Birthweight and Adult Health in a Population-Based Sample of Norwegian Twins

Andrej M. Grjibovski, Jennifer R. Harris, and Per Magnus

Population-based twin data were used to test (a) whether lower birthweight confers a greater risk of adult health disorders, and (b) whether within-pair birthweight differences in twins explain discordance for health outcomes. The sample consisted of 1201 monozygotic (MZ) male twins, 1048 dizygotic (DZ) male twins, 1679 MZ female twins, 1489 DZ female twins, and 2423 opposite-sex DZ twins, born in Norway between 1967 and 1979. The relationship between birthweight and self-reported health outcomes were studied using multivariable logistic regression. In the full sample (n = 7840), birthweight was negatively associated with risk for nearsightedness (odds ratio OR = 0.76, 95% CI: 0.65 – 0.92) and minimal brain disorder (OR = 0.27, 95% CI: 0.16-0.44) when adjusted for gestational age, sex, zygosity, age, education and body mass index after correction for intraclass correlations and multiple comparisons. Within-pair analysis of 159 MZ and 224 DZ pairs revealed that myopic twins were on average 2 g (p = .966) and 64 g (p = .040) lighter than nonmyopic twins in MZ and DZ pairs respectively, suggesting that genetic factors may play an important role in the associations between birthweight and nearsightedness. Within-pair analysis of twins discordant for a minimal brain disorder indicated that affected twins were 80 g (p = .655) and 85 g (p = .655) lighter than their healthy co-twins in MZ and DZ pairs respectively, although there were only 2 MZ and 2 DZ discordant pairs.

There is a growing body of evidence that suggests that several adult health problems have their origins in antenatal life. Growth restriction in the fetal period, clinically expressed as reduced birthweight, has been consistently shown to be a risk factor for coronary heart disease, type 2 diabetes and hypertension (Barker, 1995; Godfrey & Barker, 2001; Holness, et al., 2000) later in life. These epidemiological findings, known as the fetal origins hypothesis, suggest that diseases that present later in life may originate through fetal adaptations to inadequate nutrient supply in certain periods of antenatal development (Barker, 1998). Moreover, increased risk of adult diseases is not only associated with low birth weight (< 2500 g) but is found throughout the entire birthweight distribution. For example, the prevalence of impaired glucose tolerance and death rates from coronary heart disease fall progressively with increases in birthweight (Barker, 1995; Hales et al., 1991). Similar associations have been found between being small at birth and neurological, psychological and articulatory impairment in children (Michelsson & Noronen, 1983). Birthweight was negatively related to asthma in some (Shaheen et al., 1999; Steffensen et al., 2000) but not all studies (Hagström et al., 1998; Katz et al., 2003). Positive associations between birthweight and hayfever (Katz et al., 2003), rheumatoid arthritis (Jacobsson et al., 2003), and lower back pain (Hestbaek et al., 2003) have been recently reported. These associations could reflect fetal programming, but could also be explained by genetic factors common to antenatal growth and susceptibility to the studied outcome.

Twin studies offer unique opportunities to test aspects of the fetal origins hypothesis by resolving whether associations between impaired fetal growth and later illnesses are attributed to common genetic factors or fetal programming (Leon, 2001). The twin applications are founded on expectations of genetic similarity derived from biometric models. Monozygotic (MZ) twins are genetically similar whereas dizygotic (DZ) twins share, on average, 50% of their segregating genes. Shared environments are assumed to be equal for both types of twinships in infancy and childhood. Studying differences in size at birth and later health in twins provides optimal control for maternal characteristics, duration of gestation, and shared effects of early environments. Moreover, MZ twin design controls for the influence of genes on the association between birthweight and later health. Thus, an association between birthweight and the disease of interest within both MZ and DZ pairs provides evidence of fetal programming. If such an
association is present in DZ twins, but not in MZ twins, the role of genetic factors, which are responsible for both fetal growth and susceptibility to the disease, should be considered. No association between birthweight and the disease both in MZ and DZ pairs suggests a prominent role of environmental factors (Hubinette et al., 2003).

