AMERICAN JOURNAL OF HUMAN BIOLOGY 2:133–138 (1990)

Effects of Maternal Drinking, Smoking, Size, and Parity on Parent-Offspring Birth Weight Correlations

RUTH E. LITTLE
Department of Epidemiology, University of Michigan, Ann Arbor, Michigan 48109

ABSTRACT Parent-offspring birth weight correlations are presented by sex of parent and infant. They range from .14 to .16, except for the mother-daughter correlation, which is .32. This pattern of parent-offspring correlations varies when the parity of the infant, the size of the mother, and the mother's drinking and smoking status are considered. All parent-offspring correlations are higher when the infant is parity 2 or more. The mother-daughter correlations are significantly higher than mother-son correlations when the mother is above average in usual weight, height, or pregnancy weight gain. When the mother smoked before conception, all birth weight correlations except mother-daughter are essentially zero. The mother-son correlation is also very small if the mother was a regular drinker, independent of her smoking status. The complex relationships in this sample demonstrate that interactions with environmental variables must be taken into account in studies of familial aggregation of human birth weight.

Family resemblance for a continuous trait is frequently measured by a correlation coefficient. The degree of association between the phenotypes of two sets of family members can be expressed by the Pearson product-moment correlation, r. r is influenced by both the genes and the environment shared by the family and by environmental factors specific to individuals. It is generally assumed that r is homogeneous unless the population under study contains genetically diverse subgroups (Falconer, 1981). This assumption of homogeneity may be incorrect. Environmental variables can affect not only the level of the trait but also its covariation between family members (Bulmer, 1985). When the environment varies, r may vary too, and correlations describing resemblance of families in different environments may show significant heterogeneity.

In this paper, the correlation of parent and infant birth weights are considered. Several environmental variables that are known to affect the level of fetal growth are selected, and their influence on parent-infant birth weight correlations is examined. By presenting the familial correlations in the strata of the environmental variables and comparing across the strata, interactions of correlations with the environmental variables are detected and evaluated.

SUBJECTS AND METHODS

Subjects and methods are outlined briefly, because they have been described in detail elsewhere (Little et al., 1986, 1989). Subjects were recruited from the prenatal clinics of the Group Health Cooperative of Puget Sound, a health maintenance organization in Seattle, Washington, during a 12-month period. All prenatal patients receiving care during this period were contacted in their sixth month of gestation, and 74% agreed to participate in the study if needed. Informed consent was obtained after a full explanation of the study procedures. All infants in this study were singletons who survived for at least 1 month after delivery.

Two of the variables considered in this study were alcohol and tobacco use, which have a profound effect on birth weight and hence possibly parent-offspring correlations. To control for an expected alcohol-tobacco association and to obtain enough drinkers and smokers to detect these effects, a sample of 494 women, stratified on alcohol and tobacco use, was recruited. Of these, 377 were able to obtain information on their own birth weight and the birth weight of the child's

Received July 10, 1989; accepted October 19, 1989.

father. When a subset of these self-reported parental birth weights was compared with weights on state birth certificates, the mean absolute difference was 4 ounces; 44% of the self-reported weights were identical to the weight on the certificate, and another 38% were within 8 ounces of it (Little, 1986). Accuracy of alcohol and tobacco use reports were verified by laboratory tests, and less than 3% were judged seriously invalid (Little et al., 1986). Test-retest reliability of these self-reports was also found to be satisfactory (Little et al., 1984).

Information was obtained by personal interview and mail questionnaire on 31 secondary variables known to affect birth weight levels. The 31 variables were classified as familial traits, reproductive factors, environmental factors, maternal drug use, and paternal drug use. A stepwise regression analysis was employed to select the most important variables in each group, which were retained for use in the analysis. The retained secondary variables were parents' usual weights and races, parity, pregnancy weight gain, mother's height, mother's and father's drinking before conception, and mother's smoking before and during pregnancy. Their influence on birth weight has been confirmed in other studies (Dougherty and Jones, 1982; Mills et al., 1984; Showstack et al., 1984; Little and Sing, 1986).

