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Original article – Obstetrics

# Parental factors affecting the weights of the placenta and the offspring\*

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## Abstract

**Aim:** To determine parental, especially paternal factors associated with the weight of the placenta and offspring.

**Methods:** This population-based birth-cohort study includes 2947 singleton children born from April 2006 to 2007 and living in Drenthe, The Netherlands. Placental weight and birth weight were measured and questionnaires were filled out for this cohort. Associations between parental factors, and the weight of the placenta and the offspring were evaluated using univariate and multivariate linear regression models.

**Results:** Univariate regression revealed that the paternal birth weight and body mass index (BMI) of the father were predictors for placental and birth weight of the offspring. However, they were not independent predictors. Independent predictors for placental weight were the maternal factors of pre-pregnancy BMI, birth weight, and diabetes. The maternal factors of weight gain during pregnancy, birth weight, smoking during pregnancy, and diabetes were independent predictors for birth weight of the offspring.

**Conclusion:** Paternal as well as maternal factors influence the weight of the placenta and the offspring.

**Keywords:** Birth weight; obstetrics; parents; placenta.

\*This study was performed within the Groningen Expert Center for Kids with Obesity, supported by Hutchison Whamoa Ltd. and by the University Medical Center Groningen.

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## Introduction

The incidence of overweight and obesity are increasing very rapidly worldwide. Overweight is defined as a body mass index (BMI)  $\geq 25$ , and obesity as a BMI  $\geq 30$  [20]. In children, BMI values are gender- and age-specific. Consequently, the International Obesity Task Force determined gender- and age-specific cut-off values for BMI [3].

Especially alarming is the rapid increase of overweight and obesity in young children [28]. In the Netherlands, the obesity prevalence doubled or even tripled from 1980 to 1997 in boys and girls [9]. From 1997 to the period 2002–2004, a two or threefold increase was seen for almost all ages [25]. Birth weight is one of the factors known to influence the risk of developing overweight [17]. Both birth weight and placental weight are related to the risk of hypertension at adult age. Barker et al. [1] found high blood pressure at adult age in individuals born with a low birth weight and a large placenta. Moore et al. [16] confirmed these findings in children aged eight years. In a review, Godfrey [6] noted that both small and large placenta are associated with childhood and adult hypertension. A small placenta is also associated with an increased risk for type 2 diabetes and stroke in adulthood [6].

How birth weight and placental weight are related to long-term outcome is not completely clear. Programming is considered to be an important mechanism [4]. Programming is an epigenetic phenomenon by which nutrition, hormonal, physical, psychological, and other stressful events acting during a critical period of life cause hormonal and metabolic dearrangements [4]. The gestational period and the first months after birth have been shown to be a critical period for future nutritional and hormonal status.

High birth weight is correlated with a higher BMI in childhood and later life [17, 29]. Moreover, a high birth weight is associated with a higher lean mass rather than fat mass. Still, a high birth weight is a risk factor for diseases in later life [18]. For diabetes, an odds ratio of 1.7 was found for children with a high birth weight ( $>4000$  g). In contrast, a low birth weight is associated with a subsequent higher ratio of fat to lean mass and a higher amount of central fat [17]. In addition, low birth weight is associated with an increased risk of glucose intolerance, high blood pressure, and dyslipidemia, along with related diseases, including cardiovascular diseases, in later life [1, 18].

Treatment of existing overweight and obesity is not very effective [21]. Therefore, strategies to prevent these diseases are needed. Since the weight of the placenta as well as birth weight are related to the incidence of overweight, obesity, and its complications, interventions directed towards optimizing both placental and birth weight might be important.

In order to do so, we need to know which factors influence both placental and birth weight but previous studies [2, 5, 8, 10–12, 14, 15, 19, 22, 23, 26, 27, 32] have focused on maternal factors. Hyppönen et al. [10] investigated the role of paternal factors. They only evaluated the role of the father's BMI and did not find any effect on the birth weight.

In this study, we investigated the role of both maternal and paternal factors that might be associated with the weight of the placenta and offspring.

