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Original Contribution

Genetic and Environmental Influences on Birth Weight, Birth Length, Head Circumference, and Gestational Age by Use of Population-based Parent-Offspring Data

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Familial correlations in birth weight and gestational age have been explained by fetal and maternal genetic factors, mainly in studies on offspring of twins. The aim of the present intergenerational study was to estimate and compare fetal and maternal genetic effects and shared sibling environmental effects on birth weight and gestational age and also on crown-heel length and head circumference. The authors used path analysis and maximum likelihood principles to estimate these effects and, at the same time, to adjust for covariates. Parent-offspring data were obtained from the Medical Birth Registry of Norway from 1967 to 2004. For the analysis of birth weight and crown-heel length, 101,748 families were included; for gestational age, 91,617 families; and for head circumference, 77,044 families. Assuming no cultural transmission and random mating, the authors found that fetal genetic factors explained 31% of the normal variation in birth weight and birth length, 27% of the variation in head circumference, and 11% of the variation in gestational age. Maternal genetic factors explained 22% of the variation in birth weight, 19% of the variation in birth length and head circumference, and 14% of the variation in gestational age. Relative to the proportion of explained variation, fetal genes were most important for birth length and head circumference.

birth weight; family; gestational age; mixed linear model; path analysis; variance components

Abbreviations: MBRN, Medical Birth Registry of Norway; SD, standard deviation.

Editor's note: *A related article appears on page 742, and an invited commentary on these two articles is published on page 753.*

Size at birth is associated with not only perinatal mortality and morbidity but also with diseases in adulthood, such as cardiovascular disease and type 2 diabetes. The associations between size at birth and adult disease have been explained by alterations in fetal nutrition and endocrine status, which permanently change the structure, physiology, and metabolism of the fetus and predispose individuals to adult disease (1). Alternatively, the associations between size at birth and adult disease may be explained by genetic factors influencing both fetal growth and predisposition for adult diseases (2). Understanding the causes of variation in birth measurements is important in

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relation to their impact on outcomes in both the perinatal period and later life, in order to provide opportunities for prevention and intervention.

Efforts to locate and identify genes controlling human traits, such as birth weight, are usually done on a gene-to-gene basis, without knowing the chances of success in advance. The more traditional biometric analyses, such as path analysis, aim at estimating the overall balance between the genetic and environmental factors determining a trait. This is of interest in a population setting, when assessing the possible effects of genetic or environmental interventions targeted at a specific disorder or when assessing the feasibility of a more detailed gene search.

Both intergenerational studies and studies on offspring of twins have described familial correlations in birth weight and fetal growth, as well as in gestational age at birth (3–11). Such associations may be explained by fetal genes passed on from the father and the mother to the fetus and by maternal genes acting on the mother's capability of carrying a pregnancy, but they also may be explained by environmental factors that are shared among relatives.

Magnus (4, 5) and Clausson et al. (8) have described estimates of heritability in birth weight by use of data on offspring of twins. Magnus (4) found that 50 percent of the variability in birth weight could be explained by fetal genes, whereas Clausson et al. (8) estimated heritability to be around 40 percent. Recently, Magnus et al. (7) used mother–father–first child trios and concluded that, under the assumption of no cultural transmission on the paternal side, estimates of heritability in birth weight were 25 percent.

Clausson et al. (8) also estimated the heritability of gestational age to be around 30 percent. Earlier data from the 1958 British birth cohort showed that both maternal and paternal gestational ages had independent effects on term offspring's gestational age (10). A recent Norwegian study confirms this (12).

Few studies have focused on familial influences on newborns' length or head circumference at birth. A recent study from Norway reported full-sibling correlations for birth weight ($r = 0.48$), crown-heel length ($r = 0.39$), head circumference ($r = 0.36$), and gestational age ($r = 0.29$) (11).

The aim of the present study was to estimate and compare the contributions of fetal and maternal genetic factors and sibling environmental factors to birth weight, crown-heel length, head circumference, and gestational age and also to evaluate whether the higher sibling correlations in birth weight, compared with the other phenotypes (11), could be explained by stronger genetic or sibling environmental effects. By use of parent-offspring data including data on maternal half siblings, biometric methods in quantitative genetics (13) together with maximum likelihood principles (14, 15) provide opportunities to separate the different components of familial associations. These methods typically model (unobserved) genetic and environmental factors as latent variables that influence the variance of the observed trait. By utilization of the correlation between family members, components such as fetal genes and the shared and sporadic environment can be identified, and their relative contributions to the variance of the trait can be estimated.