Strata for height, weight, and pregnancy weight gain were defined by taking the mean value of the variable and dividing subjects into those at or below the mean and those above it. Strata for parity were 1 vs. 2 or more. Race was split into white vs. other. "Smoking" was defined to be an average of at least one cigarette daily. Drinking was classified as "occasional" or "regular," with regular drinking defined as an average of at least 30 ml ethanol (one ounce) daily or 75 ml (2.5 ounces) on one occasion at least once a month and occasional drinking defined as less than this, including none. (One ounce of ethanol is equivalent to about two standard-sized drinks of any alcoholic beverage.)

Mother- and father-infant birth weight correlations were computed by sex of infant for all families and for the subsets of families within each stratum of the secondary variables. To verify that differences in correlations were due to differences in covariance rather than differences in variance, the correlations were also computed with the z scores within each stratum. An "interaction" of the parent-offspring correlations with the secondary variables was defined to be a difference in the correlations across strata, or by sex of infant or by sex of parent within a stratum that had a P value of 0.05 or less.

Untransformed birth weights were used in the analysis of the data, since the distribution was not significantly different from normal for parents or infants. Significance tests of differences between correlations were made using the z-transformation suggested by Fisher (1958). All regression analyses used the stepwise method unless otherwise noted, with an F-to-enter criterion of $P < 0.05$ and an F-to-remove criterion of $P > 0.10$. For simplicity, P values that are 0.05 or less are termed statistically significant.

P values for the differences in two correlation coefficients are presented without adjustment for multiple testing so that the reader may see the strength and pattern of the original associations. The Bonferroni inequality (Neter et al., 1985) may be invoked to obtain an approximate estimate of the adjusted P value; assuming n simultaneous tests of the data, the sum of the individual alpha values for each test must not exceed the original alpha, and dividing each of the individual alpha values by n will satisfy this condition.

RESULTS

The families in this study were primarily white (95%), with median family income over $25,000 and median education of the parents 14 years. Maternal age ranged from 18 to 41. Mean parity (including the index birth) was 1.8; 45% of the mothers were primiparous. Mean infant birth weight in the 377 pregnancies was 3,562 g with standard deviation 511 g, which is consistent with previous studies of this population (Little, 1977).

Table 1 shows parent-offspring birth weight correlations for the entire sample by sex of infant and parent. The correlations ranged between .14 and .16, except for the mother-daughter correlation, which was about double these values. All correlations were significantly different from zero. There were no significant differences between any pair of correlations.

Table 1 also shows the parent-offspring correlation by strata of the secondary variables where an interaction was detected; these secondary variables were parity, mother's height, usual weight and pregnancy weight gain, and mother's smoking and drinking status before conception. When

TABLE 1. Parent-offspring birth weight correlations by strata of selected secondary variables[1]

	Sons	Daughters	All infants
All subjects (N = 201/176)[2]			
Mother-infant	.141	.317	.225
Father-infant	.161	.157	.150
Parity			
1 (95/76)			
Mother-infant	−.021^{a**}	.237	.101^{a***}
Father-infant	.109	.067	.081
2 or more (106/100)			
Mother-infant	.328^{a**}	.341	.319^{a***}
Father-infant	.224	.240	.221
Maternal pre-pregnancy weight			
≤160 lb (159/127)			
Mother-infant	.211	.265	.237
Father-infant	.136	.230	.166
>160 lb (42/49)			
Mother-infant	−.134^{c*}	.398^{c*}	.146
Father-infant	.279	.012	.130
Maternal height			
≤65 inches (116/110)			
Mother-infant	.222	.193	.210
Father-infant	.084	.120	.086
>65 inches (85/76)			
Mother-infant	.056^{c*}	.386^{c*}	.223
Father-infant	.255	.178	.218
Pregnancy weight gain			
≤40 lb (155/140)			
Mother-infant	.133	.175^{a**}	.147
Father-infant	.216	.198	.206
>40 lb (46/36)			
Mother-infant	.091^{c*}	.595^{a**,b**,c*}	.363^{b**}
Father-infant	.022	−.114^{b**}	−.058^{b**}
Mother's smoking before conception			
None (113/108)			
Mother-infant	.117	.272	.238
Father-infant	.246	.271	.264^{a*}
At least 1 cigarette daily (88/68)			
Mother-infant	.019^{c*}	.369^{b*,c*}	.189
Father-infant	−.005	−.006^{b*}	−.013^{a*}
Mother's drinking before conception			
Occasional (91/77)			
Mother-infant	.278	.263	.268
Father-infant	.078	.214	.151
Regular (110/99)			
Mother/infant	.027^{c*}	.363^{c*}	.181
Father-infant	.217	.136	.148

