114
Sib♀♀	3524	.317	NSib♀♀	536	.083	Mzf♂♂	153	.040	Sibl♀♀	447	.075	SND♂♀	169	−.043
Sib♂♀	4255	.224	PSib♀♂	131	−.007	Mzf♀♀	340	.191				SPDz♂♂	36	−.255
			PSib♀♀	196	.065	Mzf♂♀	449	.064	Dzl♂♀	387	.047	SPDz♂♀	68	.146
DZ♂♂	573	.292	NSib♂♂	236	.105				Dzl♀♂	603	.126	SNDz♀♂	64	.090
Dz♀♀	1164	.360	NSib♂♀	284	.059	Dzm♂♂	19	−.375	Dzl♂♂	353	.038	SNDz♀♀	95	.106
Dz♂♀	1307	.264				Dzm♀♀	41	.070	Dzl♀♀	458	−.028			
Mz♂♂	775	.692	PDz♂♂	105	.292	Dzm♂♀	52	−.072	Mzl♂♀	589	.048	SPMz♀♂	129	.014
Mz♀♀	1847	.730	PDz♂♀	137	.016	Dzf♂♂	52	.260	Mzl♀♂	1139	.109	SPMz♀♀	213	.062
			NDz♀♂	345	.152	Dzf♀♀	138	.095				SNMz♂♂	342	−.107
Fa–So	2160	.190	NDz♀♀	525	.176	Dzf♂♀	159	−.025	Fa-Dal	205	−.068	SNMz♂♀	502	.040
Fa–Da	2971	.194	PDz♀♂	118	.393	Dzo♂♂	38	.176	Fa-Sol	188	.044			
Mo–So	3035	.227	PDz♀♀	188	−.001	Dzo♀♀	71	.118	Mo-Dal	293	.024	SDzm	100	.126
Mo–Da	4476	.257	NDz♂♂	150	.185	Dzo♂♀	51	−.118	Mo-Sol	338	.102	SDzf	120	−.065
			NDz♂♀	202	.098	Dzo♀♂	72	.141				SDzmf	167	−.057
												SMzm	172	.025
			PMz♂♂	217	.141							SMzf	300	.132
			PMz♂♀	337	.264									
			NMz♀♂	673	.124									
			NMz♀♀	1040	.255									

[a] S, spouse; Sib, sibling; Dz, DZ twin; Mz, MZ twin; Fa, father; Mo, mother; So, son; Da, daughter; P, paternal; N, maternal; I, in-laws; m, male; f, female; o, opposite sex; ♂♂, male–male pair; ♀♀, female–female pair; ♂♀, male–female pair; ♀♂, female–male pair.

twins. Such an approach effectively discounts the data from twins, and can markedly decrease estimates of heritability. In our study, the special MZ environment parameter was nonsignificant, although when estimated it did substantially reduce the estimate of dominance genetic effects. This is a natural consequence as special MZ environment is highly correlated with dominance in the twin-family design.

The significance of dominance variance, as indicated by the Virginia 30,000 and other large samples, may partly account for the higher heritability estimates found in twin versus family studies. Dominance variance is correlated 1.0 in MZ twins and .25 in DZ twins and siblings but is uncorrelated between parents and offspring.

There are reasons to believe that heritability estimates based on twin data may be better than those based on other types of relative. Twins are well controlled for age effects, whereas correlations between siblings or more distan relatives may be attenuated by nonlinear changes in BMI over time. In our data, however, we did not find evidence for a significant relationship between absolute difference in age and absolute difference in BMI (r = .05, p = .04) among siblings.

One potential source of difference between twin correlations and those from other types of relative is a maternal effect. It is conceivable that there are intrauterine effects on the growth of the fetus that lead to lasting differences in body mass in later life. The data presented here that include the offspring of twins provide an indirect measure of maternal effects. If the maternal effect is of genetic origin, so that the mother's genotype influences the quality of the uterus and the nutrition and teratogens relevant to later growth of her offspring, we would expect to see higher correlations between the offspring of an MZ female twin and the offspring of her twin sister than among the offspring of an MZ male twin and the offspring of his twin brother. To a lesser extent, a similar pattern should be observed for the children of male and female DZ twin pairs. In the present study, no such effect was observed, with MZ offspring correlations approximately (.15, .11, .27) for males and (.10, .10, .20) for females. If no evidence of maternal effects is found, the special MZ twin environment might