## Patients and methods

The data for this study were collected in Drenthe, one of the northern provinces of the Netherlands. All children born between April 2006 and 2007, and living at time of birth in Drenthe were eligible. Pregnant women in this province were invited to participate in the third trimester of pregnancy. Recruitment took place through obstetricians, midwives, and general practitioners, supported by a media campaign [13]. During the recruitment period, a total of 4778 infants were born. Of these parents, 3631 (76%) wanted to be informed about the study. Finally, 2997 (63%) gave their consent to participate in the study. Multiple birth children (25 twins) were excluded from the present analyses. No other exclusion criteria were applied.

The Dutch obstetric system is traditionally characterized by extensive primary care services, supported by more specialized care. Midwives and general practitioners are responsible for normal deliveries, with obstetricians responsible for those deliveries considered high-risk. When a complication during pregnancy or delivery arises, the woman is referred to an obstetrician. Thirty-four percent of pregnant women deliver under the care of a midwife or a general practitioner; twenty-three percent of women deliver at home, most often supervised by a midwife [31]. In this study, we included all children born full-term as well as preterm, at home and in a hospital.

After signing informed consent, the parents received a questionnaire concerning social status, anthropometry (height and weight), diet and smoking habits, and medical history. Medical history was obtained by requesting a list of diseases diagnosed by a physician. Maternal clinical data during pregnancy were obtained through midwives, obstetricians, and general practitioners.

Parental age was recorded in years. Pre-pregnancy BMI was self-reported and calculated by dividing weight (in kg, recorded to one decimal place) by height squared (in m, recorded to two decimal places). Parental birth weight was self-reported, with the questionnaire filled out at home so that the parents were able to check their birth weight with their own birth records. Weight gain during pregnancy was registered in kg (without decimals). Physical activity was dichotomously coded, with positive defined as once a week or more of at least half an hour of activity of moderate intensity. Diabetes, hypertension, thyroid disease, hypercholesterolemia, and depression (according to the DSM IV) were considered present if the disease had ever been diagnosed by a medical doctor in the past or during pregnancy.

Placental weight and birth weight were measured at birth, and clinical data concerning pregnancy and delivery were collected. Placental weight was measured after the umbilical cord was cut 3 cm from the neonate, including membranes, and without blood clots. All obstetricians, midwives, and general practitioners used an electronic scale with a digital readout which recorded to the nearest 0.01 kg, when measuring both placental weight and birth weight.

This study was approved by the Medical Ethics Committee of the University Medical Center Groningen and performed in accordance with the Declaration of Helsinki.

The association between placental weight and birth weight was calculated using a linear regression model. To identify factors associated with the weight of the placenta and offspring, the data were first analyzed with univariate linear regression using the placental weight and birth weight of the offspring as dependent variables, and parental factors as independent variables. The parental factors examined were age, BMI, birth weight, physical activity, diabetes, hypertension, thyroid disease, hypercholesterolemia, depression, smoking, alcohol, and substance abuse. The maternal factors of weight gain during pregnancy, parity, and income were also tested.

Possible confounding child factors (gestational age and sex of the newborn) were included in the univariate regression analyses as independent variables. Subsequently, multivariate linear regression models with the same outcomes were used to examine the independence of variables associated with outcomes in the univariate analyses.

Since both a low and a high birth weight increase the risk of overweight, the association between parental factors and the groups with low (<2500 g) and high (>4000 g) birth weight was determined by performing univariate and multivariate logistic regression analyses. Low birth weight has been defined by the World Health Organization [24] as <2500 g, and high birth weight has been defined as >4000 g [30].

$P < 0.05$  were considered significant. All statistical analyses were performed using SPSS version 14.0 (SPSS, Chicago, IL, USA).

## Results

A total of 2947 singleton children participated in this cohort study. Of those children included, 52.3% were males, 5.6% were born prematurely (<37 weeks), and mean gestational age was 39.8 (standard deviation, SD 1.7) weeks. Moreover, 150 children (5.2%) had one or two parents with non-Dutch ethnicity. Birth weight was recorded for 2528 children and placental weight for 1651 children. Mean birth weight was 3557 g (SD 540 g) and mean placental weight was 644 g (SD 143 g). The baseline characteristics of the parents are listed in Table 1.

