Original Contribution

Birth Weight Standardized to Gestational Age and Intelligence in Young Adulthood: A Register-based Birth Cohort Study of Male Siblings

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The authors aimed to determine the relation between birth-weight variations within the normal range and intelligence in young adulthood. A historical birth cohort study was conducted. Data from the Medical Birth Register of Norway were linked with register data from the Norwegian National Conscript Service. The sample comprised 52,408 sibships of full brothers who were born singletons at 37–41 completed weeks’ gestation during 1967–1984 in Norway and were intelligence-tested at the time of mandatory military conscription. Generalized estimating equations were used to fit population-averaged panel data models. The analyses showed that in men with birth weights within the 10th–90th percentile range, a within-family difference of 1 standard deviation in birth weight standardized to gestational age was associated with a within-family difference of 0.07 standard deviation (99% confidence interval: 0.03, 0.09) in intelligence score, after adjustment for a range of background factors. There was no significant between-family association after adjustment for background factors. In Norwegian males, normal variations in intrauterine growth are associated with differences in intelligence in young adulthood. This association is probably not due to confounding by familial and parental characteristics.

birth weight; cohort studies; fetal development; gestational age; intelligence; Norway; siblings

Abbreviations: IQ, intelligence quotient; SD, standard deviation; WAIS, Wechsler Adult Intelligence Scale.

Editor’s note: An invited commentary on this article appears on page 537.

The relation between birth weight and intelligence has been examined in many studies (1–23), including studies of siblings (3, 6, 7, 15–23). This research on birth weight and intelligence indicates that small size at birth (<2,500 g) due to prematurity or low weight at term is associated with reduced intelligence. It is less clear, however, whether birth-weight variations within the normal range are associated with differences in intelligence (5). Most investigators have focused on infants born premature or small for gestational age or have included these risk groups in the sample without presenting specific analyses of birth-weight variations within the normal range. Thus, the findings of those studies may not be fully representative of the great majority of infants, who are born at term at a weight appropriate for their gestational age.

In 6 studies of children born at term at a weight higher than 2,500 g, reviewed in 2004, there was a small, positive correlation between birth weight and childhood cognitive ability (5). Later studies of the relation between birth-weight variations within the normal range and childhood intelligence gave mixed results (6–9, 22). Among the studies that examined effects of birth-weight variations within the normal range on childhood intelligence, we identified 3 studies in which comparisons between siblings were made (7, 15, 22). Only 1 of these showed a significant within-family association (15), and in that case, the association was seen only in the male sibling pairs (15).

We identified 5 studies in which the relation between birth-weight variations within the normal range and adult intelligence was analyzed (4, 11–14). This literature on adult intelligence is difficult to interpret, partly because the results are inconsistent, but also for methodological reasons. All of these studies on adult intelligence compared persons born to
different mothers and brought up in different families, and although multivariate analyses were used to adjust for some possible confounders, this method can hardly take into account the wide range of familial and parental characteristics that might influence birth weight and intelligence. Confounding by such background factors could create spurious associations, as well as a false absence of association.

Comparing siblings brought up in the same family represents a powerful method of controlling for familial and parental characteristics, since the relation between differences in birth weight and intelligence within sibships (the within-family effect) cannot be confounded by factors shared by the siblings (24). In addition, studies of siblings may provide information about between-family effects (23).

Our aim in this study was to determine the relation between birth weight and intelligence in young adulthood. We were particularly interested in the effects of birth-weight variations within the normal range. To achieve effective control for the confounding of familial and parental characteristics and to obtain information about both within-family and between-family effects, we wanted to compare siblings. Available data on Norwegian conscripts enabled us to do this for males.

**MATERIALS AND METHODS**

Population and study design

A historical birth cohort study was conducted. Data from the Medical Birth Register of Norway, which contains information on all newborn children in Norway from 1967 to the present, were linked with register data from the National Conscript Service and the national statistics agency, Statistics Norway. The original cohort consisted of the 399,239 registered infant boys who were born alive as singletons at 37–41 completed weeks’ gestation during the period 1967–1984. Intelligence test scores, recorded at military conscription, were available for 338,416 persons. For 335,640 of these persons, there were also available birth-weight data and information that permitted individuals to be identified as brothers (maternal and paternal serial numbers). Nested within this sample, there were 54,927 sibships of 2 or more men with the same mother. For sibling comparisons, we selected all sibships in which all men were full brothers—altogether, 52,408 sibships with 2–8 men.