[1]Superscripts indicate the comparison being made and its *P* value as follows: a, comparisons across secondary variable strata; b, comparisons of father vs. mother; c, comparisons of sons vs. daughters. * $P \le .05$; ** $P \le .01$; *** $P \le .001$.
[2]Numbers in parentheses are numbers of male and female infants in the group.

parity was considered, correlations for first births were lower than for later births in all four categories of parents and offspring, and significantly lower for all mother-infant pairs pooled over infant sex. The differences in the correlations in the strata of the secondary variables measuring maternal height, usual weight, and weight gain during pregnancy all arose from an increased mother-daughter correlation in the stratum of the variable where the mother's size was greater, coupled with a lower mother-son correlation in that stratum.

The data presented in Table 1 show a strong interaction between mother's smoking and parent-infant birth weight correlations. When the mother smoked before conception, father-infant correlations were essentially zero, regardless of the sex of the infant; so was the mother-son correlation. This pattern persisted for smoking during pregnancy rather than before conception (data not shown); however, the difference in the correlations was less marked and not statistically significant by the criterion used here. Table 1 also shows a significantly lower mother-son birth weight correlation when the mother drank regularly before conception.

To verify that the heterogeneity by maternal drinking and smoking status was not a reflection of the father's habits, the correlations were recomputed by both parents' drinking and smoking status (Table 2). Partial correlations were used so that the results for smoking were adjusted for drinking, and vice versa. When the mother smoked, father-infant correlations were significantly lower than when the mother did not smoke; this was true if the father himself was a nonsmoker (.004 vs. .282) or if the father smoked too (−.041 vs. .282). Father-infant correlations appeared unchanged by father's smoking (.245 vs. .282). Mother-son correlations were also smaller than mother-daughter correlations when the mother drank or smoked regularly, independent of the father's habits; however, the differences in the correlations could well have been due to chance ($P > 0.05$ for all differences).

DISCUSSION

The results of this study show a complex network of interrelationships that alter the correlations for infant and parent birth weights. Three sets of variables are involved. One set is parity alone, which is associated with higher birth weight correlations when the mother is multiparous. Another set is variables that measure the mother's size: her usual weight, height, and pregnancy weight gain. Among larger women, by any measure, mother-daughter correlations are high and mother-son correlations are low. Finally, there is significant heterogeneity of parent-offspring birth weight correlations by mother's smoking and drinking status.

There are two caveats in interpreting these findings. First, the environmental variables themselves are correlated, so the findings do not reflect the independent influence of each of them. For example, maternal height, weight, and pregnancy weight gain are correlated, and the differences in parent-offspring correlations observed across strata of maternal height (say) probably reflect the influence of maternal weight and weight gain as well. The independent effects of alco-

TABLE 2. Parent-offspring birth weight partial correlations by parents' smoking and drinking status before conception[1]

	Sons	Daughters	All infants
Neither parent smokes (104/95)[2]			
Mother-infant	.188	.294	.253
Father-infant	.260	.276	.282*,**
Only father smokes (10/15)			
Mother-infant	−.003	.062	.154
Father-infant	.033	.518	.245
Only mother smokes (39/32)			
Mother-infant	.005	.213	.164
Father-infant	.078	−.113	.004*
Both parents smoke (48/34)			
Mother-infant	.027	.445	.178
Father-infant	−.068	.046	−.041**
Neither parent drinks regularly (66/57)			
Mother-infant	.246	.273	.304
Father-infant	.022	.184	.134
Only father drinks regularly (25/20)			
Mother-infant	.248	.034	.121
Father-infant	.024	.544	.222
Only mother drinks regularly (46/34)			
Mother-infant	−.061	.364	.079
Father-infant	.331	.165	.146
Both parents drink regularly (64/65)			
Mother-infant	.071	.332	.210
Father-infant	.173	.116	.134

[1]Partial correlations by paretns' smoling status adjusted for drinking status; partial correltions by drinking status adjusted for smoking status.