The parental characteristics of the children with recorded birth weight or placental weight did not differ from the parental characteristics of children with unrecorded weights.

The paternal factors of BMI and birth weight were positively associated with placental weight (Table 2). Other factors, such as age, physical activity, smoking in the presence of the mother and paternal diseases were not significantly associated with placental weight.

The maternal factors of age, BMI, weight gain during pregnancy, parity, birth weight, diabetes, hypertension, and depression were positively associated with placental weight (Table 2). Maternal smoking during pregnancy was negatively associated with placental weight. Maternal factors, such as the use of alcohol, physical activity, income, thyroid disease and hypercholesterolemia were not significantly associated with placental weight.

Multivariate analysis revealed that maternal factors of BMI, birth weight, and diabetes were independent predictors

**Table 1** Parental baseline characteristics for the total study population (n=2947).

	Mother (n=2573)	Father (n=2550)
Age (years) (mean $\pm$ SD)	30.71 $\pm$ 4.46	33.44 $\pm$ 4.95
BMI (kg/m <sup>2</sup> ) (mean $\pm$ SD)	24.71 $\pm$ 4.73	25.52 $\pm$ 3.40
Weight gain during pregnancy (kg) (mean $\pm$ SD)	13.78 $\pm$ 5.51	
Birth weight (g) (mean $\pm$ SD)	3311 $\pm$ 591	3487 $\pm$ 588
Parity (median and range)	1.0 (0.4)	
Smoking (%)	10.5	29.4
Fathers who smoke in presence of mother (%)		21.6
Alcohol use during pregnancy (%)	0.9	84.0
Substance abuse during pregnancy (%)	0.2	1.2
Hypercholesterolemia in medical history (%)	1.5	4.4
Depression in medical history (%)	9.0	3.6
Diabetes in medical history (%)	2.6	0.8
Hypertension in medical history (%)	10.7	4.5
Thyroid disease in medical history (%)	2.8	0.4
Physical activity: once a week or more (%)	74.0	68.8
Income <sup>a</sup> (%)		
Less than EUR 850	1.2	0.5
Between EUR 850 and EUR 1150	3.6	2.5
Between EUR 1150 and EUR 3050	58.7	59.5
More than EUR 3050	24.8	25.6
Unwilling to tell	11.7	11.9

<sup>a</sup>The differences in maternal and paternal income can be explained by single parents.

BMI=body mass index.

of placental weight. Placental weight increased by 3.6 g for every additional kg/m<sup>2</sup> BMI of the mother, 49 g for every additional kg of maternal birth weight and 63 g if the mother had diabetes. The explained variance of placental weight by this multivariate model was 10.5%.

Weight gain in pregnancy is partly the result of the increasing weight of the fetus and placenta. Therefore, we performed the multivariable analysis using all variables associated with placental weight (according to the univariate analysis), excluding maternal weight gain. Maternal BMI ( $\beta$ =3.83, standard error, SE=1.12,  $P$ <0.001) and maternal birth weight ( $\beta$ =0.049, SE=0.009,  $P$ <0.001) remained independently associated with placental weight. The other independent variable associated with placental weight in the first analyses, maternal diabetes, had borderline significance in this analysis ( $\beta$ =77.99, SE=40.87,  $P$ =0.057).

Birth weight was associated with placental weight. An increase of 100 g of placental weight was associated with a 63 g higher birth weight ( $P$ <0.001). Paternal BMI and paternal birth weight were positively associated with birth weight of the offspring (Table 2). Smoking by the father in the presence of the pregnant woman was negatively associated with birth weight. Physical activity and paternal diseases were not significantly associated with birth weight.

The maternal factors of age, BMI, weight gain during pregnancy, parity, birth weight, and diabetes were each positively associated with birth weight of the offspring (Table 2). Smoking, low income, and hypertension were negatively associated with birth weight. Diseases other than diabetes and hypertension, physical activity, and the use of alcohol were not significantly associated with birth weight.

