Exercise Training in Pregnancy Reduces Offspring Size without Changes in Maternal Insulin Sensitivity

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Context: Epidemiological studies have identified the importance of the in utero environment in providing a healthy start to life. Previous studies have suggested that the maternal environment, in particular a reduction in maternal insulin sensitivity, contributes significantly to fetal growth. Regular aerobic exercise, through an effect on maternal insulin sensitivity, may influence offspring size by regulating nutrient supply to the fetus.

Objective: The aim of the study was to determine the effects of aerobic exercise training in the second half of pregnancy on maternal insulin sensitivity and neonatal outcomes.

Design and Setting: We conducted a community-based, randomized, controlled trial of exercise in pregnancy.

Participants: Eighty-four healthy nulliparous women (mean ± SD, age, 30 ± 4 yr; body mass index, 25.5 ± 4 kg/m²) participated in the study.

Intervention: Subjects participated in a home-based stationary cycling program from 20 wk gestation to delivery.

Main Outcome Measures: Maternal insulin sensitivity, neonatal auxology, body composition, and growth-related peptides in cord blood were measured.

Results: Offspring of exercisers had lower birth weight (SD score, control, 0.23 ± 0.8; exercise, −0.19 ± 0.9; P = 0.03) and body mass index at birth (SD score, control, 0.40 ± 0.9; exercise, −0.01 ± 0.09; P = 0.04). The reduction in maternal insulin sensitivity in late gestation was not affected by exercise (P = 0.45) and was unrelated to offspring size. Exercise offspring had lower cord serum IGF-I (P = 0.03) and IGF-II (P = 0.04).

Conclusions: Regular exercise was associated with lower birth weights and reduced cord concentrations of growth-related peptides, suggesting an influence of exercise on endocrine regulation of fetal growth. These effects on offspring growth were not associated with an exercise training effect on maternal insulin sensitivity. (J Clin Endocrinol Metab 95: 2080–2088, 2010)
swimming, may minimize joint and musculoskeletal stress, especially in late gestation (8). However, the small number of studies that have used non-weight-bearing exercise, although hampered by inadequate sample size, have not shown a significant effect on birth size (4–6).

At present, there are minimal data on the metabolic consequences of exercising during pregnancy for mother and offspring. Regular exercise persistently improves insulin sensitivity in nonpregnant individuals (9–11), an effect that is maintained as long as regular exercise is continued (9). Therefore, regular sustained aerobic exercise in pregnant women may counteract the normal state of insulin resistance present in late gestation (12–15). To date, there have been no randomized controlled trials examining the effects of regular aerobic exercise on maternal insulin sensitivity in healthy nondiabetic pregnant women. However, limited data on surrogate markers of insulin action suggest that exercise training may modify glucose metabolism in pregnancy (16–19).

During late pregnancy, the marked reduction in maternal insulin sensitivity has been linked to the preservation of fetal nutrient availability for growth (20). This has been suggested by an inverse relationship between offspring birth size and both very low and very high maternal insulin sensitivity (21–24). Physical activity, by improving insulin sensitivity, may reduce nutrient delivery to the fetus. In addition to the well-documented impact of exercise on blood flow and oxygen-carrying capacity, endocrine adaptations to exercise during pregnancy may provide one physiological mechanism underlying any exercise-associated effects on fetal growth. In addition, the effects of maternal exercise on the fetal IGF axis and leptin concentrations are unexplored and could provide a hormonal basis for an exercise impact on nutrient partitioning and fetal growth.

The aim of this study was to determine the effects of aerobic exercise training during pregnancy on maternal insulin sensitivity and neonatal outcomes (including auxology, body composition, and cord blood concentrations of growth-associated peptides). We hypothesized that regular non-weight-bearing aerobic exercise during the second half of pregnancy would 1) lead to a reduction in offspring birth size and percentage body fat; and 2) be associated with an exercise-induced attenuation of the normal reduction in maternal insulin sensitivity with advancing gestation.