The study is part of a large register-based project. Approval was given by the Norwegian Data Inspectorate before the project started.

Intelligence

In Norway, military service is compulsory for every able young man, and before the men enter military service, their medical and psychological suitability for such service is assessed. The great majority of conscripts (approximately 95%) are tested between their 18th and 21st birthdays.

The intelligence test data used in the present study comprised general ability scores in the form of standard 9 scores, that is, single-digit scores with the values 1–9. The scores were distributed as a normal distribution with mean 5.0 and standard deviation (SD) 2.0. The scoring norms were the same for all men examined here.

General ability is a composite score from 3 speeded subtests. The Arithmetic Test (25 minutes) has 30 items in prose and measures logical reasoning and arithmetic and algebraic ability; it is similar to the arithmetic test in the Wechsler Adult Intelligence Scale (WAIS) (25). The Word Similarities Test (8 minutes) is a multiple-choice test with 54 items, akin to the vocabulary test in WAIS. The Figures Test (20 minutes) has 36 multiple-choice items with 6 or 8 alternatives and is similar to Raven’s Progressive Matrices (26).

The test-retest reliabilities of these 3 subtests, calculated on data from a sample of 800 adolescents in the seventh grade, were 0.84, 0.90, and 0.72, respectively (27). In a small sample of adults ($n = 48$), the correlation between the general ability score and WAIS, measured with a time lag varying from 2 years to 25 years, was 0.75 (28). The data on the general ability of Norwegian conscripts have been used in several studies (4, 28–30). The subtest scores were available for only some of the cohorts examined in the present study.

Birth weight and background factors

Data on birth weight (in grams), gestational age (in completed weeks from the first day of the last menstrual period), birth year, birth month, birth order (among the mothers’ live-born children), and maternal age and marital status were obtained from the Medical Birth Register. Paternal age (birth year of child minus birth year of father) and the mother’s total number of children (including sisters and brothers who had not been conscripted) were calculated on the basis of data from Statistics Norway. Data on the highest attained maternal and paternal educational levels, divided into low (<11 years), medium (11–13 years), and high (>13 years), were obtained from Statistics Norway. In the study base, there was missing information on birth order for 562 persons, on maternal marital status for 169 persons, on maternal educational level for 301 persons, and on paternal educational level for 336 persons.

Statistical analyses

Birth weights were converted into $z$ scores representing birth weight standardized to gestational age (birth weight $z$ scores), calculated as birth weight minus birth weight mean divided by the SD, using gestational age-specific birth weight means and SDs from the Norwegian population standards (31). The gestational age-specific birth weight means for 37–41 weeks were within the range of 3,235–3,810 g (31). The gestational age-specific SDs for 37–41 weeks were within the range of 450–475 g (31). Normal birth weight was defined as birth weight within the range of the gestational age-specific 10th–90th percentiles, according to Norwegian population standards (31).

The relation between birth weight $z$ score and intelligence score was examined by means of generalized estimating equations (32) with an exchangeable correlation structure and robust standard error estimation via the xtgee procedure in Stata 11 (Stata Corporation, College Station, Texas).
A general model for simultaneously estimating the within-family and between-family associations between birth weight z score and intelligence score (23) can be expressed as

$$E(Y_{ij}) = \alpha + \beta X_{ij} + \gamma X_i,$$

where $E(Y_{ij})$ represents the expected intelligence score for an individual $j$ of sibship $i$, $X_{ij}$ represents the individual’s birth weight z score, and $X_i$ represents the mean birth weight z score for the sibship.

