

# Altered Fat Tissue Distribution in Young Adult Men Who Had Low Birth Weight

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Numerous studies have implicated impaired early growth (low birth weight [LBW]) as a risk factor for the development of obesity (1) and type 2 diabetes (2). Obesity, particularly abdominal obesity, is associated with an increased risk of insulin resistance and type 2 diabetes, and although the mechanistic basis is not fully known, several characteristics of the metabolically active visceral fat depot, including ready release of free fatty acids and adipokines into the portal circulation, have been proposed as potential mediators of whole-body insulin resistance. In contrast, leg fat appears to be protective against the development of glucose intolerance (3). Little is known about time of onset of fat accumulation and the regional distribution of fat tissue in LBW subjects. Previous studies have used indirect methods such as BMI, waist and hip circumference, and waist-to-hip ratio to assess adiposity and body fat distribution. The limitation of those measurements was recently demonstrated (4).

We determined whole-body fat content and regional fat distribution by anthropometrical measurements (BMI and waist and hip circumference) and dual-energy X-ray absorptiometry (DEXA) (Norland XR-26 Mark II; Norland, Fort Atkinson, WI) in two independent cohorts of randomly se-

lected healthy young men identified through the Danish Medical Birth Registry according to birth weight. All subjects were born at term in 1980 (weeks 39–41). Cohort 1 was studied in 1999 and cohort 2 in 2003. LBW was defined as a birth weight below the 10th percentile for gestational age (Table 1) and normal birth weight (NBW) as a birth weight between the 50th and 90th percentile for gestational age (Table 1). Subjects with a family history of diabetes, hypertension, ischemic heart disease, and/or BMI  $\geq 30$  kg/m<sup>2</sup> were excluded. All participants had normal fasting plasma glucose according to World Health Organization and American Diabetes Association criteria.

Estimates of whole-body and regional body composition (i.e., lean mass, fat mass, and fat mass percentage) were obtained for the following regions: total body, trunk, abdomen, and leg. Regions of interest were positioned according to the operator's guide (Norland XR-26 Mark II Software 2.5.3A, resolution 6.5  $\times$  13.0 mm). The same experienced technician performed all scans of cohorts 1 and 2. In addition, we calculated the proportion of regional fat mass relative to total body fat and the relative contributions of upper and lower body fat (Table 1). The study protocol was approved by the re-

gional ethical review committee, and all participants gave their written consent.

Initially, the cohorts were analyzed independently (Table 1), but as the overall trends for differences between birth weight groups were very similar, we decided to pool the data. A general linear model with systematic fixed effect of cohort (1,2) and birth weight group (LBW, NBW) was used to test the effect of LBW on total and regional body fat content (SAS Statistical Software version 8.2; SAS Institute, Cary, NC). All variability between cohorts 1 and 2 within birth weight group was summarized as one model estimate (cohort effect). Tests for variance homogeneity and normal distribution were done. There was no significant interaction between birth weight and cohort for any of the tested parameters.

Interestingly, in spite of virtually similar body weights, BMIs, and waist-to-hip ratios in the two birth weight groups, the LBW subjects had significantly higher total abdominal fat mass and higher proportion of trunk and abdominal fat mass but less leg fat relative to total fat mass and therefore a shift in body fat distribution with more fat located on the upper body (trunk, abdomen) compared with lower body (leg), when assessed by the DEXA technique (Table 1). In accordance with previous reports, the LBW subjects of this study were significantly shorter than their matched peers. Lower final height is also a characteristic of type 2 diabetic patients (5).

In conclusion, we have shown that a birth weight within the lowest 10th percentile of the NBW distribution is associated with significant changes in body fat content and distribution in early adulthood. These subtle differences were not evident by conventional anthropometrical measurements such as BMI or waist-to-hip ratio, which illustrates the importance of using more exact methods such as DEXA scans when evaluating (regional) adiposity. The DEXA technique does not discriminate between subcutaneous and visceral abdominal fat, the latter depot being primarily associated with insulin resistance. However, both increased abdominal fat mass and reduced leg fat mass assessed by DEXA have pre-

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**Abbreviations:** DEXA, dual-energy X-ray absorptiometry; LBW, low birth weight; NBW, normal birth weight.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—LBW effect by cohort