MATERIALS AND METHODS

The study was based on parent-offspring data from the Medical Birth Registry of Norway (MBRN). Based on compulsory notification, the MBRN comprises data on all livebirths and stillbirths from 16 weeks' gestation in the country since 1967, with a total of more than 2.2 million births. A standardized notification form is used to collect data on demographic variables, maternal health before and during pregnancy, previous reproductive history, complications during pregnancy and delivery, and pregnancy outcomes. A national identification number is given to all liveborn infants, enabling linkage of data on the mother's successive births to the mother's and father's own birth records, thus providing generation files with birth records on families.

Data selection

The original study sample consisted of 133,638 families with birth records of the father, mother, and their offspring—all singletons. We included the first three offspring, as well as families with only one and only two offspring. Both full siblings and maternal half siblings were included and identified by means of fathers' national identification numbers. If information on the father was missing, this child was excluded (5,475 births). Only the birth record of the first known father was included. Families were included in the cohort if inclusion criteria were met by both parents (first generation). Families where individual infants (second generation) had missing information or did not fulfill inclusion criteria might, however, be included but without those specific births. As generational differences in survival might affect the variables of interest, families with stillbirths or neonatal deaths (first month) in the second generation were not included (2,149 families). Finally, deliveries by cesarean section (both generations) were excluded (18,120 families), as these deliveries may be indicated as the result of pathologic conditions disturbing the normal processes of growth and pregnancy duration that we wanted to evaluate.

Data screening

We excluded births with missing birth weight or birth length (2,979 families). As the parameters of interest (path coefficients) and correlations are generally sensitive to extreme values, the data were screened for possible errors by use of polynomial regression, using birth weight as the dependent variable and birth length as the independent variable (975 families excluded). We further excluded births delivered before 35 completed weeks of gestation (2,725 families), where gestational age was based on the mother's reported date of the last menstrual period. The cutoff point of 35 weeks was chosen because we wanted to describe and compare the normal variation in the studied phenotypes, without a large influence of different pathologic conditions and without truncating any of the distributions. Likewise, to avoid the influence of extremely growth-restricted infants, we excluded births with birth weight less than 3 standard deviations below the mean birth weight at 35 gestational weeks, i.e., below 1,400 g (16). For births with missing

gestational age, we excluded births with birth weight less than 2,500 g. The final data set after these exclusions comprised 101,748 families. Table 1 shows the sample sizes used in the different analyses, plus the mean and standard deviation, stratified by type of family and family member.

For the analysis of gestational age, we excluded births with missing data on gestational age (10,580 families). Because of the acknowledged uncertainty in gestational age estimations based on menstrual dates, gestational age was screened by calculating birth weight z scores for each gestational week, and we excluded births with z scores (absolute values) greater than 3.5 (4,687 families) (16). Gestational ages above 44 completed weeks were also excluded, and we were left with 91,617 families (table 1).

Head circumference has been registered for a shorter time period in the MBRN (since 1978); thus, we had only 5,611 families with data on both parents but a total of 80,010 families if we did not require parental data (before screening). Therefore, infants (second generation) were included even if one or both of the parents had missing data on head circumference. Again, outliers were excluded by use of polynomial regression, using birth weight as the dependent variable and head circumference as the independent variable, and the final data set comprised 77,044 families (table 1).

Statistical analysis

For an initial evaluation of how the different phenotypes were distributed, we calculated Pearson's correlation coefficients for different familial relations (table 2). The correlations were based on a weighted average of the correlation coefficients stratified by the infants' birth order (second generation). By use of Fisher's z transformation (17), 95 percent confidence intervals were calculated.

To explain the correlations and the phenotypic variation in the study population in terms of genetic and environmental effects, we used path analysis (13, 18, 19). Central to path analysis is the idea of expressing phenotypic correlation between relatives as a combination of genotypic and environmental correlations. Using a path diagram (figure 1) and a simple set of tracing rules, the phenotypic correlations between the relatives can be found (table 3). The genetic effects were assumed to be polygenic, i.e., many genes with small and independent effects acting on the phenotype. No interactions between the effects were assumed, and both the genetic and environmental effects were assumed to be constant over time.