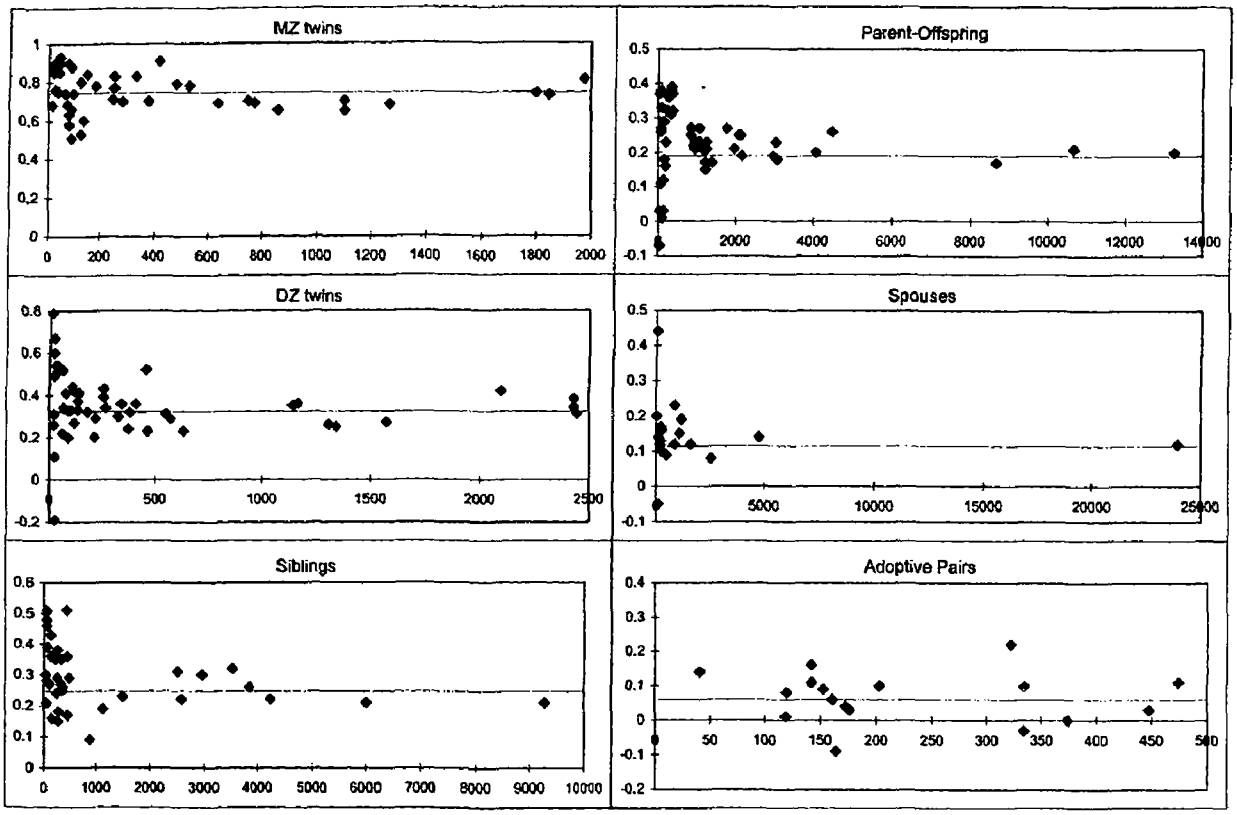

Fig. 2. Reported correlations by sample size for MZ twins, DZ twins, siblings, parent–offspring pairs, spouses, and adoptive relationships. *x* axis, sample size; *y* axis, correlations.

most logically be interpreted as epistatic effects from the interaction of genes at two or more loci. Such effects, known as "emergenesis" when the number of loci is large (Lykken *et al.*, 1992), would contribute substantially to the MZ twin correlation but would have negligible effects on correlations between other relatives. Given that BMI is a complex trait stemming from many possible genetic and environmental mechanisms, it seems quite plausible that epistatic/emergenetic effects influence it. A summary of the assumptions of different types of studies and their effect on the correlations and the estimates of genetic and environmental variance is presented in Table VII.

The results presented in this article are subject to at least six potential limitations. First, as with any study where participation is voluntary, the sample used may not be representative of the population. Part of the Virginia 30,000 sample was initially drawn from population records in the state of Virginia, but a substantial portion was strictly volunteer-based, being recruited as a result of an article in the AARP newsletter. For nonrandom sampling to affect the results of the study, it would need to be relevant to BMI. In a previous report, significant differences were found in the means or variances of twins whose cotwin had responded vs. twins whose cotwin had not (Neale and Cardon, 1992), suggesting that there may be some effects of volunteering. Comprehensive modeling of volunteer bias, using methods like those of Neale and Eaves (1993) is beyond the scope of this article.

Second, another possible limitation of these data also concerns sampling, in that even a representative sample of twins may not be representative of the population, and therefore conclusions from twins may not generalize. To some extent this might seem to be the case for previously reported studies of BMI, with heritability estimates from classical twin studies higher than those of nontwins. In the present analyses, both twins and nontwins were used to obtain parameter estimates, so

Table VII. Assumptions of Twin, Family, and Adoption Studies and Their Effect on Familial Correlations and Estimates of Genetic and Environmental Variance[a]