Evidence from twin studies suggests that genetic factors might account for the associations between birthweight and blood pressure (IJzerman et al., 2000), low-density lipoprotein cholesterol (IJzerman et al., 2001), and plasma fibrinogen (IJzerman et al., 2003a), whereas intrauterine environmental influences might contribute to the associations between birthweight and type 2 diabetes (Poulsen et al., 2002). Importantly, these studies were performed on relatively small samples (53 MZ and 61 DZ twin pairs in the former three studies, and 104 MZ and 88 DZ pairs in the latter study) and demonstrate the capability of this study design to detect the importance of genetic and/or intrauterine factors in the associations between birthweight and adult diseases (IJzerman et al., 2003b).

Despite the great potential of twin studies to examine the possible influence of genetic factors and intrauterine environment on the associations between fetal growth indices and later health in a number of diseases, most of the research has concentrated on the common degenerative conditions, such as coronary heart disease and type 2 diabetes, and their risk factors.

This study uses data from a large population-based twin cohort to examine birthweight effects on 30 health outcomes, which are poorly studied with respect to birthweight. A further goal is to investigate how the relationship between birthweight and later health is influenced by genetic and intrauterine factors.

### Materials and Methods

#### Sample and Data Collection

The data are from a population-based sample of Norwegian twins participating in a study on health and development at the Norwegian Institute of Public Health (NIPH) in Oslo (Harris et al., 2002). A total of 15,374 twins were born in Norway between 1967 and 1979. All twins were identified through the National Medical Birth Registry. A postal questionnaire was sent out in 1992 to take part in the research projects, and to 4472 twins born between 1975 and 1979 belonging to the pairs in which both twins were alive and residing in Norway in 1998. Responses were received from 8045 twins (63.3%) and included 3334 complete pairs and 1377 single responders.

The questionnaire included a checklist for 30 illnesses and symptoms (listed in Table 1), which was prefaced with ‘do you have or have you ever had, any of the following health problems’. Zygosity classification was based on responses to 7 items, which showed 97% accuracy (Magnus et al., 1983). Information on height, weight and education were also obtained from the questionnaire. Education was classified in three groups: secondary, upper secondary and higher levels of education. Body mass index (BMI) was calculated as weight(kg)/height(m²). Data on birthweight and gestational age were obtained from the Medical Birth Registry.

After excluding pairs with missing data on birthweight or length of gestation, the final sample included 7840 twins: 1201 MZ and 1048 DZ male twins, 1679 MZ and 1489 DZ female twins, and 2423 opposite-sex DZ twins.

#### Analyses

Sex and zygosity differences in the overall prevalences of the health outcomes were tested with chi-square statistics. Differences in birthweight, gestational age,
age and BMI across zygosity categories were tested using one-way ANOVA with Bonferroni post-hoc tests. The relationships between birthweight and the health outcomes were studied by multivariable logistic regression. Crude and adjusted odds ratios (OR) with 95% CI were calculated for each disease or symptom. Birthweight, gestational age, BMI and age were introduced into the models as continuous variables. Zygosity and education were entered as categorical dummy variables. Adjustments for intraclass correlations were performed. Given that 30 outcomes were studied and a large number of tests were performed, a conventional $p$-value of 0.05 was divided by 30 and a $p$-value < 0.0016 was chosen as the significance level to adjust for multiple comparisons.

Within-pair analyses were performed only for those outcomes which were significantly associated with birthweight in the regression models after Bonferroni correction. Opposite-sex pairs were excluded as the effects of gender difference within a pair may influence both birthweight and the outcome. For the within-pair analyses, 510 male MZ, 763 female MZ, 390 male DZ, and 643 female DZ pairs, of which both twins responded to the questionnaire, were available. The birthweight distribution of the pairs in the study sample was assessed by Shapiro-Wilk and Kolmogorov-Smirnov tests. Paired $t$ tests (for normally distributed data) and Wilcoxon signed ranks tests were used to test within-pair differences in birthweight in health discordant twins in MZ and DZ twins separately. Stata version 7.0 (StataCorp., 2001) and SPSS version 12.0 (SPSS Inc., 2003) software packages were used for all calculations.