Figure 1 shows a path diagram for a family with two full siblings, where unobserved genetic and environmental factors (circles) contribute to the correlations among the relatives. The unobserved genotypic variables for the father, mother, and the two infants are represented by G_F, G_M, G_1, and G_2, all with an equal effect h (degree of penetrance) on the phenotypes (P_F, P_M, P_1, and P_2). The genotypic mother-child and father-child correlations are both assumed to be 0.5, i.e., an equal paternal and maternal contribution to the fetal genes explaining the phenotype. We assumed random mating and no cultural transmission between the generations, which means that only fetal (paternal) genes contributed to the father-child correlation (7). However, maternal genes also influence the fetus through the intrauterine

TABLE 1. Characteristics of the data, stratified by sex (first generation), type of family, and birth order (second generation), for the analysis of birth weight and birth length, head circumference, and gestational age, Norway, 1967–2004

	Mother	Father	Full sibling families						Half sibling families					
			First sibling		Second sibling		Third sibling		First sibling		Second sibling		Third sibling	
			Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys
Birth weight (g)														
Mean	3,465	3,610	3,501	3,614	3,638	3,782	3,693	3,821	3,452	3,555	3,586	3,724	3,627	3,761
Standard deviation	474	500	460	488	476	493	493	510	458	475	473	502	490	520
Birth length (cm)														
Mean	50.2	51.2	49.9	50.7	50.2	51.1	50.4	51.2	49.6	50.4	50.0	50.9	50.1	51.0
Standard deviation	1.95	2.04	1.95	2.07	1.93	1.98	1.92	2.02	1.93	2.06	1.93	2.02	1.95	2.05
No. of births	101,748	101,748	41,003	42,460	24,561	25,847	5,956	6,154	4,423	4,512	4,345	4,573	1,993	2,036
Head circumference (cm)														
Mean	34.8	35.5	34.9	35.5	35.1	35.8	35.2	35.9	34.7	35.3	35.0	35.6	35.1	35.8
Standard deviation	1.33	1.40	1.38	1.48	1.30	1.36	1.31	1.38	1.39	1.45	1.39	1.45	1.34	1.36
No. of births	15,042	6,838	30,800	32,409	25,724	27,108	6,627	6,792	5,324	5,336	5,188	5,469	2,303	2,407
Gestational age (weeks)														
Mean	40.49	40.36	40.51	40.35	40.52	40.38	40.52	40.38	40.56	40.43	40.60	40.53	40.67	40.51
Standard deviation	1.51	1.55	1.57	1.62	1.44	1.50	1.44	1.50	1.53	1.62	1.39	1.42	1.41	1.46
No. of births	91,617	91,617	36,568	37,754	22,204	23,447	5,808	5,895	2,794	2,897	2,940	3,002	1,063	1,203

TABLE 2. Empirical (observed) correlation coefficients, adjusted for infant's birth order (second generation), Norway, 1967–2004

Relationship	Birth weight		Birth length		Head circumference		Gestational age	
	Correlation	95% confidence interval	Correlation	95% confidence interval	Correlation	95% confidence interval	Correlation	95% confidence interval
Father-child	0.161	0.157, 0.166	0.164	0.159, 0.169	0.139	0.117, 0.161	0.060	0.055, 0.065
Mother-child	0.254	0.249, 0.258	0.242	0.237, 0.246	0.223	0.209, 0.236	0.126	0.121, 0.131
Full siblings	0.506	0.500, 0.512	0.408	0.401, 0.414	0.381	0.375, 0.387	0.316	0.309, 0.324
Maternal half siblings	0.401	0.386, 0.415	0.313	0.297, 0.328	0.284	0.270, 0.299	0.215	0.195, 0.234

environment. Thus, maternal genotypic variables for the mother (GI_M) and mother's mother (GI_{MM}), with a correlation of 0.5, were included to account for the higher mother-child correlation (table 2), both with an effect m on the offspring phenotypes.