Multivariate analysis revealed that the maternal factors of weight gain during pregnancy, birth weight, smoking during

pregnancy, and diabetes were independent predictors for birth weight of the offspring. Birth weight increased 10 g for every additional kg of maternal weight gain during pregnancy, 181 g for every additional kg of maternal birth weight, and 420 g if the mother had diabetes. Birth weight decreased by 364 g when the mother smoked during pregnancy. The explained variance in this multivariate regression model of birth weight was 30.3%.

Multivariate analysis, excluding maternal weight gain as an independent variable, showed that maternal birth weight ( $\beta$ =0.217, SE=0.028,  $P$ <0.001) and smoking during pregnancy ( $\beta$ =−384.67, SE=65.05,  $P$ <0.001) remained independently associated with the birth weight. In this analysis, parity ( $\beta$ =93.65, SE=20.18,  $P$ <0.001) was independently associated with birth weight but diabetes ( $\beta$ =228.27, SE=148.39,  $P$ =0.125) was not.

Table 3 presents the results of the logistic regression analysis of the low birth weight group (<2500 g) and high birth weight group (>4000 g). In the low birth weight group, none of the mothers drank alcohol during pregnancy and none of the fathers had diabetes, depression, or thyroid disease; therefore no results are presented for these variables. Smoking during pregnancy ( $\beta$ =2.785,  $P$ =0.014) was independently associated with low birth weight. Weight gain during pregnancy ( $\beta$ =0.058,  $P$ <0.001) and maternal diabetes ( $\beta$ =2.203,  $P$ <0.001) were independently associated with high birth weight.

## Discussion

The results of the study indicate that both maternal and paternal factors are related to the weight of the placenta as well