**Subjects and Methods**

**Subjects**

Volunteers were recruited between December 2004 and May 2007 using advertisements and the assistance of maternity providers in Auckland. Healthy nulliparous women between 20 and 40 yr of age, with a singleton pregnancy of less than 20 wk gestation, were eligible. Exclusion criteria included alcohol consumption or tobacco use at recruitment, a personal or family history of type 2 diabetes mellitus, or the development of any medical condition for which participation in an exercise program was contraindicated by the American College of Obstetricians and Gynecologists (25) (e.g., preeclampsia, fetal growth restriction, preterm birth). All women completed baseline assessments of insulin sensitivity and aerobic fitness at approximately 19 wk gestation. All participants were then randomly assigned to exercise or control groups. Control participants were asked to continue their normal daily activities for the duration of their pregnancy.

This study was approved by the Northern Ethics Committee of New Zealand (AKX/04/08/227) and registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12605000497606). Written informed consent was obtained from maternal participants on behalf of themselves and their offspring.

**Exercise intervention**

The aerobic exercise program was home-based, using stationary cycling, and was individually prescribed to a maximum of five sessions of 40-min aerobic exercise per week. Exercise programs aimed to achieve a moderate exercise intensity of approximately 65% of predicted aerobic capacity (VO2max). The study protocol recommended that regular exercise was maintained until at least 36 wk gestation. After this time, participants were encouraged to maintain as close to their prescribed exercise program as possible until delivery (subject to capacity). During a fortnightly supervised exercise session, maternal heart rate and blood pressure responses were monitored, and exercise prescription was updated to maintain the prescribed exercise intensity.

Compliance to the exercise program was assessed by self-reported exercise diaries and downloadable heart rate monitors (Polar S625; Polar, Kempele, Finland). The required workload was estimated using linear regression of oxygen uptake and workload obtained from aerobic fitness testing, with standard equations (8) used to calculate energy expenditure for all exercise sessions. Weekly energy expenditures, exercise duration (minutes), and exercise intensity (in metabolic equivalents) were averaged for each phase of the exercise program: familiarization (20–27 wk), maintenance (28–35 wk), and subject to capacity (36–40 wk). Compliance was reported as the percentage of prescribed weekly exercise duration completed.

**Measurement techniques**

**Maternal insulin sensitivity**

Insulin sensitivity was assessed at 19 and 34–36 wk gestation. After an overnight fast, participants underwent a 180-min iv glucose tolerance test for minimal model analysis of parameters of insulin sensitivity, as previously described (26). At zero time, dextrose (300 mg/kg body weight as a 25% solution in normal saline) was infused over 60 sec. Blood samples for insulin and glucose were drawn at 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 35, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 min. Paired insulin and glucose values were entered into the MINMOD Millennium computer program (27) to calculate the insulin sensitivity index (SIr), acute insulin response (AIR), disposition index (DI; the product of SI and AIR), glucose effectiveness, and glucose disappearance.
Aerobic fitness

All subjects performed a submaximal graded exercise test in mid and late pregnancy on a stationary cycle to 150 beats/min (peak work capacity) as previously described (4, 28). In addition to standard heart rate measurements, respiratory gas analysis was used to assess changes in cardiorespiratory response to exercise. Direct gas analyses and the calculation of VO₂ at 150 beats/min were performed using the MOXUS Modular VO₂ System (AEI Technologies, Pittsburgh, PA). Each participant completed a 3-min warm-up on an unloaded cycle, after which time the workload was increased to 30 watts (W). Thereafter, the workload increased 10 W every minute until subjects maintained a target heart rate of 150 beats/min for a period of at least 10 sec. Submaximal VO₂peak was defined as the average of the last two consecutive values on attainment of the target heart rate.

Additional maternal assessments

Maternal height was measured using a fixed wall-stadiometer (Harpenden Stadiometer; Holtain Ltd., Crymych, UK). Body weight was measured using calibrated electronic scales (Tanita TBF-105 Body Fat Analyzer; Tanita Corp., Arlington Heights, IL). Dietary intake was assessed by means of two 7-d food records at 20 and 33 wk gestation. The Foodworks Professional Edition 2007 software with the New Zealand FOODfiles 2004 database was used to analyze energy intake and nutrient content of the food records.