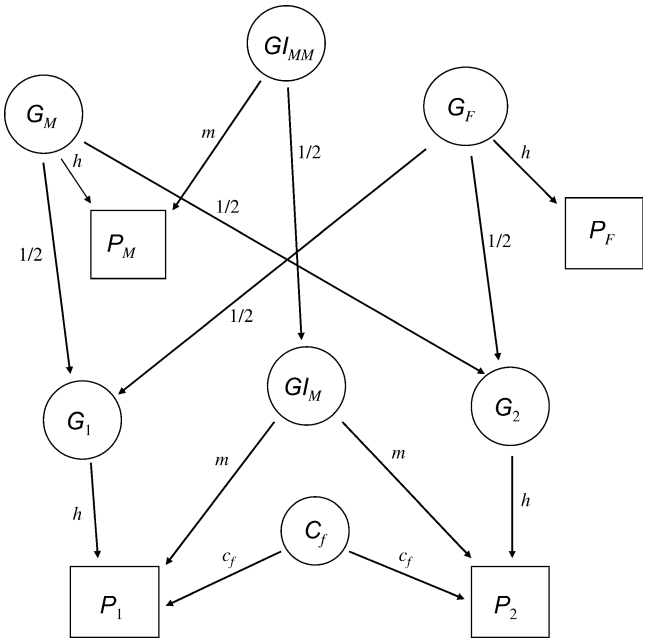

FIGURE 1. Path analytical diagram for a family consisting of mother (*M*), father (*F*), and two full siblings (1 and 2), together with mother's mother (*MM*). Arrows show how phenotypes (*P*) are influenced by fetal genes (*G*), maternal genes (*GI*), and a common sibling environment (C_f). Subscripts denote family member such that, for instance, P_M is the mother's phenotype. Rectangles denote observed quantities (phenotypes), while circles denote unobserved quantities (genes/environment). By use of a standard set of tracing rules (Li CC. *Path Analysis—A Primer*. Pacific Grove, CA: The Boxwood Press, 1975 (13)), the phenotypic correlations between the relatives can be found (table 3). The squared path coefficients (h^2, m^2, c_f^2) express the relative contribution of fetal and maternal genotypes, as well as the full sibling's environment, to the total population variance. The genotypic correlation between full siblings is 0.5, and between maternal half siblings it is 0.25. The model correlation between maternal half siblings can be found by removing the arrow between G_F and G_2 and between G_2 and P_2.

The genotypic correlation between full siblings is 0.5 and between (maternal) half siblings, 0.25. For the phenotypes studied, the difference in empirical correlation between full siblings and half siblings (table 2) was larger than the predicted difference of $1/4h^2$ (table 3). To account for this difference, the variables C_f and C_h were included to represent shared full sibling and half sibling environments, respectively, with effects c_f and c_h on the sibling phenotypes. Finally, a residual environment (unexplained variability) E also affects the phenotypes and accounts for the individual specific (sporadic) environment, as well as measurement errors. We estimated separate effects for the full and the half sibling environments and estimated the corresponding proportions of unexplained variability, represented by e_f^2 and e_h^2, respectively.

The squared path coefficients (figure 1; table 3) express the relative contribution of the fetal (h^2) and maternal (m^2) genotype, the full (c_f^2) and the half (c_h^2) siblings' shared environment, and the respective proportions of unexplained variability e_f^2 and e_h^2 to the total population variance. Together with the equations of complete determination, $h^2 + m^2 + c_f^2 + e_f^2 = 1$ and $h^2 + m^2 + c_h^2 + e_h^2 = 1$, the squared path coefficients can be found. The proportion of unexplained variability for half siblings is, thus, $e_h^2 = c_f^2 - c_h^2 + e_f^2$.

Computational details

We used maximum likelihood techniques to estimate the path coefficients, while adjusting for covariates using a linear mixed-effects regression model (14, 15). The family

TABLE 3. Model correlations, derived from the path diagram in figure 1, expressed in terms of the fetal genetic effect, maternal genetic effect, and the full and half sibling environmental effects

Relationship	Correlation*
Father-infant	$1/2h^2$†
Mother-infant	$1/2h^2 + 1/2m^2$
Full siblings	$1/2h^2 + m^2 + c_f^2$
Maternal half siblings	$1/4h^2 + m^2 + c_h^2$

* The genotypic correlation between full siblings is 0.5, and between (maternal) half siblings it is 0.25.

† h^2, fetal genetic effect; m^2, maternal genetic effect; c_f^2, full sibling environmental effect; c_h^2, half sibling environmental effect.

phenotypic values, consisting of the phenotype of each family member, were assumed to be multivariate normally distributed with a correlation structure as given in table 3. We used as covariates birth order (three levels), sex and generation (two levels), and interactions among these. However, the interaction terms were not all significant for all the phenotypes (significance level of 0.05).