[2]Numbers in parentheses are numbers of male and female infants in the group.

*P value for differences in father-infant correlations for families where neither parent smokes vs. only mother smokes is ≤.05.

**P value for difference in father-infant correlations between families where neither parent smokes vs. both parents smoke is ≤.05.

hol and tobacco use on parent-offspring correlations are seen more clearly since partial correlations have been used (smoking adjusted for drinking and vice versa).

Second, the purpose of this paper is not to test a specific hypothesis but to describe the influence of several environmental variables on parent-offspring birth weight correlations. Therefore the reader has been given as much information about the statistical significance of the difference in the correlations as possible. However, there have been multiple tests of the data. Considering only the six environmental variables presented in Table 1, there were 18 tests of mother-infant correlations; only one of these (parity 1 vs. parity >1) is significant by the criterion used here after adjustment for multiple testing. The reader should keep in mind that there is a much greater probability that a single finding is due to chance than the stated *P* value would indicate.

There are previous reports of heterogeneity of birth weight covariance among siblings when environmental conditions vary. The interaction of sibling birth weight correlations with parity has been reported by several authors (Karn and Penrose, 1951–52; Robson, 1977; Nance et al., 1983). Mueller and Pollitt (1982) found that sibling correlations in Rohrer's index (w/l^3) at birth were notably lower when the mother was given dietary supplementation before and during the second pregnancy, when compared to no supplementation during either pregnancy. However, a thorough search of the literature revealed no study of parent-offspring correlations that has addressed their interactions with environmental variables.

Magnus writes that ". . . gene expression [of birth weight] may depend on or interact with environmental factors such as . . . use of tobacco and alcohol" (1984, p. 295). The findings presented in this paper provide evidence of such an interaction, not only for the level of the trait, but for its covariance. If these results hold in other populations, parent-offspring birth weight correlations will vary with the distribution of parity, maternal size, and maternal smoking and drinking. For example, young inner-city primiparae who smoked and drank heavily could have parent-son birth weight correlations of zero. In a sample of nonsmoking, nondrinking multiparae, parent-offspring correlations could all be .2 or more. If correlations are used to infer the genetic contribution to birth weight, different conclusions would be reached from the two samples.

It is not clear what the biological mechanism for these interactions might be, especially for the decreased father-infant correlations when the mother smokes. Could there be a maternal effect on paternal gene transmission that alters the relationship of parent and infant birth weight phenotypes? Such a selection process has been reported in the transmission of transferrin alleles, which are associated with spontaneous abortion (Weitkamp and Schacter, 1985) and prematurity (Auconi et al., 1982). There is evidence also that maternal cigarette smoking is associated with covalent damage to DNA in human placentas (Everson et al., 1986). Alternatively, some investigations suggest the hypothesis that the cause of smoking-related effects on the fetus is maternal genotype selection on smoking (Silverman, 1977). A recent study of offspring of twins whose smoking during pregnancy was discordant does not support this hypothesis (Magnus et al., 1985). Finally, there is the possibility that the interactions in this sample are chance findings that will not occur in subsequent studies.

The degree to which genetic factors determine human birth weight remains to be addressed. Heterogeneity of the parent-offspring correlations must be taken into account, creating complex analytic problems. The way in which this can be done, and the resulting implications for genetic transmission of human birth weight, is the subject of another report (Little and Sing, 1987).