**Table 2** Associations between parental factors and the weights of the placenta and the offspring.

	Placental weight (univariate)			Placental weight (multivariate)			Birth weight (univariate)			Birth weight (multivariate)		
	$\beta$	SE	P-value	$\beta$	SE	P-value	$\beta$	SE	P-value	$\beta$	SE	P-value
Child factors												
Gender	-13.46	7.11	0.059				-130.16	25.95	<0.001	-143.78	37.24	<0.001
Gestational age	<b>2.53</b>	<b>0.33</b>	<0.001	2.432	0.494	<0.001	<b>20.15</b>	<b>0.86</b>	<0.001	<b>19.88</b>	<b>1.88</b>	<0.001
Paternal factors												
Age	1.41	0.78	0.072				4.28	2.33	0.066			
BMI	<b>2.51</b>	<b>1.18</b>	<b>0.034</b>	-1.77	2.73	0.516	<b>7.77</b>	<b>3.46</b>	<b>0.025</b>	7.25	10.23	0.479
Birth weight	<b>0.035</b>	<b>0.011</b>	<b>0.001</b>	0.026	0.016	0.103	<b>0.148</b>	<b>0.032</b>	<0.001	0.075	0.055	0.176
Smoking of father	-11.16	10.57	0.292				-154.05	<b>31.81</b>	<0.001	-56.45	117.76	0.632
in presence of mother												
Alcohol	5.12	10.06	0.611				-10.90	138.23	0.937			
Substance abuse	-18.74	71.34	0.793				-558.64	307.99	0.070			
Physical activity	-5.75	8.22	0.484				13.38	24.66	0.588			
Diabetes	-48.86	49.81	0.327				-75.24	119.43	0.529			
Hypertension	-15.83	20.28	0.435				-42.92	56.43	0.447			
Thyroid disease	-8.70	42.46	0.838				-119.23	119.16	0.317			
Cholesterolemia	-9.59	20.25	0.637				-57.07	56.35	0.311			
Depression	-21.14	21.69	0.330				-34.10	60.55	0.573			
Maternal factors												
Age	<b>2.62</b>	<b>0.833</b>	<b>0.002</b>	-1.44	2.49	0.555	<b>7.75</b>	<b>2.49</b>	<b>0.002</b>	-3.90	9.97	0.696
BMI	<b>5.91</b>	<b>0.806</b>	<0.001	<b>3.632</b>	<b>1.12</b>	<0.001	<b>17.61</b>	<b>2.38</b>	<0.001	16.12	8.74	0.067
Weight gain during pregnancy	<b>2.09</b>	<b>0.78</b>	<b>0.008</b>	2.70	1.80	0.135	<b>14.98</b>	<b>2.17</b>	<0.001	<b>10.41</b>	<b>3.60</b>	<b>0.004</b>
Parity	<b>18.92</b>	<b>4.23</b>	<0.001	13.43	12.40	0.280	<b>114.32</b>	<b>14.92</b>	<0.001	75.93	47.53	0.112
Birth weight	<b>0.057</b>	<b>0.009</b>	<0.001	<b>0.049</b>	<b>0.009</b>	<0.001	<b>0.210</b>	<b>0.025</b>	<0.001	<b>0.181</b>	<b>0.032</b>	<0.001
Smoking	-32.73	<b>11.59</b>	<b>0.005</b>	-12.42	38.69	0.748	-376.79	<b>41.02</b>	<0.001	-363.75	<b>74.61</b>	<0.001
Alcohol	-25.21	35.87	0.482				-10.90	138.23	0.937			
Substance abuse	-18.74	71.34	0.793				-558.64	307.99	0.070			
Physical activity	1.64	8.68	0.850				-25.70	25.90	0.321			
Income												
• Less than EUR 850	-39.18	39.45	0.321				-325.32	<b>115.05</b>	<b>0.005</b>	-202.38	457.29	0.659
• EUR 850-1150	-33.47	22.84	0.143				-105.45	63.15	0.095			
• EUR 3051 or more	0.720	8.94	0.936				-29.78	27.09	0.272			
• Unwilling to tell	13.57	12.60	0.282				-57.80	38.28	0.131			
Diabetes	<b>102.93</b>	<b>25.97</b>	<0.001	<b>62.86</b>	<b>30.38</b>	<b>0.039</b>	<b>234.56</b>	<b>70.34</b>	<b>0.001</b>	<b>420.22</b>	<b>109.73</b>	<0.001
Hypertension	<b>23.39</b>	<b>12.69</b>	<b>0.066</b>	11.50	34.92	0.742	-81.91	<b>36.37</b>	<b>0.024</b>	15.23	127.62	0.905
Thyroid disease	-9.43	12.98	0.468				18.86	38.52	0.624			
Hypercholesterolemia	-4.62	31.13	0.882				51.19	92.46	0.580			
Depression	<b>31.06</b>	<b>13.32</b>	<b>0.020</b>	25.79	33.84	0.447	34.46	40.39	0.394			

The bold values are values with a significant P-value ( $P < 0.05$ ). BMI = body mass index.