	LBW		NBW		LBW versus NBW corr. P value
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	
Demographics	21	14	19	20	
Age (years)	19.0 ± 0.0	22.9 ± 0.8	19.0 ± 0.0	22.4 ± 0.5	
Birth weight (g)	2,702 ± 202	2,764 ± 109	3,801 ± 98.7	3,965 ± 162	
Height (cm)	178.1 ± 3.9	181.4 ± 7.6	181.1 ± 5.1*	186.2 ± 7.6	0.01
Weight (kg)	73.9 ± 8.7	77.3 ± 10.3	73.3 ± 9.6	77.7 ± 9.2	0.96
BMI (kg/m <sup>2</sup> )	23.3 ± 2.8	23.5 ± 3.4	22.3 ± 2.4	22.5 ± 3.0	0.13
Waist (cm)	80.7 ± 7.2	83.4 ± 8.1	78.0 ± 4.9	82.5 ± 8.4	0.25
Hip (cm)	99.0 ± 5.1	99.3 ± 6.9	97.9 ± 5.1	98.1 ± 6.0	0.40
Waist-to-hip ratio	0.81 ± 0.04	0.84 ± 0.04	0.81 ± 0.06	0.84 ± 0.07	0.76
Systolic blood pressure (mmHg)	111.3 ± 11.7	120.0 ± 8.4	114.0 ± 11.3	121.5 ± 11.5	0.42
Diastolic blood pressure (mmHg)	65.5 ± 8.9	63.9 ± 10.3	67.6 ± 10.1	67.2 ± 8.9	0.30
Fasting plasma glucose (mM)	5.6 ± 0.4	5.7 ± 0.3	5.4 ± 0.4	5.6 ± 0.4	0.03
Whole-body estimates					
Total lean mass (g)	54,895 ± 4,327	54,615 ± 4,409	55,986 ± 6,247	56,315 ± 5,384	0.21
Total fat mass (g)	15,546 ± 6,779	19,609 ± 6,930	14,382 ± 4,590	17,6434 ± 5,778	0.29
Total fat mass (%)	20.6 ± 6.7	24.7 ± 6.0	19.2 ± 4.2	22.5 ± 5.4	0.18
Regional estimates					
Trunk lean mass (g)	26,196 ± 2,292	26,070 ± 2,202	26,392 ± 2,931	26,730 ± 2,351	0.48
Trunk fat mass (g)	7,597 ± 3,822	9,902 ± 4,606	6,390 ± 2,404	8,688 ± 2,965	0.14
Trunk fat mass (%)	21.0 ± 7.5	25.7 ± 8.4	18.5 ± 5.0	23.4 ± 6.2	0.13
Abdominal lean mass (g)	10,405 ± 764	10,388 ± 1,157	10,910 ± 1,185	10,957 ± 1,264	0.04
Abdominal fat mass (g)	3,309 ± 1811	5,026 ± 2,106	2,654 ± 1,178	3,875 ± 1,402	0.02
Abdominal fat mass (%)	22.3 ± 8.6	30.6 ± 8.9	18.4 ± 6.3	24.9 ± 7.6	0.01
Leg lean mass (g)	18,950 ± 1,601	18,371 ± 1,863	19,605 ± 2,500	20,242 ± 3,199†	0.04
Leg fat mass (g)	5,787 ± 2,335	7,010 ± 2,357	5,896 ± 1,967	6,871 ± 2,460	0.99
Leg fat mass (%)	21.8 ± 6.7	25.8 ± 5.9	21.7 ± 4.7	23.9 ± 6.3	0.49
Relative fat distribution					
Trunk fat mass (g)/total fat mass (g)	0.51 ± 0.04	0.53 ± 0.11	0.47 ± 0.05*	0.51 ± 0.05	0.06
Abdominal fat mass (g)/total fat mass (g)	0.22 ± 0.04	0.26 ± 0.03	0.19 ± 0.04*	0.23 ± 0.04†	0.00
Leg fat mass (g)/total fat mass (g)	0.40 ± 0.04	0.38 ± 0.04	0.44 ± 0.05*	0.41 ± 0.05	0.03
Trunk fat mass (%) / leg fat mass (%)	0.96 ± 0.12	0.99 ± 0.20	0.86 ± 0.14*	0.98 ± 0.16	0.03
Abdominal fat mass (%) / leg fat mass (%)	1.02 ± 0.20	1.18 ± 0.18	0.85 ± 0.24*	1.04 ± 0.23†	0.00

Data are means ± SD. \*P < 0.05 LBW vs. NBW (cohort 1); †P < 0.05 LBW vs. NBW (cohort 2).

viously been shown to correlate negatively with fasting and postload glucose concentrations after an oral glucose tolerance test (3). Furthermore, the changes in body fat distribution observed in this study were seen in lean healthy individuals with fasting plasma glucose in the normal range and therefore appear to precede and perhaps underlie the development of impaired glucose tolerance and type 2 diabetes in LBW subjects.

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