### Results

Self-reported rates of the illnesses and symptoms were greater in women with the exceptions of hay fever, asthma, psoriasis, inflammatory bowel disease (IBD), diabetes, epilepsy, Bechterew’s disease, rheumatoid arthritis, hyperactivity and minimal brain disorder (MBD), where sex differences were not significant (Table 1). No differences in lifetime prevalences of the studied outcomes were found across zygosity categories.

The distribution of birthweight, gestational age and sociodemographic characteristics of the participants by sex and zygosity is presented in Table 2. In same-sex pairs, MZ twins were lighter than DZ twins for both sexes, MZ males were heavier than MZ females, and DZ males were heavier than DZ females. Boys in opposite-sex DZ pairs were on average 128 g heavier than girls. There were no differences in birthweight between males or females from same-sex DZ pairs compared to twins from opposite-sex pairs. Gestational length was similar in MZ male and MZ female twins. There were no differences in gestational length between all groups of DZ twins. Gestational age differed significantly between MZ and DZ males, but not females. There were no age differences among participants in same-sex pairs. BMI was significantly greater in males than in females across all zygosity categories.

Crude and adjusted odds ratios for the relationships between birthweight and health outcomes are summarized in Table 3. In the unadjusted analysis, birthweight was negatively associated with risks of developing nickel allergy, headache, nearsightedness, astigmatism, ear infections and neck/shoulder pain. Adjustment for gestational age, sex, age, zygosity, BMI and education

### Table 2

<table>
<thead>
<tr>
<th>Mean (SD) Birthweight, Gestational Age, Age and BMI by Sex and Zygosity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZ male pairs</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Birthweight: g</td>
</tr>
<tr>
<td>Gestational age: days</td>
</tr>
<tr>
<td>Age: years</td>
</tr>
<tr>
<td>BMI: kg/m²</td>
</tr>
<tr>
<td>Education: %</td>
</tr>
<tr>
<td>Secondary</td>
</tr>
<tr>
<td>Upper secondary</td>
</tr>
<tr>
<td>Higher</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

Note: * Significantly different from MZ males at $p < .05$ after Bonferroni correction.

* Significantly different from same-sex DZ males at $p < .05$ after Bonferroni correction.

* Significantly different from MZ females at $p < .05$ after Bonferroni correction.

* Significantly different from same-sex DZ females at $p < .05$ after Bonferroni correction.

* Significantly different from opposite-sex DZ males at $p < .05$ after Bonferroni correction.

* Significantly different from opposite-sex DZ females at $p < .05$ after Bonferroni correction.

* The sum is not always 100% due to rounding.

* $p$-value for the chi-square test.
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reduced the observed risks to nonsignificant levels except for the risk of nearsightedness, while the risk for developing MBD became significant. The results suggest that a 1 kg increase in birthweight is associated with a 1.3 times decreased risk of developing nearsightedness, and a 3.7 times decreased risk of minimal brain disorder later in life. Besides birthweight, education was also an important factor associated with nearsightedness: individuals with upper secondary and higher education had 1.6 and 3.0 higher risks respectively (both at \(p < .001\)) of developing myopia than the twins with secondary education.

Given that the length of education is an important confounder, birthweight differences were calculated only in those myopia-discordant pairs who were concordant for education (159 MZ and 224 DZ pairs).

Significant differences in birthweight between myopic and nonmyopic twins were found in DZ twins (2686 g vs. 2750 g, \(p = .040\)), but not in MZ twins (2610 g vs. 2612 g, \(p = .966\)), indicating that genetic factors are important in the association between birthweight and nearsightedness later in life.

The low number of MBD discordant (2 MZ and 2 DZ) pairs did not allow conclusions to be drawn about the origins of the associations between birthweight and MBD, though affected twins were lighter than unaffected twins, 80 g (\(p = .655\)) and 85 g (\(p = .655\)) in MZ and DZ pairs respectively.

**Discussion**

Population-based twin data were used to study the associations between birthweight and 30 health outcomes.