Neonatal outcomes

Neonatal auxological measures were obtained by a study investigator within 48 h of birth. Birth weight was measured to the nearest 10 g using electronic infant scales. Crown-heel length was measured using a neonatometer (Holtain Ltd.), and circumferential measurements of the head and chest were obtained to the nearest millimeter. Between-group comparisons of birth size included uncorrected birth weight (grams), crown-heel length (millimeters), and head circumference (millimeters), and their sd scores, corrected for gender and gestational age (29, 30). Body mass index (BMI) at birth was calculated as weight/height² (kilograms/meter²), with sd scores corrected for gender only (29). Ponderal index was calculated as birth weight in grams (×100) divided by the cube of the crown-heel length in centimeters. Small for gestational age (SGA) was defined as birth weight less than the 10th customized centile that was adjusted for maternal height, weight, ethnicity, infant sex, and gestation at delivery (31). In addition to auxology, a venous cord blood sample was collected at delivery to assess fetal concentrations of growth-related peptides [IGF-I, IGF-II, IGF binding protein (IGFBP)-1, IGFBP-3, leptin, glucose, and insulin].

Body composition

Maternal and offspring body compositions were evaluated 2–3 wk postpartum by dual-energy x-ray absorptiometry (DXA) (Lunar Prodigy BX-II; Lunar Corp., Madison, WI). All scans were analyzed for total fat mass, lean mass, percentage body fat, and bone mineral density by the same operator using standard pediatric software packages (GE Corp., Madison, WI).

Assays

Levels of plasma glucose were measured by an automatic random-access analyzer (Hitachi 911; Hitachi, Tokyo, Japan) with an interassay coefficient of variation of 1.2% (32). Plasma insulin concentrations were measured by an automated micro-particle enzyme immunoassay (IMX MEIA assay; Abbott Laboratories, North Chicago, IL) with an interassay coefficient of variation in our laboratory of less than 5%. Serum IGF-I, IGF-II, IGFBP-1, and IGFBP-3 were measured in duplicate using commercially available ELISA kits (Diagnostic Systems Laboratories Inc., Webster, TX). Manufacturer intra- and interassay coefficients of variation range from 1.7 to 7.3% and 6.2 to 8.2%, respectively. Leptin was measured in cord blood serum using a direct sandwich ELISA kit (LINCO Research, St. Charles, MO). The manufacturer intraassay and interassay coefficients of variation were 2.6 and 2.6%, respectively.

Calculations and statistical analysis

Sample size calculations were planned to detect differences in our two main outcomes, offspring birth weight and maternal insulin sensitivity. Variance observed in earlier studies of exercise effects on birth weight indicated that a sample size of 20 per group was required to detect a 10% difference in birth weight at the 0.05 level, with a power of 0.80. Secondly, based on previous pregnancy data (14, 15, 33), a sample size of 50 per group had 80% power at the 0.05 level of significance to detect a 20% difference between groups in the change in insulin sensitivity.

All variables were checked for normality and transformed where necessary (logarithmically or by square root). Simple group comparisons were conducted using independent samples t test or χ² test for categorical data. Within comparison blocks, the Bonferroni method was used to adjust for multiple comparisons. Intention to treat analyses were performed using repeated measures ANOVA to investigate differences in insulin sensitivity, aerobic fitness, and maternal size between groups from baseline to late pregnancy. All data were analyzed using SPSS version 15 for Windows, (SPSS Inc., Chicago, IL).

Results

Of the 98 women recruited, 84 (47 exercise, 37 control) completed both baseline and late pregnancy data collection and had auxological data collected on their offspring (Fig. 1). There were no significant differences in age, ethnicity, or body size between women who completed the study and those that were lost to follow-up (data not shown). Maternal physical characteristics were not different between exercise and control groups at the start of the study (Table 1). However, mean maternal age was higher in the exercise group (control, 29 ± 4 yr; exercise, 31 ± 3 yr; P < 0.005). Ethnicity (93% European), years of education (16.5 ± 2.5 yr), and self-reported maternal birth weight (3.4 ± 0.4 kg) were not different in the two groups; and paternal age (control, 33 ± 5 yr; exercise, 33 ± 5 yr), body weight (control, 84.0 ± 10.2 kg; exercise, 86.9 ± 12.4 kg), and BMI (control, 25.5 ± 2.9 kg/m²; exercise, 26.7 ± 3.3 kg/m²) were not different. Exercise volumes and compliance with the exercise program are displayed in Fig. 2. Overall compliance in the exercise
commitments (n = 253) and moving out of the study area. In the control group, two exercise) withdrew from the study for personal reasons. In the exercise group these were the result of increased work commitments (did not complete baseline testing) and wanting to take part in another exercise program during pregnancy. Three women, all in the control group, met exclusion criteria in late pregnancy with the development of pregnancy complications that were stated as absolute contraindications for exercise training. These included preeclampsia (n = 1), gestational hypertension with intraterine growth restriction (n = 1), and preterm labor (<30 wk gestation) (n = 1). These women delivered before the late gestation follow-up period, and no neonatal auxology was collected. Eleven women (nine control, two exercise) withdrew from the study for personal reasons. In the exercise group these were the result of increased work commitments and moving out of the study area. In the control group reasons included health concerns that did not meet exclusion criteria and not wanting to have the follow-up insulin sensitivity test (n = 1).