We fitted population-averaged panel data models with intelligence score as the dependent variable and individual birth weight z score and sibship mean of birth weight z score as the principal predictors. We conducted 1 series of analyses in the total study base and 1 series restricted to siblings with birth weights within the normal range. In addition to the basic model, in which only the principal predictors were entered, we tested more complex models with the following covariates: birth order, birth year, birth season, parental age (years), maternal marital status at the time of the birth, mean age difference between the siblings (months), parental educational level, mother’s total number of children, and the interaction terms “birth weight z score \times birth order” and “birth weight z score \times mean age difference between siblings.” The great majority (89%) of the sibships that were examined included only 2 siblings, and sibship size was not significantly associated with intelligence score after adjustment for background factors in preliminary generalized estimating equations analyses.

We tested the linearity assumption for each covariate by including alternative expressions (quadratic and categorical terms) together with the simple continuous terms in preliminary generalized estimating equations analyses. The contribution of the terms was examined by means of the Wald test. In the final models, the individual-level birth weight z score was entered as a simple continuous term plus a squared term. The sibship mean of birth weight z score was entered as a simple continuous term. Birth order was entered as a continuous term plus 6 dummy variables (for orders 1, 2, 3, 4, 5, and 6), birth season as a dichotomous term (summer or autumn vs. winter or spring), birth year as 3 dummy variables (1970–1974, 1975–1979, or 1980–1984), parental age as a continuous term (years) plus 7 dummy variables (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, or ≥50 years), maternal marital status as 1 dummy variable (married), the mother’s total number of children as 3 dummy variables (2, 3, or 4), parental educational level as the original ordinal terms divided into 3 categories, and the mean age difference between siblings as a continuous term (months).

We used listwise deletion for handling missing data and 2-sided $P$ values. Because we made several comparisons, we used the 99% confidence interval as the measure of statistical significance.

## RESULTS

### Characteristics of the study base

Persons included in the study base had a higher mean birth weight, were less likely to be the firstborn child in the family, were more likely to have parents with more than 13 years of education, and were more likely to have married mothers than the original cohort (Table 1).

### Analyses of the total study base

In the total study base, the within-family association between birth weight z score and intelligence score was characterized by both a significant simple term and a significant squared term for birth weight z score (Table 2). Based on the adjusted unstandardized regression coefficients of these terms (0.10 and −0.02, respectively), one can infer by derivation that the within-family association between birth weight z score and intelligence score was curvilinear, with a slope that decreased with increasing birth weight z score and turned negative for birth weight z scores higher than 2.5 (calculated as $0.10/(0.02 \times 2)$). There was no significant between-family association after adjustment for background factors.

### Analyses of men with birth weights within the normal range

In men with birth weights within the normal range, a within-family difference of 1 SD in birth weight standardized to gestational age was associated with a within-family difference in intelligence score of 0.12 (99% confidence interval: 0.06, 0.17), after adjustment for background factors and interaction terms (Table 3). This corresponds to a 0.07-SD (99% confidence interval: 0.03, 0.09) change in intelligence score per SD change in birth weight. There was no significant between-family association after adjustment for background factors. Entering birth order and parental educational level into the model had a strong impact on the relative strength of the within- and between-family associations.

The within-family association between birth weight z score and intelligence score was weaker in sibships with a mean between-sibling age difference in the highest quartile than in the other sibships (Table 4).

### DISCUSSION

Among Norwegian male siblings born at term with birth weights within the range of the gestational age-specific 10th–90th percentiles, after adjustment for background factors, there was a positive within-family association (but no between-family association) between birth weight standardized to gestational age and intelligence score.

### Strengths and limitations

This study was based on a large, nationwide birth cohort. Intelligence test scores were available for the great majority of the cohort. The intelligence testing of Norwegian conscripts is comprehensive, and the test scores seem to be reliable and valid (27, 28). The sample included only males, and the relation between birth weight and intelligence could be different in females (15). The persons in the study base had a higher mean birth weight, were less likely to be the
firstborn child in the family, and were less likely to have unmarried mothers and less-educated parents than the original cohort. However, because siblings share the effects of parental socioeconomic characteristics to a large extent and because we adjusted for birth order, the modestly biased selection of the study base in the present study probably had no important effects on the estimates.

Comparisons with other studies

The relation between birth weight and intelligence has been explored in many studies (1–23). However, most investigators have not conducted specific analyses of birth-weight variations within the normal range.