Table 3

<table>
<thead>
<tr>
<th>Problems with:</th>
<th>Crude OR (95% CI)</th>
<th>(p)</th>
<th>Adjusted OR (95% CI)*</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hay fever</td>
<td>0.97 (0.85–1.10)</td>
<td>.615</td>
<td>0.97 (0.82–1.14)</td>
<td>.670</td>
</tr>
<tr>
<td>Nettle rash</td>
<td>0.80 (0.69–0.94)</td>
<td>.005</td>
<td>0.95 (0.78–1.21)</td>
<td>.565</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.94 (0.79–1.12)</td>
<td>.498</td>
<td>0.95 (0.76–1.18)</td>
<td>.528</td>
</tr>
<tr>
<td>Nickel allergy</td>
<td>0.80 (0.70–0.91)</td>
<td>.001</td>
<td>0.94 (0.79–1.11)</td>
<td>.430</td>
</tr>
<tr>
<td>Childhood eczema</td>
<td>1.05 (0.87–1.28)</td>
<td>.596</td>
<td>1.21 (0.96–1.54)</td>
<td>.110</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1.02 (0.81–1.29)</td>
<td>.871</td>
<td>1.19 (0.90–1.57)</td>
<td>.216</td>
</tr>
<tr>
<td>Other skin disease</td>
<td>0.92 (0.80–1.05)</td>
<td>.220</td>
<td>0.97 (0.82–1.15)</td>
<td>.728</td>
</tr>
<tr>
<td>Migraine</td>
<td>0.95 (0.80–1.12)</td>
<td>.503</td>
<td>1.01 (0.82–1.23)</td>
<td>.949</td>
</tr>
<tr>
<td>Other headache</td>
<td>0.89 (0.60–0.79)</td>
<td>&lt; .001</td>
<td>0.78 (0.65–0.92)</td>
<td>.004</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>0.89 (0.72–1.10)</td>
<td>.279</td>
<td>0.85 (0.65–1.11)</td>
<td>.230</td>
</tr>
<tr>
<td>IBD(^b)</td>
<td>0.87 (0.56–1.34)</td>
<td>.517</td>
<td>0.80 (0.45–1.43)</td>
<td>.449</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>0.81 (0.69–0.96)</td>
<td>.013</td>
<td>0.92 (0.75–1.12)</td>
<td>.388</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.82 (0.54–1.25)</td>
<td>.352</td>
<td>0.59 (0.33–1.05)</td>
<td>.073</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>0.71 (0.50–1.01)</td>
<td>.054</td>
<td>0.75 (0.46–1.20)</td>
<td>.227</td>
</tr>
<tr>
<td>Nearsightedness</td>
<td>0.84 (0.76–0.92)</td>
<td>&lt; .001</td>
<td>0.76 (0.67–0.86)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Farsightedness</td>
<td>0.86 (0.74–1.00)</td>
<td>.045</td>
<td>0.98 (0.81–1.18)</td>
<td>.837</td>
</tr>
<tr>
<td>Astigmatism</td>
<td>0.83 (0.75–0.92)</td>
<td>.001</td>
<td>0.82 (0.72–0.94)</td>
<td>.003</td>
</tr>
<tr>
<td>Ear infections</td>
<td>0.79 (0.68–0.91)</td>
<td>.001</td>
<td>0.81 (0.68–0.97)</td>
<td>.022</td>
</tr>
<tr>
<td>Tonsilitis</td>
<td>0.81 (0.70–0.93)</td>
<td>.003</td>
<td>0.81 (0.68–0.97)</td>
<td>.022</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>0.91 (0.76–1.09)</td>
<td>.288</td>
<td>0.98 (0.78–1.25)</td>
<td>.874</td>
</tr>
<tr>
<td>Bladder infections</td>
<td>0.85 (0.75–0.97)</td>
<td>.014</td>
<td>1.12 (0.95–1.23)</td>
<td>.176</td>
</tr>
<tr>
<td>Neck/shoulder pain</td>
<td>0.77 (0.78–0.88)</td>
<td>&lt; .001</td>
<td>0.81 (0.68–0.96)</td>
<td>.017</td>
</tr>
<tr>
<td>Lumbar pain</td>
<td>0.91 (0.81–1.01)</td>
<td>.087</td>
<td>0.88 (0.77–1.01)</td>
<td>.078</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>0.80 (0.64–0.99)</td>
<td>.038</td>
<td>0.85 (0.64–1.13)</td>
<td>.258</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>0.82 (0.43–1.58)</td>
<td>.562</td>
<td>0.89 (0.33–1.48)</td>
<td>.340</td>
</tr>
<tr>
<td>Bechterew's disease</td>
<td>0.97 (0.41–2.33)</td>
<td>.948</td>
<td>1.98 (0.77–5.16)</td>
<td>.164</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0.72 (0.45–1.15)</td>
<td>.165</td>
<td>0.82 (0.45–1.47)</td>
<td>.500</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0.86 (0.67–1.09)</td>
<td>.211</td>
<td>1.07 (0.80–1.45)</td>
<td>.640</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>0.53 (0.31–0.92)</td>
<td>.024</td>
<td>0.61 (0.30–1.23)</td>
<td>.168</td>
</tr>
<tr>
<td>MBD(^d)</td>
<td>0.38 (0.16–0.90)</td>
<td>.028</td>
<td>0.27 (0.16–0.44)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Note: * Adjusted for sex, age, gestational length, BMI, zygosity and education.
\(^b\) Inflammatory bowel disease.
\(^c\) Minimal brain disorder.
\(^d\) Not adjusted for education, because all cases had the same educational level.
in young adulthood. The findings indicate that lower weight at birth may confer a higher risk of developing nearsightedness and MBD later in life.