All the estimated path coefficients were significant (refer to confidence intervals), and the full and half sibling environments were significantly different from one another (tested by introducing a parameter for the difference between c_f^2 and c_h^2). Because of the large sample sizes, all submodels were significantly worse than the model we present.

The likelihood function was maximized with respect to the fixed effects, the path coefficients, and the population variance, using the AD Model Builder software package (20) for parameter estimation in linear and nonlinear models. The data were preprocessed by use of R, version 2.1.1, language and environment for statistical computing and graphics for UNIX (The Open Group, San Francisco, California).

RESULTS

For the phenotypes studied, the correlations among the relatives (table 2) followed the same pattern for the different phenotypes: The mother-child correlation was higher than the father-child correlation, and the highest correlations were found between the siblings. Here, the correlation between full siblings was higher than that between half siblings.

Maximum likelihood estimates of the squared path coefficients (h^2, m^2, c_f^2, c_h^2, e_f^2) were calculated for all four phenotypes (table 4). For gestational age, the covariates (birth order, sex, and generation) had only a small influence on the path coefficients, and the corresponding total variance reduction was only 0.16 percent. For birth weight, birth length, and head circumference, the variance reduction was 2.5, 3.1, and 3.2 percent, respectively.

Maternal age was also considered as a covariate, modeled as a factor with five levels, where interaction with type of family (full siblings/half siblings) and generation was considered. Maternal age had only a minor effect on the estimated path coefficients for the phenotypes studied.

The ordering of the path coefficients was $h^2 > m^2 > c_f^2 > c_h^2$ for all phenotypes except gestational age (table 4). Further, birth weight had the lowest proportions of unexplained variability (e_f^2, e_h^2) and the highest proportions of all the other effects. To compare the path coefficients across phenotypes, we divided each coefficient by its respective proportion of explained variation ($1 - e_f^2$, full siblings). The relative importance of fetal genes on the phenotypes was then greatest for birth length (52 percent) and somewhat less important for head circumference (49 percent) and birth weight (46 percent). The maternal genetic factors were most important for head circumference (35 percent) and equally important for birth length (33 percent) and birth weight (33 percent). The common full sibling environment was most

TABLE 4. Estimated squared path coefficients* (relative variances), adjusted for covariates (birth order, sex, and generation), explained in terms of a fetal genetic effect, a maternal genetic effect, shared full and half sibling environmental effects, and unexplained variation for full siblings and half siblings, Norway, 1967–2004

Effects	Birth weight		Birth length		Head circumference		Gestational age	
	Estimated squared path coefficient	95% confidence interval	Estimated squared path coefficient	95% confidence interval	Estimated squared path coefficient	95% confidence interval	Estimated squared path coefficient	95% confidence interval
Fetal genetic effect (h^2)	0.310	0.299, 0.320	0.306	0.295, 0.316	0.266	0.224, 0.308	0.113	0.102, 0.125
Maternal genetic effect (m^2)	0.221	0.206, 0.236	0.193	0.178, 0.208	0.188	0.137, 0.239	0.142	0.126, 0.158
Full sibling environmental effect (c_f^2)	0.148	0.135, 0.160	0.092	0.079, 0.105	0.087	0.051, 0.123	0.131	0.117, 0.146
Unexplained variation for full sibling (e_f^2)	0.322	0.314, 0.329	0.410	0.401, 0.418	0.459	0.437, 0.481	0.613	0.603, 0.623
Half sibling environmental effect (c_h^2)	0.112	0.094, 0.130	0.068	0.049, 0.087	0.050	0.005, 0.095	0.042	0.019, 0.065
Unexplained variation for half sibling (e_h^2)†	0.357	0.357, 0.372	0.434	0.417, 0.450	0.496	0.462, 0.531	0.702	0.681, 0.722

* Constraints: $h^2 + m^2 + c_f^2 + e_f^2 = 1$, and $h^2 + m^2 + c_h^2 + e_h^2 = 1$.
† $e_h^2 = c_f^2 - c_h^2 + e_f^2$.

important for birth weight (22 percent) and almost equally important for birth length and head circumference (both around 16 percent). Finally, looking at explained variation in the half sibling families (relating the proportions to $1 - e_h^2$), the common half sibling environment was most important for birth weight (17 percent) and less important for birth length (12 percent) and head circumference (10 percent).