In some studies, researchers examined the relation of birth-weight variations within the normal range to childhood intelligence (5–9, 15, 22). The majority of these studies showed a positive association. However, the evidence from the sibling studies is weak (7, 15, 22): Among 812 male sibling pairs from the United States, a 1-kg difference in birth weight was associated with a 0.33-SD difference in intelligence quotient (IQ) (5.0 standard IQ points) across the full range of birth weights, and Matte et al. (15) stated that the effect was essentially identical to this in siblings with birth weights higher than 2,500 g. This association in boys was twice as strong as the within-family association seen in our young men, as our findings correspond to a 0.15-SD change in intelligence score per kg of birth weight. However, Matte et al. (15) found no significant intrapair association among the 871 female sibling pairs. In 1,645 sibling pairs from the United Kingdom, Lawlor et al. (22) found no significant within-family association. They found a significant between-family association (22), but they used a model specification which gives a between-family coefficient that is identical to the sum of the within-family and between-family coefficients in the model we used (23). Among 3,083 siblings from the United States, Yang et al. (7) found a significant between-family association in their crude model, but this association was reduced and lost its significance after adjustment for background factors, as in our study.

We identified 5 studies in which the relation of birth-weight variations within the normal range to adult intelligence was analyzed (4, 11–14). One of these was a study of Norwegian conscripts based on data from the same registers as those we used, but that study was not restricted to siblings, did not include sibling comparisons, and did not adjust for a series of potential confounders that sibling comparisons indirectly control for, such as maternal health, behavior, and anthropometric characteristics; parental education; parental intelligence; and the family’s financial situation, social position, and social network (4). In that study, Eide et al. (4) found that the mean standard 9 intelligence score was 0.33 points higher in men with a birth weight of

| Table 1. Characteristics of a Cohort of Males Born in Norway in 1967–1984 and Followed up at Military Conscription and a Study Base Comprising the Sibships of Full Brothers in the Cohort |
|-----------------|-----------------|-----------------|
|                | Original Cohort | Study Base (Sibships) |
| No. of participants | 399,239         | 110,862          | 77,506 |
| Mean (SD) gestational age, completed weeks | 39.7 (1.1) | 39.7 (1.1) | 39.7 (1.1) |
| Range of birth weights, g | 550–7,270 | 900–6,400 | 2,630–4,415 |
| Mean (SD) birth weight, g | 3,599 (495) | 3,625 (482) | 3,636 (328) |
| Range of birth weight z scores | –6.8 to 7.4 | –6.0 to 5.8 | –1.3 to 1.3 |
| Mean (SD) birth weight z score | –0.1 (1.0) | –0.1 (1.0) | –0.1 (0.6) |
| Birth in summer or autumn, % | 48.3 | 48.0 | 48.1 |
| Firstborn child, % | 40.4 | 34.0 | 33.8 |
| Mean (SD) maternal age, years | 26.1 (5.3) | 26.0 (4.8) | 25.9 (4.8) |
| Mean (SD) paternal age, years | 29.5 (6.1) | 29.3 (5.7) | 29.2 (5.6) |
| High parental educational level, % |
| Mother | 20.7 | 22.5 | 22.9 |
| Father | 23.3 | 25.1 | 25.7 |
| Married mother, % | 89.8 | 95.8 | 96.0 |
| Mean (SD) intelligence score | 5.3 (1.8) | 5.3 (1.8) |
| Mean (SD) no. of siblings per sibship | 2.2 (0.4) | 2.2 (0.4) |
| Mean (SD) age difference between siblings, months | 46.9 (27.1) | 47.1 (27.5) |