Assumption	Study	Effect on correlations	Effect on estimate ($/V_p$)		
			h^2	c^2	e^2
Twins = singletons	T		?	?	?
Correct self-report zygosity: systematic discrepant MZ as DZs	T	MZ ↗ DZ ?	+	−	−
Equal environment	T	MZ ↗	+	−	−
Special twin environment	T	MZ ↗ DZ ↗	=	+	−
GE correlation	TF	MZ 2 ↗ DZ ↗	+	=	−
GC covariance < cultural transmission	TF	MZ ↗ DZ ↗ PO ? SI ↗	=	+	−
G × E interaction	TF	MZ 2 ↘ DZ ↘ PO ↘ SI ↘	−	=	+
Random mating	T	MZ ↗ DZ ↗	+AE/−	=/+ACE	≈
Intrauterine/prenatal environment	TA	MZ ↗ DZ ↗ ABSI ↗ ASI ↘	+	=	−
Chorionicity	T	MZ ↗	+	=	−
Epistatis/emergenesis	F	MZ	+	=	−
AgexG/C/E interaction	FA	PO ↘ SI	−	+	≈
Random placement	A	APO ↗ ASI ↗	+	=	−
Separation age/postnatal environment	A	ABSI ↗ ASI ↘	+	=	−

[a] T, twin studies; F, family studies; A, adoption studies; MZ and DZ, twins; PO, parent-offspring; SI, sibling; APO, adoptive PO; ASI, adoptive sibling; ABSI, adoptee with biological sibling; ↗, increase; ↘, decrease; $/V_p$, over the phenotypic variance; h^2, heritability; c^2, shared environment; e^2, unique environment; ?, unknown; +, overestimation; −, underestimation; =, no effect; AE, AE model; ACE, ACE model.

the impact of using twins would be attenuated compared to studies of twins alone.

Third, self-reported height and weight used to calculate BMI is not an optimal index of obesity, and therefore caution should be exercised when generalizing the results to other related measures of fatness. While self-report BMI is likely to be quite highly correlated with such measures, the correlation is less than perfect. A related issue is that the analyses presented concern population-based samples that were not specifically ascertained because they met some clinical or other criteria for obesity. Our findings may not generalize to the study of extreme pathological levels of obesity if these have a different cause than extreme deviations on the hypothesized normal continuum of variation.

Fourth, heritability estimates based on twin studies can be biased if MZ twins have greater levels of contact than DZ twins and if contact affects intrapair similarity. In our data, we correlated two measures of contact with the absolute intrapair difference in BMI and found small but significant correlations ($r = .10, p < .001$, and $r = .14\ p < .001$) for both measures, indicating greater similarity between twins in closer contact. Quite possibly, these effects are reflected in the MZ and DZ special twin environment parameters in the Stealth model. More explicit modeling of contact effects such as those described by Kendler *et al.* (1993) could test this hypothesis if incorporated into the stealth model.

Fifth, the structural equation model we used is a simple linear model, but the relationship between genes and phenotype or between environment and phenotype may be nonlinear. The relationship between these variables may also be moderated by a variety of other genetic, environmental, or phenotypic factors, which have not been taken into account here. Nevertheless, a linear model is a good place to begin the analysis of complex phenotypes, being simple, easily communicated, and easily falsified, which are all desirable properties of a scientific model (Popper, 1961).

Finally, we emphasize that the heritability of a trait as estimated from twin, adoption, and family studies does not exclude environmental pathways. For example, a genetic predisposition to select or request a large proportion of fatty foods from the available diet is clearly dependent on the availability of such foods. Therefore while predisposition to obesity might be due largely to individual differences in metabolism, it is also possible that behavioral and environmental pathways are significant. Simultaneous measurement of plausible metabolic and nutritional factors in a genetically informative

design is needed to distinguish between these alternatives. It seems quite likely that there exists heterogeneity in the population, such that what is a primary cause of obesity in one individual may be a minor cause in another. Commingling analysis may reveal some of this heterogeneity, but experience in the relative power and robustness of segregation analysis vs linkage analysis implies that heterogeneity would most effectively be discerned when associated with some external, measurable factor.

ACKNOWLEDGMENTS

This research was supported by NIH Grants MH-45268 and RR-08123 and grants from the J. M. Templeton Foundation and the Carman Trust. We are grateful to Dr. K. S. Kendler for helpful comments on an early draft of this paper.

REFERENCES

Allison, D. B. (1995). Methodological issues in obesity research: Examples from biometrical genetics. In Vanltallie, T. B., and Simopoulos, A. P. (eds.), *Obesity. New Directions in Assessment and Management*, Charles Press, Philadelphia, pp. 122–132.

Allison, D. B., Heshka, S., Neale, M. C., and Heymsfield, S. B. (1994). Race effects in the genetics of adolescents' body mass index. *Int. J. Obes.* **18**:363–368.

Allison, D. B., Paultre, F., Heymsfield, S. M., and Pi-Sunyer, F. X. (1995). Is the intra-uterine period really a critical period for the development of adiposity? *Int. J. Obes.* **19**: 397–402.

Allison, D. B., Kaprio, J., Korkeila, M., Koskenvuo, M., Neale, M. C., and Hayakawa, K. (1996a). The heritability of body mass index among an international sample of monozygotic twins reared apart. *Int. J. Obes.* **20**:501–506.