In general, large-scale epidemiological studies rely on self-reported measures of symptoms and diseases. Several studies report an acceptable quality of questionnaire-based self-reported rates of hay fever (Duffy et al., 1990), asthma (Duffy et al., 1990), ear infections (Stephenson, 1995) and diabetes (Martin et al., 2000). Moreover, studies from Nordic countries report the acceptable validity of questionnaires in detecting migraine, headache (Hagen et al., 2000) and skin diseases (Susitaival et al., 1995). The estimates of refractive disorders in this survey are close to those found in other studies from Norway (Kinge et al., 1998) and thereby indirectly support the reliability of our data. Haugland and Wold (2001) found that survey methods provide adequate quality of data on headache, sleeping problems, dizziness, neck ache and other subjective health complaints in Norwegian adolescents. Although recall bias may result in either overestimation or underestimation of prevalence rates for some outcomes in our sample, we do not think that this bias is differentially related to birthweight.

The response rate was 71.0% for women and 55.1% for men (p < 0.001). Those who did not return the questionnaires were 44g (p = .001 [males]) and 41g (p = .004 [females]) lighter at birth than those who responded. This could lead to a slight underestimation of the odds ratios for those illnesses/symptoms for which lower birthweight confers increased risks, and overestimations of the odds ratios for the outcomes where the association occurs in the opposite direction. At the same time, analyses in pairs where only one twin responded did not reveal birthweight differences between those who responded and those who did not in either male or female twin pairs, which suggests little effect of recall bias in our co-twin control analyses. Only pairs for which both twins were alive at the age of 18 years were included in the study. Twins who did not survive were 1412 g (males) and 1154 g (females) lighter than those who survived. Therefore we must restrict our conclusions to the variations in birthweight within the relatively normal range of birthweight.

Several studies have reported higher prevalence of childhood myopia in children who were born preterm or with low birthweight (Holmström et al., 1998; Larsson et al., 2003). Children born preterm have altered growth of the eye that contributes to the higher risk of developing myopia in these children (O’Connor et al., 2002). While the eye of a small infant is smaller in length, the reduced radius of curvature of the cornea and/or lens may promote development of myopia (Saunders et al., 2002). Flederius (1976) reported that 10-year-old children who were born preterm had shorter axial length, more curved corneas, and thicker lenses. Contrary to myopia in children born at term, which is characterized by increased axial length, myopia in prematurely born children has been shown to be attributed to an increase in corneal curvature and/or lens thickness, and a decrease in the anterior chamber depth (Choi et al., 2000; Gallo & Fagerholm, 1993; O’Connor et al., 2002), although there is still no consensus on the mechanisms of myopia development in preterm infants.