ACKNOWLEDGMENTS

This work was done while the author was a Senior Research Fellow in Human Genetics at the University of Michigan (grant HD06608). The support of Dr. Charles F. Sing is very gratefully acknowledged. Dr. Patricia Moll made significant contributions to this paper. Assistance was also provided by the Department of Human Genetics, University of Michigan, and the Alcoholism and Drug Abuse Institute of the University of Washington.

LITERATURE CITED

Auconi P, Biagini R, Colarizi P, et al. (1982) Transferrin C subtypes in extremely premature newborn infants. Pediatr. Res. *16*:1022–1024.

Bulmer MG (1985) The Mathematical Theory of Quantitative Genetics. Oxford: Clarendon Press.

Dougherty CRS, and Jones AD (1982) The determinants of birth weight. Am. J. Obstet. Gynecol. *144*:190–200.

Everson RB, Randerath E, Santella RM, Cefalo RC, Avitts TA, and Randerath K (1986) Detection of smoking-related covalent DNA adducts in human placenta. Science *231:*54–57.

Falconer DS (1981) Introduction to Quantitative Genetics. London: Longman.

Fisher RA (1958) Statistical Methods for Research Workers. New York: Hafner.

Karn M, and Penrose LS (1951–52) Birthweight and gestation time in relation to maternal age, parity and infant survival. Ann. Eugen. *16:*147–164.

Little RE (1977) Moderate alcohol use during pregnancy and decreased infant birth weight. Am. J. Public Health *67:*1154–1156.

Little RE (1986) Birth weight and gestational age: Mother's estimates compared with state and hospital records. Am. J. Public Health *76:*1350–1351.

Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, and Clarren S (1989) Maternal alcohol use during lactation and infant mental and motor development at one year. N. Engl. J. Med. *321:*425–430.

Little RE, and Sing CF (1986) Association of father's drinking and infant birth weight. N. Engl. J. Med. *314:*1644–1645.

Little RE, and Sing CS (1987) Genetic and environmental influences on human birth weight. Am. J. Hum. Genet. *40:*512–526.

Little RE, Uhl CN, Labbe RF, et al. (1986) Agreement between laboratory tests and self reports of alcohol, tobacco, caffeine, marijuana, and other drug use in post-partum women. Soc. Sci. Med. *22:*91–98.

Little RE, Worthington-Roberts B, Mann S, et al. (1984) Test-retest reliability of diet and drinking estimates for pregnancy and post-partum. Am. J. Epidemiol. *120:*794–797.

Magnus P (1984) Further evidence for a significant effect of fetal genes on variation in birthweight. Clin. Genet. *26:*289–296.

Magnus P, Berg K, Bjerkedal T, et al. (1985) The heritability of smoking behavior in pregnancy, and the birth weights of offspring of smoking-discordant twins. Scand. J. Soc. Med. *13:*29–34.

Mills JL, Graubard BI, Harley MS, Rhoads GG, and Berendes HW (1984) Maternal alcohol consumption and birth weight. J.A.M.A. *252:*1875–1879.

Mueller WH, and Pollitt E (1982) The Bacon Chow study: Effects of nutrition supplementation on sibling-sibling anthropometric correlations. Hum. Biol. *54:*455–468.

Nance WE, Kramer AA, Corey LA, Winter PM, and Eaves LJ (1983) A causal analysis of birthweight in the offspring of monozygotic twins. Am. J. Hum. Genet. *35:*1211–1223.

Neter J, Wasserman W, and Kutner MH (1985) Applied Linear Statistical Models. Homewood, IL: Irwin.

Robson EB (1977) The genetics of birthweight. In F Faulkner and GM Tanner (eds.): Human Growth. New York: Plenum Press, pp. 285–297.

Showstack JA, Budeti PP, and Minkler D (1984) Factors associated with birthweight: An exploration of the roles of prenatal care and the length of gestation. Am. J. Public Health *74:*1003–1008.

Silverman DT (1977) Maternal smoking and birthweight. Am. J. Epidemiol. *105:*513–521.

Weitkamp LR, and Schacter BZ (1985) Transferrin and HLA: Spontaneous abortion, neural tube defects and natural selection. N. Engl. J. Med. *313:925–932.*