Allison, D. B., Neale, M. C., Kezis, M. I., Alfonso, V. C., Heshka, S., and Heymsfield, S. B. (1996b). Assortative mating for relative weight: Genetic implications. *Behav. Genet.* **26**:103–111.

Annest, J. L., Sing, C. F., Biron, P., and Mongeau, J. G. (1983). Familial aggregation of blood pressure and weight in adoptive families. *Am. J. Epidemiol.* **117**:492–506.

Austin, M. A., King, M. C., Bawol, R. D., Hulley, S. B., and Friedman, G. D. (1987). Risk factors for coronary heart disease in adult female twins. *Am. J. Epidemiol.* **125**:308–318.

Ayatollahi, S. M. T. (1992). Obesity in school children and their parents in southern Iran. *Int. J. Obes.* **16**:845–850.

Bayley, N. (1954). Some increasing parent-child similarities during the growth of children. *J. Educ. Psych.* **45**:1–21.

Beunen, G., Maes, H. H., Vlietinck, R., Malina, R. M., Thomis, M., Feys, E., Loos, R., and Derom, C. (1997). Univariate and multivariate genetic analysis of subcutaneous fat distribution in early adolescence (submitted for publication).

Biron, P., Mongeau, J. G., and Bertrand, D. (1977). Familial resemblance of body weight and weight/height in 374 homes with adopted children. *J. Pediatr.* **91**:555–558.

Bodurtha, J. N., Mosteller, M., Hewitt, J. K., Nance, W. E., Eaves, L. J., Moskowitz, W. B., Katz, S., and Schieken, R. M. (1990). Genetic analysis of anthropometric measures in 11-year-old twins: The Medical College of Virginia Twin Study. *Pediatr. Res.* **28**:1–4.

Borjeson, M. (1976). The aetiology of obesity in children. *Acta Paediatr. Scand.* **65**:279–287.

Bouchard, C. (1987). Genetics of body fat, energy expenditure and adipose tissue metabolism. In Blondheim, B., and Shafrir, E. (eds.), *Recent Advances in Obesity Research V*, J. Libby, London.

Bouchard, C. (1995). Genetic epidemiology, association, and sib-pair linkage: Results from the Quebec Family Study. In Bray, G. A., and Ryan, D. H. (eds.), *Molecular and Genetic Aspects of Obesity*. Louisiana State University Press, Baton Rouge, pp. 470–481.

Bouchard, C., and Pérusse, L. (1988). Heredity and body fat. *Annu. Rev. Nutr.* **8**:259–277.

Bouchard, C., and Pérusse, L. (1993). Genetic aspects of obesity. In Williams, C. L., and Kimm, S. Y. S. (eds.), *Prevention and Treatment of Childhood Obesity* (Annals of the New York Academy of Sciences, Vol. 699), New York Academy of Sciences, New York, pp. 26–35.

Bouchard, C., and Pérusse, L. (1994). Genetics of obesity: Family studies. In Bouchard, C. (ed.), *The Genetics of Obesity*, CRC Press, Boca Raton, FL, pp. 79–92.

Bouchard, C., Savard, R., Després, J. P., Tremblay, A., and Leblanc, C. (1985). Body composition in adopted and biological siblings. *Hum. Biol.* **57**:61–75.

Bouchard, C., Pérusse, L., Leblanc, C., Tremblay, A., and Theriault, G. (1987). Inheritance of the amount and distribution of human body fat. *Int. J. Obes.* **12**:205–215.

Bouchard, C., Tremblay, A., Després, J. P., Nadeau, A., Lupien, P. J., Thériault, G., Dussault, J., Moorjani, S., Pinault, S., and Fournier, G. (1990). The response to long-term overfeeding in identical twins. *N. Engl. J. Med.* **322**:1477–1482.

Brook, C. G. D., Huntley, R. M. C., and Slack, J. (1975). Influence of heredity and environment in determination of skinfold thickness in children. *Br. Med. J.* **2**:719–721.

Burns, T. L., Moll, P. P., and Lauer, R. M. (1989). The relation between ponderosity and coronary risk factors in children and their relatives. The Muscatine Ponderosity Family Study. *Am. J. Epidemiol.* **129**:973–987.

Byard, P. J., Siervogel, R. M., and Roche, A. F. (1983). Sibling correlations for weight/stature^2 and calf circumference: Age changes and possible sex linkage. *Hum. Biol.* **55**: 677–685.

Byard, P. J., Siervogel, R. M., and Roche, A. F. (1989). X-linked pattern of inheritance for serial measures of weight/stature^2. *Am. J. Hum. Biol.* **1**:443–449.

Cardon, L. R. (1995). Genetic influences on body mass index in early childhood. In Turner, J. R., Cardon, L. R., and Hewitt, J. K. (eds.), *Behavior Genetic Approaches in Behavioral Medicine*, Plenum Press, New York, London, pp. 133–143.