**Table 3** Associations between parental factors and high and low birth weight of the offspring.

	Low birth weight (univariate)			Low birth weight (multivariate)			High birth weight (univariate)			High birth weight (multivariate)		
	$\beta$	SE	P-value	$\beta$	SE	P-value	$\beta$	SE	P-value	$\beta$	SE	P-value
Child factors												
Gender	0.040	0.333	0.904				-0.446	0.123	<0.001	<b>-0.561</b>	<b>0.162</b>	<b>0.001</b>
Gestational age	<b>-0.089</b>	<b>0.008</b>	<b>&lt;0.001</b>	-0.030	0.042	0.467	0.071	0.006	<0.001	<b>0.095</b>	<b>0.011</b>	<b>&lt;0.001</b>
Paternal factors												
Age	-0.011	0.029	0.693				<b>0.023</b>	<b>0.011</b>	<b>0.031</b>	0.031	0.072	0.672
BMI	-0.061	0.046	0.184				0.031	0.016	0.053			
Birth weight	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.023</b>	<0.001	<0.001	0.704	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.005</b>	0.001	<0.001	0.104
Smoking of father in presence of mother	0.212	0.370	0.567				<b>-0.044</b>	<b>0.171</b>	<b>0.009</b>	-1.034	0.953	0.278
Alcohol	-0.546	0.326	0.094				0.214	0.152	0.160			
Substance abuse	0.677	1.033	0.513				0.176	0.512	0.731			
Physical activity	0.008	0.304	0.979				0.142	0.118	0.230			
Diabetes							-1.547	1.027	0.132			
Hypertension	0.327	0.604	0.589				-0.252	0.287	0.380			
Thyroid disease							-0.125	0.604	0.837			
Cholesterolemia	-0.090	0.729	0.902				-0.430	0.304	0.158			
Depression							-0.063	0.292	0.828			
Maternal factors												
Age	0.005	0.030	0.870				<b>0.043</b>	<b>0.012</b>	<b>&lt;0.001</b>	-0.103	0.083	0.214
BMI	<b>-0.129</b>	<b>0.041</b>	<b>0.002</b>	-0.053	0.138	0.703	<b>0.064</b>	<b>0.010</b>	<b>&lt;0.001</b>	0.100	0.057	0.080
Weight gain during pregnancy	<b>-0.068</b>	<b>0.028</b>	<b>0.016</b>	0.021	0.102	0.836	<b>0.055</b>	<b>0.010</b>	<b>&lt;0.001</b>	<b>0.058</b>	<b>0.015</b>	<b>&lt;0.001</b>
Parity	-0.325	0.216	0.132				<b>0.352</b>	<b>0.067</b>	<b>&lt;0.001</b>	0.125	0.304	0.681
Birth weight	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>0.014</b>	<0.001	<0.001	0.577	<b>0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.001	<0.001	0.155
Smoking	<b>1.874</b>	<b>0.336</b>	<b>&lt;0.001</b>	<b>2.785</b>	<b>1.145</b>	<b>0.014</b>	<b>-1.189</b>	<b>0.285</b>	<b>&lt;0.001</b>	-0.607	1.292	0.639
Alcohol							0.359	0.587	0.541			
Physical activity	-0.304	0.297	0.306				0.156	0.125	0.210			
Income												
• Less than EUR 850	0.927	1.044	0.374				-0.481	0.625	0.442			
• EUR 850–1150	1.081	0.553	0.051				-0.411	0.333	0.217			
• EUR 3051 or more	0.512	0.321	0.111				-0.062	0.177	0.627			
• Unwilling to tell	0.649	0.415	0.118				-0.076	0.181	0.674			
Diabetes	0.808	0.609	0.185				<b>0.905</b>	<b>0.275</b>	<b>&lt;0.001</b>	<b>2.203</b>	<b>0.466</b>	<b>&lt;0.001</b>
Hypertension	0.216	0.411	0.559				-0.060	0.173	0.729			
Hypercholesterolemia	0.954	0.742	0.199				0.379	0.392	0.334			
Thyroid disease							-0.045	0.184	0.807			
Depression	0.087	0.476	0.855				0.327	0.176	0.063			

The bold values are values with a significant P-value ( $P < 0.05$ ). BMI = body mass index.

as birth weight in the offspring. The paternal factors of BMI and the father's own birth weight are related to placental weight. Both factors, together with smoking in the environment of the mother, influence birth weight. The influence of the maternal factors of age, BMI, weight gain during pregnancy, parity, birth weight, and diabetes were positively related to both the weights of the placenta and the offspring; hypertension and depression were positively related to placental weight, and smoking was negatively related. Moreover, the maternal factors of smoking, hypertension, and low income were negatively related to birth weight.

In the Netherlands, birth weight is measured in virtually all newborns, but the weight of the placenta is not routinely measured and, therefore, it had to be especially measured for our cohort study. Unfortunately a number of the weight measurements of the placenta were missing in our data. We have no reason to assume that a bias has occurred regarding which placentas were measured. Therefore, we are convinced that the weights of the placenta provide a reliable sample of the whole population.

We observed a significant relationship between placental weight and birth weight. This was also found by Hindmarsh et al. [8], which provides further support to the observation of Gruenewald [7] that the placenta is a fetal organ and that placental size is largely a reflection of the determinant for fetal size. This is also in accord with our findings that almost all factors influencing placenta weight also influenced birth weight.