Abbreviation: SD, standard deviation.  
* Birth weights within the 10th–90th percentiles.  
b Standardized to gestational age.  
c More than 13 years of education.
4,000–4,499 g than in men with a birth weight of 2,500–2,999 g, after adjustment for maternal age, maternal education, and parity. This implies a mean difference of 0.12 SD in intelligence score per kg of birth weight, which is slightly lower than the within-family difference in the present study. We had expected the estimates for the within-family association to be lower than the estimates of Eide et al. However, our study suggested that an expected change in intelligence score for a given change in birth weight is the same irrespective of whether the comparison is made between siblings or between unrelated persons (no between-family association). Besides, the fact that Eide et al. included persons born at 42–44 weeks’ gestation (4), a group with higher birth weight but lower intelligence scores than persons born at term, may have reduced their estimates. When Eide et al. also adjusted for adult height, the estimates turned out even lower (4), but including adult height as a covariate may represent overadjustment for factors on the causal pathway and may lead to underestimation of the association. In a study of Danish conscripts, Sørensen et al. (12) presented results that implied an unadjusted mean difference of 0.17 SD in intelligence score per kg of birth weight, which is slightly higher than the within-family difference seen in our study. Richards et al. (13) studied a mixed sample of men and women from the United Kingdom who had been intelligence-tested as both children and adults. The results of the tests conducted at age 26 years implied a mean increase of 0.11 SD in intelligence score per kg of birth weight across the birth weight range 2,500–4,000 g (13). However, there was a drop in intelligence scores for birth weights higher than 4,000 g, so the relation between birth weight and intelligence score across the full range of normal birth weights was not statistically significant (13). In a study of 1,576 British men and women aged 48–74 years (11) and in another study of 128 British men and women aged 75–81 years (14), there was no significant association between birth weight and intelligence score.

### Possible explanations

The most likely explanation for these results is a causal association between intrauterine growth and adult intelligence. Background factors that are fully shared by siblings, such as parental intelligence and maternal anthropometric characteristics, can be ruled out as confounders in our study.
Many environmental factors may change from one birth to another and exert differential effects on siblings. However, differences between siblings in environmental exposures will tend to increase with an increasing age difference, so the fact that the within-family association was not stronger in sibships with a large age difference between siblings than in sibships with a small age difference suggests that unmeasured environmental confounders did not increase the estimates. If this interpretation is correct, the within-family association between birth weight and intelligence can hardly be explained by changes in the family’s financial situation and social position or in the parents’ experience, lifestyle, and health. Thus, our study suggests that environmental confounders other than birth order and parental education play a minor role. Birth order was a strong negative confounder in the within-family association, however, and birth order and parental educational level explained all of the between-family association seen in our crude model. Because siblings share, on average, 50% of their genes, measuring within-family associations also represents control for genetic factors to some extent. Even so, one should take into account that confounding by genetic factors may create a spurious within-family association between birth weight and intelligence (20).

Clinical implications

From a maternal-care perspective, it is important to know the consequences of intrauterine growth variations for later cognitive function. The present study indicates, in line with earlier studies (3, 4, 13), that there are such effects, that these effects persist into young adulthood, and that they are strongest for babies with low birth weights and ignorable or negative for babies with high birth weights.

For babies born at term with birth weights within the normal range, the consequences of additional intrauterine growth seem to be modest. In these infants, a difference of 1 kg in birth weight is associated with a difference of 2 points on a standard IQ scale (mean = 100; SD, 15).

Unanswered questions and future research

These results require replication. It would also be interesting to see whether the findings can be generalized to women and to persons in other countries. Comparisons of monozygotic twins may be used to control for the confounding effects of genetic factors, and among the studies of monozygotic twins that have examined the relation of birth weight to childhood intelligence (6, 16, 17, 20), there is a preponderance of studies that show a significant association (6, 16, 17). However, only 1 small study of monozygotic twins seems to have examined the effects on adult intelligence (19), and low statistical power could be the reason for the lack of association seen in that study. Thus, there is a call for studies of adult intelligence in monozygotic twins. It is questionable, however, whether findings from twin studies are representative of the majority of the population, which is born singleton, especially when the aim is to determine effects of birth-weight variations within the normal range.

It is unclear whether the impact of lower birth weight on intelligence depends upon the cause of the intrauterine growth restriction. During the Dutch Hunger Winter of World War II, third-trimester exposure to famine reduced birth weight but had no impact on intelligence score at military conscription (33, 34).

Conclusions

In Norwegian males, normal variations of intrauterine growth are associated with differences in intelligence in young adulthood. This association is probably not due to confounding by familial and parental characteristics.

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