It remains unclear whether most of the reported associations between size at birth and subsequent nearsightedness are primarily attributed to prematurity or to fetal growth restriction. We focused on the effects of fetal growth restriction on later health; therefore adjustment for gestational age was performed in the regression analysis. Saw et al. (2004) showed that 7- to 9-year-old Singaporean Chinese children who were lighter or less mature at birth had shorter axial length, shallower vitreous chambers, and more curved corneas in dose-response fashion across the normal range of birthweight and gestational age that corresponds with the previous studies, although no differences in refraction data were found. Failure to detect refractive errors despite significant changes in ocular biometric parameters at a young school age in the Singaporean study, followed by a significant relationship between birthweight and myopia across the whole birthweight spectrum in individuals aged between 18 and 31 years in this study, may raise speculations that some compensatory mechanisms that may still be present at a young school age are exhausted with increased years of schooling. However, since these studies were performed in two different populations and this study does not include biometric data, these speculations should be considered with due caution.

Twin studies have shown that myopia is mainly genetically determined (Hammond et al., 2001; Lyhne et al., 2001), while studies in selected population groups indicate that environmental factors are important (Mutti et al., 2002; Saw et al., 2002). Therefore, the multifactorial aetiology of nearsightedness in which both genetic and environmental factors contribute to the susceptibility to myopia has to be considered (Goldschmidt, 2003). Little is known as to whether the associations between birth parameters and myopia are due to genes that may be associated with both impaired fetal growth and myopia, or due to growth restriction per se. No difference in birthweight in discordant MZ twins suggests that intrauterine growth restriction per se cannot explain the revealed association between birthweight and nearsightedness. Given that the birthweight difference between affected and nonaffected twins in DZ pairs was significant, we hypothesize that there may be some genetic factors that are associated with both reduced fetal growth and susceptibility to myopia later in life.

It has been reported that females from opposite-sex pairs have lower visual acuity (Miller, 1995) and an increased rate of fetal growth than females from same-sex twin pairs (Corey et al., 1979), suggesting influences of the male sex hormones on the female fetus development in opposite-sex twin pairs. However, in
this large study, female twins from opposite-sex DZ pairs were only 17 g heavier than female twins from same-sex DZ pairs, no difference in gestational duration was found, and the prevalences of the studied outcomes including myopia were similar across zygosity categories.

Several studies have identified low birthweight as a risk factor for hyperactivity disorders, behavioral problems and anxiety disorders in childhood and adolescence (Breslau, 1995; Elgen et al., 2002), which may support our findings in relation to MBD. We were unable to examine how the relationship between birthweight and MBD was explained by genes or intrauterine environment, due to a low number of discordant pairs.

Several other outcomes may deserve attention in future studies given that the Bonferroni adjustment for multiple comparisons is rather conservative; our data suggest that there may also be relationships between birthweight and increased risks of developing astigmatism, ear infections, tonsillitis, neck/shoulder pain, and headaches.

The results may not necessarily be generalizable to singletons given the different biology of twin pregnancies. The average birthweight among twins is lower than that of singletons and twins are more likely to be born preterm. However, the growth retardation experienced by twins compared to singletons does not result in increased risk of mortality in adulthood (Christensen et al., 1995). Nevertheless, in total groups of twins, negative associations between birthweight and blood pressure (Ijzerman et al., 2000), cholesterol levels (Ijzerman et al., 2001) and other outcomes were found to be similar to the findings in singletons, suggesting that differences in birthweight in twins can be used as a model for differences in birthweight in singletons. The prevalence of refractive errors was comparable in preterm twins and triplets with preterm singletons, and in within-pair analyses, the twins with lower birthweight were more likely to have ametropia than their heavier co-twins, though these results were not significant (Tomazzoli et al., 2003). Twins are at higher risk of neurological and behavioral problems than singletons, but these differences are mainly related to the shorter twin gestation, rather than to being a twin (Shinwell, 2002). While the findings in dichorionic twins regarding birthweight and later health can be valid for singletons, caution is needed regarding data from monochorionic twins (Morley et al., 2003). About two thirds of MZ twins are monochorionic, and the intrauterine environment may also be different for MZ and DZ twins, which in turn may influence the associations between intrapair differences in birthweight and adult health.

In summary, lower birthweight conferred increased risks of nearsightedness and MBD in the full sample. In relation to myopia, the findings are unlikely to be attributed to intrauterine growth restriction per se and suggest that genetic factors may account for the associations between birthweight and nearsightedness.

Acknowledgments

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