Although the path coefficients for birth weight, birth length, and head circumference seemed to follow the same pattern, the path coefficients for gestational age differed markedly from the others (table 4). For gestational age, the maternal genetic factors and the shared full sibling environment were almost equally important. Relative to the proportion of explained variation ($1 - e_f^2$), these factors were more important (and thus the fetal genetic factors less important) for gestational age than for the other phenotypes. Further, the difference between the full and the half sibling environmental effects ($c_f^2 - c_h^2$) was largest for gestational age, giving the largest contribution to the half sibling error (e_h^2), compared with the other phenotypes.

For full siblings and for all phenotypes, the correlation between the first and second sibling was significantly lower than between the second and third sibling. For half siblings, there were only minor differences between these correlations, except for birth length, where we found the opposite (but not significant) effect. We excluded third siblings from the data and repeated the estimation. For birth length, we got mainly an increase in the half sibling environmental effect and, thus, there was no significant difference between the full and the half sibling environmental effect. For the other studied phenotypes, there were only minor changes in the path coefficients.

We repeated the estimation with adjustment for the unequal phenotypic variance (heteroscedasticity), stratified by birth order, sex, and generation. Adjustment for unequal variance gave mainly a decrease in the maternal genetic effect and an increase in the full and half siblings' environmental effects, mainly for birth weight ($m^2 = 0.204$, $c_f^2 = 0.161$) and birth length ($m^2 = 0.176$, $c_f^2 = 0.104$). Adjustment for unequal variance and relative to explained variation, the fetal genes were even more important to birth length (53 percent) and head circumference (50 percent), and the maternal genetic factors were less important to birth weight and length (30 percent) and less important to head circumference (32 percent). Finally, there was an increase of about 2 percentage points in both shared sibling environmental effects, for all phenotypes except gestational age.

DISCUSSION

We confirm that there is a fetal genetic effect (4–8), a maternal genetic effect, and an effect from the sibling environment on birth weight, birth length, head circumference, and gestational age. We find that heritability and especially fetal genes to a large extent explain the normal variation in birth weight, birth length, and head circumference.

According to our analysis, fetal genes explain about 31 percent of the normal variation in birth weight and birth length and 27 percent of the normal variation in head circumference. Our estimate for birth weight was somewhat higher than what has recently been reported by Magnus et al. (7), also using data from the MBRN (mother–father–first child trios), probably because we excluded the most preterm infants in our study in order to focus on the normal processes of fetal growth and gestational duration. We also included infants with higher birth order and used birth order as a covariate in our model.

Maternal genetic effects explained another 19–22 percent of the natural variation of the studied variables, so that about 50 percent of the variation may be explained by what is modeled as genetic factors. Further, the shared full sibling environmental factors explain about 9–15 percent of the variation, all significantly higher than the half sibling environmental factors. Maternal lifestyle habits, diet, and socioeconomic status are factors that may constitute the sibling environment, and such factors are more likely to differ between two pregnancies when there is a new partner.

We found that the different proportions of unexplained variation may account for the differences between the correlations and the path coefficients across phenotypes, except for gestational age. Relative to the explained variation, we found that fetal genetic effects were of more importance, and that the common full and half sibling environmental effects were of less importance, for birth length and head circumference than for birth weight. This may suggest that birth weight is more influenced by nutritional factors and placental function than are birth length and head circumference (21–23).

For gestational age, the maternal genetic effect and the full sibling environment explained most of the variation, 14 percent and 13 percent, respectively. This suggests that there are factors associated with the mother that are more important than the fetal genes for the normal duration of pregnancy. However, the larger full sibling environmental effect, compared with the half sibling effect, suggests that the father is also important for the duration of pregnancy (12). We suggest that the large proportions of unexplained variability in gestational age compared with the other phenotypes (e_f^2, e_h^2) are due to individual specific conditions during pregnancy, but errors in the reported menstrual dates may also contribute.

Birth length and head circumference are measured on a coarser scale (rounded to the nearest centimeter) compared with birth weight and gestational age, and this will normally give lower correlations and therefore higher unexplained variability. However, based on sensitivity analysis, measurement error alone is less likely to explain the larger proportion of unexplained variation in birth length and head circumference. For birth length, varying muscle tonus and to what extent the child is stretched during the measuring will cause random variation. For head circumference, the presentation at birth (breech or cephalic), the way the head is placed in the pelvis toward the end of pregnancy, and the duration of the second stage of labor may be of importance. For all phenotypes, individual specific conditions during the pregnancy will cause random variation.