Carmichael, C. M., and McGue, M. (1995). A cross-sectional examination of height, weight, and body mass index in adult twins. *J. Gerontol.* **50A**:B237–B244.

Comuzzie, A. G., Blangero, J., Mahaney, M. C., Mitchell, B. D., Stern, M. P., and MacCluer, J. W. (1994). Genetic and environmental correlations among skinfold measures. *Int. J. Obes.* **18**:413–418.

Donahue, R. P., Prineas, R. J., Gomez, O., and Hong, C. P. (1992). Familial resemblance of body fat distribution: The Minneapolis Children's Blood Pressure Study. *Int. J. Obes.* **16**:161–167.

Eaves, L. J., Heath, A. C., and Martin, N. G. (1997). Comparing the biological and cultural inheritance of stature and conservatism in the kinships of monozygotic and dizygotic twins. In Cloninger, C. R. (ed.), *Proceedings of 1994 APPA Conference* (in press).

Esposito-Del Puente, A., Scalfi, L., De Filippo, E., Peri, M. R., Caldara, A., Caso, G., Contaldo, F., Valerio, G., Franzese, A., Di Maio, S., and Rubino, A. (1994). Familial and environmental influences on body composition and body fat distribution in childhood in Southern Italy. *Int. J. Obes.* **18**:596–601.

Fabsitz, R. R., Garrison, R. J., Feinleib, M., and Hjortland, M. (1978). A twin analysis of dietary intake: Evidence for a need to control for possible environmental differences in MZ and DZ twins. *Behav. Genet.* **8**:15–25.

Fabsitz, R., Feinleib, M., and Hrubec, Z. (1980). Weight changes in adult twins. *Acta Genet. Med. Gemellol.* **29**: 273–279.

Fabsitz, R., Carmelli, D., and Hewitt, J. K. (1992). Evidence for independent genetic influences on obesity in middle age. *Int. J. Obes.* **16**:657–666.

Feinleib, M., Garrison, R. J., Fabsitz, R., Christian, J. C., Hrubec, Z., Borhani, N. O., Kannel, W. B., Rosenman, R., Schwartz, J. T., and Wagner, J. O. (1977). The NHLBI Twin Study of cardiovascular disease risk factors: Methodology and summary of results. *Am. J. Epidemiol.* **106**: 284–295.

Friedlander, Y., Kark, J. D., Kaufmann, N. A., Berry, E. M., and Stein, Y. (1987). Familial aggregation of body mass index in ethnically diverse families in Jerusalem. The Jerusalem Lipid Research Clinic. *Int. J. Obes.* **12**:237–247.

Fulker, D. W. (1982). Extensions of the classical twin method. In Bonne-Tamir, B. (ed.), *Human Genetics, Part A: The Unfolding Genome* (Progress in Clinical and Biological Research 103A), Alan R. Liss, New York, pp. 395–406.

Garn, S. M., Cole, P. E., and Bailey, S. M. (1979). Living together as a factor in family-line resemblances. *Hum. Biol.* **51**:565–587.

Garn, S. M., Sullivan, T. V., and Hawthorne, V. M. (1989). Fatness and obesity of the parents of obese individuals. *Am. J. Clin. Nutr.* **50**:1308–1313.

Grilo, C. M., and Pogue-Geile, M. F. (1991). The nature of environmental influences on weight and obesity: A behavior genetic analysis. *Psych. Bull.* **110**:520–537.

Guillaume, M., Lapidus, L., Beckers, F., Lambert, A., and Bjorntorp, P. (1995). Familial trends of obesity through three generations: the Belgian-Luxembourg child study. *Int. J. Obes.* **19**(Suppl. 3):S5–S9.

Harris, J. R., Tambs, K., and Magnus, P. (1995). Sex-specific effects for body mass index in the new Norwegian Twin Panel. *Genet. Epidemiol.* **12**:251–265.

Hartz, A., Giefer, E., and Rimm, A. A. (1977). Relative importance of the effect of family environment and heredity on obesity. *Ann. Hum. Genet.* **41**:185–193.

Hawk, L. J., and Brook, G. D. (1979). Family resemblances of height, weight, and body fatness. *Arch. Dis. Child.* **54**: 877–879.

Heller, R., Garrison, R. J., Havlik, R. J., Feinleib, M., and Padgett, S. (1983). Family resemblances in weight and relative weight in the Framingham Heart Study. *Int. J. Obes.* **8**:399–405.

Heller, R. F., O'Connell, D. L., Roberts, D. C. K., Allen, J. R., Knapp, J. C., Steele, P. L., and Silove, D. (1988). Lifestyle factors in monozygotic and dizygotic twins. *Genet. Epidemiol.* **5**:311–321.

Herskind, A. M., McGue, M., Sorensen, T. I. A., and Harvald, B. (1996). Sex and age specific assessment of genetic and environmental influences on body mass index in twins. *Int. J. Obes.* **20**:106–113.

Hewitt, J. K., Stunkard, A. J., Carroll, D., Sims, J., and Turner, J. R. (1991). A twin study approach towards understanding genetic contributions to body size and metabolic rate. *Acta Genet. Med. Gemellol.* **40**:133–146.

