Early Life Programming of Abdominal Adiposity in Adolescents: The HELENA Study

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OBJECTIVE — To examine the relationship between birth weight and abdominal adiposity in adolescents.

RESEARCH DESIGN AND METHODS — A total of 284 adolescents (49.3% of whom were female) aged 14.9 ± 1.2 years were included in the study. Birth weight and gestational age were obtained from parental records. Abdominal adiposity (in three regions: R1, R2, and R3) and trunk and total body fat mass were measured by dual-energy X-ray absorptiometry. Regional fat mass indexes (FMIs) were thereafter calculated as fat mass divided by the square of height (Trunk FMI and abdominal FMI R1, R2, and R3).

RESULTS — Birth weight was negatively associated with abdominal FMI R1, R2, and R3 independently of total fat mass, gestational age, sex, breast-feeding duration, pubertal stage, physical activity, and socioeconomic status (all $P < 0.01$).

CONCLUSIONS — Our study shows an inverse association between birth weight and abdominal adiposity in adolescents independently of total fat mass and other potential confounders. These findings suggest that fetal nutrition, as reflected by birth weight, may have a programming effect on abdominal adiposity later in life.

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Low birth weight seems to increase the risk of type 2 diabetes and cardiovascular disease by programming a more central fat deposition (1). However, the association between birth weight and fat distribution remains controversial (2–4). Studies using advanced methods to assess body composition such as dual-energy X-ray absorptiometry (DEXA) may help to better describe these asso- ciations.

The aim of this study was to examine the relationship between birth weight and abdominal adiposity measured by DEXA in Spanish adolescents participating in the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross-Sectional study (HELENA-CSS).

RESEARCH DESIGN AND METHODS

The HELENA study was designed to examine the interactions between personal, environmental, and lifestyle influences on the risk factors for future cardiovascular diseases (5).

The present study comprised 284 healthy Caucasian adolescents (140 female and 144 male) aged 14.9 ± 1.2 years from Zaragoza, Spain, with complete data on birth weight, gestational age, and abdominal fat measured by DEXA. Birth at >37 weeks' gestation (95.1%) was an additional inclusion criterion.

The study was approved by the Human Research Ethics Committee of Aragon. Written informed consent to participate was obtained from both the parents and the adolescents. Birth weight and duration of gestation were obtained from the health booklets (6).

Body composition and abdominal fat distribution

Body weight and height, waist circumference, and subscapular and tricipital skinfold thicknesses were measured in triplicate (7). Waist circumference, waist-to-height ratio, and subscapular to tricipital skinfold were used as surrogate markers of central body fat.

We measured fat mass with DEXA using an extended research model (pediatric version of the software QDR-Explorer, version 12.4; Hologic, Waltham, MA). Abdominal adiposity was assessed at three different regions: R1, R2, and R3 (8,9). A rectangle was drawn on the digital scan image to establish every region. All had the lower horizontal border on the top of the iliac crest. For R1, the upper border was established parallel to the end of the lowest rib. The upper border of R2 was parallel to the junction of the T12 and L1 vertebrae, and that for R3 was parallel to the middle of the costo-vertebrae articulation of the last rib. The lateral sides were adjusted to include the maximal

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Table 1—*Unstandardized regression coefficients (β) and SEM showing the association between birth weight and abdominal fat deposition indexes in adolescents*

	Model 1 (n = 284)			Model 2 (n = 258)			Model 3 (n = 258)			Model 4 (n = 252)		
	β	SEM	P	β	SEM	P	β	SEM	P	β	SEM	P
Trunk FMI (kg/m^2)	−0.317	0.158	**0.045**	−0.129	0.047	**<0.001**	−0.210	0.048	**<0.001**	−0.204	0.050	**<0.001**
Abdominal R1 FMI (kg/m^2)	−0.055	0.032	0.091	−0.037	0.014	**0.009**	−0.045	0.015	**0.002**	−0.044	0.015	**0.004**
Abdominal R2 FMI (kg/m^2)	−0.090	0.043	**0.036**	−0.060	0.017	**0.001**	−0.059	0.018	**0.001**	−0.055	0.019	**0.004**
Abdominal R3 FMI (kg/m^2)	−0.104	0.048	**0.031**	−0.069	0.020	**0.001**	−0.069	0.020	**0.001**	−0.067	0.021	**0.002**
Waist (cm)*	0.001	0.007	0.916	0.007	0.004	0.128	−0.001	0.003	0.735	0.001	0.004	0.831
Waist-to-height ratio	−0.015	0.007	**0.031**	−0.008	0.004	0.070	−0.011	0.004	**0.008**	−0.012	0.004	**0.010**
Subscapular SFT (mm)†	−1.387	0.534	**0.001**	−1.601	0.467	**0.001**	−1.7744	0.490	**<0.001**	−1.711	0.512	**0.001**