Our results indicate that BMI and birth weight of the father are related to placental weight. In the multivariate analysis, these factors were not independent. The effect size of the determinant for the father was, in this univariate analysis, much smaller when compared to the factors for the mother. This might explain why effects disappeared in the multivariate analysis. That the paternal factors might influence the weight of the placenta seems remarkable. Hindmarsh et al. [8] showed that paternal as well as maternal height was related to placental weight. We observed a relationship with the BMI and the birth weight of the father. The relationship with birth weight, as well as the observation of Hindmarsh et al. [8], might be fixed in biological terms. How the BMI of the father might influence the placental weight is less clear.

A number of maternal conditions are described which influence placental weight. Maternal BMI [22], diabetes [23], maternal weight, and height [8] have a positive effect on placental weight whereas smoking has a negative effect [8]. Our results are in line with these observations but we also found that age, weight gain during pregnancy, maternal own birth weight, hypertension, and depression were positively related to the weight of the placenta. In the univariate analysis we observed a positive relationship between parity and placental weight. The same positive correlation was found by Bleker et al. [2]. The negative effect of parity on placental weight as found by Hindmarsh et al. [8] disappeared when birth weight was included in the analysis. It is, from a physiological point of view, understandable that parity would be positively related to placental weight, at least for the first three to four pregnancies.

As shown in the univariate analysis, the paternal factors of BMI, birth weight, and smoking in the presence of the mother, were related to birth weight of the offspring. Since the multivariate linear regression analysis revealed that maternal factors were independent predictors, while paternal factors were not, we concluded that the maternal factors did have a stronger influence than the paternal factors. Little [14] also found a relationship between paternal birth weight and the birth weight of his children. The effect, however, was smaller when compared to the birth weight of the mother. Nevertheless, these results indicate an effect from paternal genes or gene expression on birth weight. In contrast to the study by Hyppönen [10], we observed a relationship between BMI of the father and birth weight of the offspring. Our finding might be caused by a correlation between the BMIs of both parents, while the real effect was due to the maternal BMI only.

Our results regarding the effect of maternal factors on birth weight are in line with previous studies. BMI as well as weight gain during pregnancy were found to be related to birth weight [5, 15, 26]. The combination of pre-pregnant BMI and weight gain during pregnancy was also a predictor for birth weight [12]. Our results show that maternal BMI and weight gain during pregnancy were related to birth weight of the offspring. However, maternal BMI was not an independent predictor.

Maternal smoking during pregnancy was independently associated with birth weight. Interestingly, maternal smoking predicted birth weight, but not placental weight. This suggests that the size of the placenta does not decrease the function of the placenta, but that the function of the placenta is impaired, resulting in a decrease in birth weight. Zdravkovic et al. [32] found that tobacco had a direct effect on trophoblast proliferation and differentiation, thereby influencing placental function. Pringle et al. [19] showed that smoking was associated with a significantly increased abnormal umbilical arterial blood flow. These two findings underscore the possibility that smoking might have an effect on placental function rather than size.

The relationship between maternal diabetes and birth weight has frequently been described [11, 27]. Jovanovic-Peterson et al. [11] showed that more infants of diabetic mothers are at or above the 90<sup>th</sup> percentile for birth weight as compared to infants of control mothers. Voldner et al. [27] showed that overweight women with a rise in fasting plasma glucose from early to late pregnancy had a 4.5-fold increase in risk of newborn macrosomia as compared to mothers with only a high BMI.

Our prospective birth cohort study was specially designed to answer questions focused on childhood growth [13]. Compared with other cohort studies, more detailed data regarding parental medical history and obstetric data (such as placental weight, parity, smoking, use of alcohol during pregnancy) were collected. Therefore, in our opinion, the results of our study are more accurate when compared to other studies that focused on this specific facility of one variable on one outcome [5, 10, 12], or when data were collected retrospectively [12, 15].

Unfortunately, our data are not very helpful in designing interventions to prevent the occurrence of overweight and obesity in infants. The factors influencing the weights of the placenta and the offspring are hard to manipulate. The only factors that might be changed during pregnancy are smoking and weight gain. The other factors, such as BMI of the mother and the father need to be addressed long before pregnancy.

In conclusion, paternal as well as maternal factors influence the weights of the placenta and offspring.

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