Hunt, S. C., Hasstedt, S. J., Kuida, H., Stults, B. M., Hopkins, P. N., and Williams, R. R. (1989). Genetic heritability and common environmental components of resting and stressed blood pressures, lipids, and body mass index in Utah pedigrees and twins. *Am. J. Epidemiol.* **129**:625–638.

Kapoor, S., Kapoor, A. K., Bhalla, R., and Singh, I. P. (1985). Parent-offspring correlation for body measurements and subcutaneous fat distribution. *Hum. Biol.* **57**:141–150.

Kaur, D. P., and Singh, R. (1981). Parent-adult offspring correlations and heritability of body measurements in a rural Indian population. *Ann. Hum. Biol.* **8**:333–339.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., and Eaves, L. J. (1993). A test of the equal-environment assumption in twin studies of psychiatric illness. *Behav. Genet.* **23**:21–27.

Khoury, P., Morrison, J. A., Laskarzewski, P. M., and Glueck, C. J. (1983). Parent-offspring and sibling body mass index associations during and after sharing of common household environments: The Princeton School District Family Study. *Metabolism* **32**:82–89.

Knuiman, M. W., Divitini, M. L., Bartholomew, H. C., and Welborn, T. A. (1996). Spouse correlations in cardiovascular risk factors and the effect of marriage duration. *Am. J. Epidemiol.* **143**:48–53.

Korkeila, M., Kaprio, J., Rissanen, A., and Koskenvuo, M. (1991). Effects of gender and age on the heritability of body mass index. *Int. J. Obes.* **15**:647–654.

Korkeila, M., Kaprio, J., Rissanen, A., and Koskenvuo, M. (1995). Consistency and change of body mass index and weight. A study on 5967 adult Finnish twin pairs. *Int. J. Obes.* **19**:310–317.

Longini, I. M., Higgins, M. W., Hinton, P. C., Moll, P. P., and Keller, J. B. (1984). Genetic and environmental sources of familial aggregation of body mass in Tecumseh, Michigan. *Hum. Biol.* **4**:733–757.

Luke, B., Leurgans, S., Keith, L., and Keith, D. (1995). The childhood growth of twin children. *Acta Genet. Med. Gemellol.* **44**:169–178.

Lykken, D. T., McGue, M., Tellegen, A., and De Rubeis, R. (1987). Recruitment bias in twin research: The rule of two-thirds reconsidered. *Behav. Genet.* **17**:343–362.

Lykken, D. T., McGue, M., Bouchard, T. J., Jr., and Tellegen, A. (1990). Does contact lead to similarity or similarity to contact? *Behav. Genet.* **20**:547–561.

Lykken, D. T., McGue, M., Tellegen, A., and Bouchard, T. J. (1992). Emergenesis. Genetic traits that may not run in families. *Am. Psychol.* **47**:1565–1577.

Lytton, H. (1977). Do parents create, or respond to, differences in twins? *Dev. Psych.* **13**:456–459.

Macdonald, A., and Stunkard, A. (1990). Body-mass indexes of British separated twins. *N. Engl. J. Med.* **24**:1530.

Maes, H. (1992). *Univariate and Multivariate Genetic Analysis of Physical Characteristics of Twins and Parents*, Unpublished doctoral dissertation, Katholieke Universiteit Leuven, Leuven.

Maes, H. H. M., Beunen, G. P., Vlietinck, R. F., Neale, M. C., Thomis, M., Vanden Eynde, B., Lysens, R., Simons,

J., Derom, C., and Derom, R. (1996). Inheritance of physical fitness in 10-year-old twins and their parents. *Med. Sci. Sports Exerc.* **28**:1479–1491.

Martin, N. G., Eaves, L. J., Kearzey, M. J., and Davies, P. (1978). The power of the classical twin study. *Heredity* **40**:97–116.

Meyer, J. M. (1995). Genetic studies of obesity across the life span. In Turner, J. R., Cardou, L. R., and Hewitt, J. K. (eds.), *Behavior Genetic Approaches in Behavioral Medicine*, Plenum Press, New York, London, pp. 145–166.

Meyer, J. M., and Stunkard, A. J. (1993). Genetics and human obesity. In Stunkard, A. J., and Wadden, T. A. (eds.), *Obesity: Theory and Therapy*, Raven Press, New York, pp. 137–149.

Meyer, J. M., and Stunkard, A. J. (1994). Twin studies of human obesity. In Bouchard, C. (ed.), *The Genetics of Obesity*, CRC Press, Boca Raton, FL, pp. 63–78.

Meyer, J. M., Silberg, J. L., Eaves, L. J., Maes, H. H., Simonoff, E., Pickles, A., Rutter, M. L., and Hewitt, J. K. (1996). Variable age of gene expression: Implications for developmental genetic models. In LaBuda, M. C., and Grigorenko, E. L. (eds.), *On the Way to Individuality: Current Methodological Issues in Behavioral Genetics*, Progress Publishers, Moscow (in press).