A recent study from the MBRN has shown that the sibling correlation for head circumference (first and second birth) decreased with increasing interpregnancy interval (11). In

our study, for head circumference, the mean interval between the first and the second birth (full siblings) was 3.0 years (standard deviation (SD): 1.4) and between the second and the third birth was 3.4 years (SD: 1.6). For half siblings, the corresponding numbers were 5.8 (SD: 2.6) and 5.9 (SD: 2.5) years. These numbers were approximately the same for the other phenotypes. Thus, the longer interval between the births of half siblings relative to full siblings could partly explain the lower effect of the half sibling environment (as compared with the full sibling environment). The difference could also possibly be explained by dominant genes (18). However, for birth length, this difference diminished when we excluded the third sibling from the data. This may indicate that maternal factors such as diet and lifestyle habits are of less importance for length than for birth weight (21). Further studies should try to model this difference in sibling correlation as a function of interpregnancy interval and as a function of birth order.

Compared with the results reported by Samuelsen et al. (11), our results found higher sibling correlations for all the studied phenotypes, possibly as the result of different data screening. Our study was intergenerational, and both infants and parents were born after 1967 and thus ascertained in the MBRN. The majority of the second generation births were therefore concentrated over a shorter time period.

We assumed that the different genetic and environmental effects are independent of sex, birth order, and time period. Earlier studies have reported sex-limited fetal genetic variation in birth weight (4), while later studies have not (6, 7).

We assumed that the genetic effects are polygenic, with many independently segregating loci acting on the phenotype in a simple, additive fashion (18). During the last two decades, several studies have described single-gene effects on birth measurements, such as birth weight and length at birth (24–30), as well as imprinting of genes important for fetal growth (31). In our model, such single-gene effects would be incorporated in the estimated *h*. The fact that we find a significant heritability for birth length, head circumference, and birth weight increases the chances of identifying specific genes for these traits.

Models including the environment, culturally transmitted from parent to child, might possibly explain the correlations seen in this material (7). Factors constituting the common sibling environment, such as lifestyle (smoking), living conditions, and diet, may be culturally transmitted factors ''inherited'' from one or both parents. Based on nuclear family data with maternal half siblings, culturally transmitted factors on the maternal side cannot be separated from the maternal genetic effect. Similarly, on the paternal side, this factor cannot be separated from the fetal genetic effect. Extended-family data (paternal half siblings, cousins/half-cousins) are needed to estimate these effects along with the genetic effects (18, 19).

We have excluded cesarean births from our study, as they may represent truncated values of the phenotypes (16). However, the impact of the exclusion on our estimates is not large. For instance, excluding cesarean births increases the fetal and the maternal genetic effects by 0.6 and 1.7 percentage points, respectively, for birth weight and birth length and by 1.0 percent point for both effects for birth length. Hence, the corresponding proportion of unexplained variance decreases by about 2.0 percentage points for full siblings and 1.6 percentage points for half siblings, for both variables.

Compared with earlier studies of heritability in birth measurements (5–8), this study excluded the most preterm births, as they may be under a different genetic and environmental control than are normal births at term. When the very preterm births, from 22 to 34 weeks' gestation, are included, genetic effects became somewhat less important. The fetal genetic effects were reduced by 2–3 percentage points, and the full siblings' environmental effects were increased by 1–2 percentage points for all phenotypes. Further, there was an increase in the proportions of unexplained variance, 1.0–1.5 percentage points for full siblings and 2 percentage points for half siblings, except for gestational age, where there was an opposite but small effect. There were only minor changes in the maternal genetic effects.

In Norway, the number of births due to induction of labor was 12 percent in 2002. This information on the individual birth was not included in the present study. Many of these births are postterm, i.e., births after 42 completed weeks of gestation. However, excluding the postterm births gave only minor changes to the estimates in table 4.

In conclusion, we found that about 50 percent of the variation in birth weight, birth length, and head circumference may be explained by genetic factors. Relative to the proportion of explained variation, fetal genetic effects were of more importance, and the common full and half sibling environmental effects were of less importance, for birth length and head circumference than for birth weight. Gestational age showed a different pattern than the other phenotypes, where the maternal genetic effect and the full sibling environment were most important for the explained variation. Further studies using extended family data (paternal half siblings, cousins/half-cousins) are needed to separate culturally transmitted factors from the genetic effects estimated in our study, as well as to evaluate possible interactions between maternal and paternal genes and the environment.

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