Model 1, birth weight adjusted for gestational age; model 2, adjustments for model 1 plus total body fat; model 3, adjustments for model 2 plus sex, breast-feeding duration, pubertal stage, and physical activity; model 4, adjustments for model 3 plus SES (mother's and father's educational levels). Data in bold are statistically significant ($P < 0.05$). *Analysis was performed on log-transformed data. †Birth weight controlling also for tricipital skinfold thickness. SFT, skinfold thickness.

amount of abdominal tissue within each region. Trunk fat mass and abdominal fat mass R1, R2, and R3 were used as surrogates of abdominal adiposity.

Confounders

Several factors potentially related to birth weight or fat distribution were investigated. Pubertal status was evaluated by a trained physician (6,10). Physical activity was objectively assessed by accelerometry (Actigraph MTI) (11). Socioeconomic status (SES) was assessed via questionnaire and defined by maternal and paternal educational status (1, lower education; 2, lower secondary education; 3, higher secondary education; and 4, higher education or university degree). Exclusive breast-feeding duration was coded as follows: 0, never; 1, <3 months; 2, 3–6 months; and 3, >6 months (6).

Pubertal status was obtained in 97.9% of adolescents (96.4% of those male and 97.9% of those female), physical activity in 94.7% (95% of those male and 94.4% of those female), SES in 97.9% (99.3% of those male and 98.6% of those female), and information on breast-feeding duration in 98.9% (99.6% of those male and 99.3% of those female).

Statistical analysis

Statistical analyses were performed using SPSS software (version 16.0), and the level of significance was set at 0.05. We adjusted abdominal fat deposition variables by the square of height. Regional fat mass indexes (FMIs) were then calculated as fat mass divided by the square of height (trunk FMI and abdominal FMI R1, R2, and R3).

The association of birth weight with fat distribution was analyzed by linear regression in an extended model approach: Model 1 included the predictor (birth weight) and the dependent variable (trunk FMI; abdominal FMI R1, R2, and R3; waist circumference; waist-to-height ratio; or subscapular to tricipital skinfold) adjusted for gestational age. For model 2, total fat mass was entered into the model. For model 3, a set of confounders (sex, pubertal stage, breast-feeding duration, and physical activity) was added. For model 4, SES was added to the model. We also tested the interaction effect between sex and birth weight. Pubertal stage, SES, and breast-feeding duration were entered as dummy variables.

RESULTS — Mean ± SD birth weight was 3.31 ± 0.44 kg (3.36 ± 0.50 kg in male subjects and 3.26 ± 0.39 kg in female subjects). Because there was no evidence that the associations of birth weight with trunk FMI and abdominal FMI R1, R2, and R3 differed between female and male subjects (P for interaction 0.256, 0.301, 0.243, and 0.304, respectively), the results are presented jointly for both sexes (Table 1).

Birth weight adjusted for gestational age was negatively associated with trunk and abdominal FMI R1 and R2 (all $P < 0.05$). When total fat mass was entered into the model (model 2), these relationships were strengthened ($P < 0.01$). The results did not change after further adjustment for potential confounders (models 3 and 4). A decrease of 1 kg in birth weight predicted an increase of ~50 g/m^2 in abdominal FMI. The adjustment for age instead of pubertal stage did not substantially change the results (data not shown).

CONCLUSIONS — The present study shows a negative association between birth weight and central and abdominal fat deposition independently of total body fat mass in adolescents. These associations were independent of gestational age, pubertal stage, physical activity, breast-feeding duration, and SES.

Although our sample size was not comparable to that of larger epidemiological studies, a major strength of our study was the use of DEXA in an extended model, which is a very accurate technique to measure abdominal adiposity (9).

Results from the limited number of studies that have investigated this issue using direct measures of central fat in adolescents are controversial. Our findings are in agreement with those of Dolan et al. (2) in a study conducted in 101 young adolescents. One other report found no relationship between birth weight and central fat deposition but included children and adolescents with a very large age range (from 4 to 20 years) (3).

In conclusion, our findings further support the concept that fetal undergrowth, as reflected by lower birth weight, may have a programming effect on increased abdominal adiposity later in life. These results may help to explain the relationship between low birth weight and later metabolic disorders such as diabetes or cardiovascular disease.

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