Meyer, J. M., Bodurtha, J. N., Eaves, L. J., Hewitt, J. K., Mosteller, M., Nance, W. E., Neale, M. C., and Schieken, R. M. (1997). Tracking genetic and environmental effects on adolescent BMI: The MCV Twin Study (submitted for publication).

Moll, P. P., Burns, T. L., and Lauer, R. M. (1991). The genetic and environmental sources of body mass index variability: The Muscatine Ponderosity Family Study. *Am. J. Hum. Genet.* **49**:1243–1255.

Mueller, W. H. (1978). Transient environmental changes and age-limited genes as causes of variation in sib-sib and parent-offspring correlations. *Ann. Hum. Biol.* 5:395–398.

Mueller, W. H., and Malina, R. M. (1980). Genetic and environmental influences on growth of Philadelphia Black and White schoolchildren. *Ann. Hum. Biol.* 7:441–448.

Neale, M. C. (1995). *Mx: Statistical Modeling*, 3rd ed., Department of Psychiatry, Medical College of Virginia, Richmond.

Neale, M. C., and Cardon, L. R. (1992). *Methodology for Genetic Studies of Twins and Families*, Kluwer Academic, Dordrecht.

Neale, M. C., and Eaves, L. J. (1993). Estimating and controlling for the effects of volunteer bias with pairs of relatives. *Behav. Genet.* **23**:271–277.

Neale, M. C., and Eaves, L. J. (1995). Research design and methods to study the genetic epidemiology of obesity. In Allison, D. B., and Pi-Sunyer, F. X. (eds.), *Obesity Treatment*, Plenum Press, New York, pp. 225–238.

Ness, R., Laskarzewski, P., and Price, R. A. (1991). Inheritance of extreme overweight in black families, *Hum. Biol.* **63**:39–52.

Nirmala, A., Mitchell, L. E., Rice, T., Chengal Reddy, P., and Rao, D. C. (1993). Assessment of adiposity in an Indian population: Familial correlations. *Genet. Epidemiol.* **10**: 133–143.

Pérusse, L., Leblanc, C., Tremblay, A., Allard, C., Thériault, G., Landry, R., Talbot, J., and Bouchard, C. (1987). Familial aggregation in physical fitness, coronary heart disease risk factors, and pulmonary function measurements. *Prev. Med.* **16**:607–615.

Pérusse, L., Leblanc, C., and Bouchard, C. (1988). Inter-generation transmission of physical fitness in the Canadian population. *Can. J. Spt. Sci.* **13**:8–14.

Phillips, K., and Fulker, D. W. (1989). Quantitative genetic analysis of longitudinal trends in adoption designs with application to IQ in the Colorado Adoption Project. *Behav. Genet.* **19**:621–658.

Plomin, R., and DeFries, J. C. (1990). *Behavioral Genetics: A Primer*, 2nd ed., W. H. Freeman, New York.

Popper, K. R. (1961). *The Logic of Scientific Discovery*, Science Editions, New York (translation; original work published 1934).

Price, R. A. (1987). Genetics of human obesity. *Ann. Behav. Med.* **9**:9–14.

Price, R. A., and Gottesman, I. I. (1991). Body fat in identical twins reared apart: Roles for genes and environment. *Behav. Genet.* **21**:1–7.

Price, R. A., Cadoret, R. J., Stunkard, A. J., and Troughton, E. (1987). Genetic contributions to human fatness: An adoption study. *Am. J. Psychiatry* **144**:1003–1008.

Price, R. A., Stunkard, A. J., Ness, R., Wadden, T., Heshka, S., Kanders, B., and Cormillot, A. (1990). Childhood onset (age <10) obesity has high familial risk. *Int. J. Obes.* **14**:185–195.

Province, M. A., and Rao, D. C. (1985). Path analysis of family resemblance with temporal trends: Applications to height and weight, and Quetelet Index in northeastern Brazil. *Am. J. Hum. Genet.* **37**:178–192.

Ramirez, M. E. (1993). Familial aggregation of subcutaneous fat deposits and the peripheral fat distribution pattern. *Int. J. Obes.* **17**:63–68.

Rice, J., Cloninger, C. R., and Reich, T. (1978). Multifactorial inheritance with cultural transmission and assortative mating. I. Description and basic properties of the unitary models. *Am. J. Hum. Genet.* **30**:618–643.

Rice, T., Bouchard, C., Pérusse, L., and Rao, D. C. (1995). Familial clustering of multiple measures of adiposity and fat distribution in the Québec family study: A trivariate analysis of percent body fat, body mass index, and trunk-to-extremity skinfold ratio. *Int. J. Obes.* **19**:902–908.

Rose, R. J., Kaprio, J., Williams, C. J., Viken, R., and Obremski, K. (1990). Social contact and sibling similarity: Facts, issues, and red herrings. *Behav. Genet.* **20**:763–778.

Rotimi, C., and Cooper, R. (1995). Familial resemblance for anthropometric measurements and relative fat distribution among African Americans. *Int. J. Obes.* **19**:875–880.

Scarr, S., and Carter-Saltzman, L. (1979). Twin method: Defense of a critical assumption. *Behav. Genet.* **9**:527–542.

Selby, J. V., Reed, T., Newman, B., Fabsitz, R. R., and Carmelli, D. (1991). Effects of selective return on estimates of heritability for body mass index in the National Heart, Lung, and Blood Institute Twin Study. *Genet. Epidemiol.* **8**:371–380.

Sellers, T. A., Drinkard, C., Rich, S. S., Potter, J. D., Jeffery, R. W., Hong, C. P., and Folsom, A. R. (1994). Familial aggregation and heritability of waist-to-hip ratio in adult women: The Iowa Women's Health Study. *Int. J. Obes. Relat. Metab. Disord.* **18**:607–613.

Sorensen, T. I. A. (1995). Adoption studies of obesity. In Bray, G. A., and Ryan, D. H. (eds.), *Molecular and Genetic Aspects of Obesity*, Louisiana State University Press, Baton Rouge, pp. 462–469.

Sorensen, T. I. A., and Stunkard, A. J. (1994). Overview of the adoption studies. In Bouchard, C. (ed.), *The Genetics of Obesity*, CRC Press, Boca Raton, FL, pp. 49–61.

Sorensen, T. I. A., Price, R. A., Stunkard, A. J., and Schulsinger, F. (1989). Genetics of obesity in adult adoptees and their biological siblings. *Br. Med. J.* **298**:87–90.

Sorensen, T. I. A., Holst, C., and Stunkard, A. J. (1992a). Childhood body mass index—Genetic and familial envi-

ronmental influences assessed in a longitudinal study. *Int. J. Obes.* **16**:705–714.

Sorensen, T. I. A., Holst, C., Stunkard, A. J., and Skovgaard, L. T. (1992b). Correlations of body mass index of adult adoptees and their biological and adoptive relatives. *Int. J. Obes.* **16**:227–236.

Stunkard, A. J. (1991). Genetic contributions to human obesity. In McHugh P. R, and McKusick, V. A. (eds.), *Genes, Brain, and Behavior*, Raven Press, New York, pp. 205–218.

Stunkard, A. J., Foch, T. T., and Hrubec, Z. (1986a). A twin study of human obesity. *JAMA* **256**:51–54.

Stunkard, A. J., Sorensen, T. I. A., Hanis, C., Teasdale, T. W., Chakrabory, R., Schull, W. J., and Schulsinger, F. (1986b). An adoption study of human obesity. *N. Engl. J. Med.* **314**:193–198.

Stunkard, A. J., Harris, J. R., Pedersen, N., and McClearn, G. E. (1990). The body mass index of twins who have been reared apart. *N. Engl. J. Med.* **322**:1483–1487.

Tambs, K., Mourn, T., Eaves, L., Neale, M., Midthjell, K., Lund-Larsen, P. G., Næss, S., and Holmen, J. (1991). Genetic and environmental contributions to the variance of the body mass index in a Norwegian sample of first- and second-degree relatives. *Am. J. Hum. Biol.* 3:257–267.

Tanner, J. M., and Israelsohn, W. J. (1963). Parent-child correlations for body measurements of children between the ages one month and seven years. *Ann. Hum. Genet.* **26**: 245–259.

Truett, K. R., Eaves, L. J., Walters, E. E., Heath, A. C., Hewitt, J. K., Meyer, J. M., Silberg, J., Neale, M. C., Martin, N. G., and Kendler, K. S. (1994). A model system for analysis of family resemblance in extended kinships of twins. *Behav. Genet.* **24**:35–49.

Turula, M., Kaprio, J., Rissanen, A., and Koskenvuo, M. (1990). Body weight in the Finnish Twin Cohort. *Diabetese Res. Clin. Pract.* **10**:533–536.

Vogler, G. P., Sorensen, T. I. A., Stunkard, A. J., Srinivasan, M. R., and Rao, D. C. (1995). Influences of genes and shared family environment on adult body mass index assessed in an adoption study by a comprehensive path model. *Int. J. Obes.* **19**:40–45.

Wang, Z., Ouyang, Z., Wang, D., and Tang, X. (1990). Heritability of blood pressure in 7- to 12-year-old Chinese twins, with special reference to body size effects. *Genet. Epidemiol.* **7**:447–452.

Wilson, R. S. (1986). Growth and development of human twins. In Falkner, F., and Tanner, J. M. (eds.), *Human Growth. A Comprehensive Treatise*, Plenum Press, New York, pp. 197–211.

Withers, R. F. J. (1964). Problems in the genetics of human obesity. *Eugen. Rev.* **56**:81–90.

Zonta, L. A., Jayakar, S. D., Bosisio, M., Galante, A., and Pennetti, V. (1987). Genetic analysis of human obesity in an Italian sample. *Hum. Hered.* **37**:129–139.

Edited by David B. Allison and Myles S. Faith