FIG. 1. Flow of participants through the study. During the study period, 14 participants (two exercise, 12 control) were lost to follow-up (4% of exercise, 24% of control participants). Allocation stage. Two control participants withdrew as a result of increased work commitments (did not complete baseline testing) and wanting to take part in another exercise program during pregnancy. Three women, all in the control group, met exclusion criteria in late pregnancy with the development of pregnancy complications that were stated as absolute contraindications for exercise training. These included preeclampsia (n = 1), gestational hypertension with intraterine growth restriction (n = 1), and preterm labor (<30 wk gestation) (n = 1). These women delivered before the late gestation follow-up period, and no neonatal auxology was collected. Eleven women (nine control, two exercise) withdrew from the study for personal reasons. In the exercise group these were the result of increased work commitments and moving out of the study area. In the control group reasons included health concerns that did not meet exclusion criteria (n = 2), moving out of the Auckland area (n = 2), increased work commitments (n = 2), and not wanting to have the follow-up insulin sensitivity test (n = 1).

Exercise training had no impact on changes in maternal body weight and BMI during late pregnancy (Table 1). In contrast, exercise training resulted in an increase in total test time and VO₂ at submaximal peak exercise in the training group (P < 0.05). Table 2 displays indices of glucose regulation obtained during minimal model analyses. The Sf decreased in both groups from baseline to late gestation, indicating increased peripheral insulin resistance. In contrast, AIR increased with advancing gestation, as would be expected to maintain euglycemia. Exercise training had no effect on the changes in Sf and AIR from baseline to late gestation and did not affect any other parameters of glucose regulation.

The auxological characteristics of the offspring are detailed in Table 3. Exercise had no impact on the average length of gestation. Offspring of exercisers were on average 143 ± 94 g lighter than their control counterparts; however, there was no group difference in birth length. Exercise training resulted in lower offspring BMI. When birth weight was adjusted for gender and gestational age at delivery and reported as an SD score, there was a significant reduction in exercise offspring compared with controls.

This reduction in body size persisted at the time of postnatal DXA scans. DXA analysis suggested that body composition was unaffected by maternal exercise, with similar percentage body fat. Cord serum concentrations of IGF-I and IGF-II were lower in exercise compared with control offspring (Table 4). In contrast, there were no differences between exercise and control in cord blood concentrations of IGFBP-1, IGFBP-3, leptin, plasma glucose, or insulin.

**Discussion**

In this randomized, controlled study, 15 wk of non-weight-bearing aerobic exercise during the second half of pregnancy was associated with reduced birth weight after correction for gender and gestational age at delivery. However, exercise had no effect on offspring body composition assessed by DXA, with a proportional decrease in both lean and fat mass in exercise offspring compared with controls. Consistent with their smaller birth size, cord blood concentrations of IGF-I and IGF-II were lower in exercise offspring. The reduction in concentrations of known fetal growth-promoting peptides suggests that maternal exercise elicited adaptations in nutrient partitioning to the fetus, leading to decreased endocrine stimulation of fetal growth. These changes were not associated with an increased incidence of SGA or reductions in neonatal bone density. Therefore, we conclude that exercise resulted in a modest shift in the birth weight distribution within the normal range when compared with the control group. In contrast, 15 wk of exercise training had no impact on pregnancy-related alterations in insulin sensitivity compared with controls, refuting our hypothesis that maternal insulin sensitivity may provide a physiological link between maternal exercise and the observed reduction in birth weight.

This is the first study to evaluate longitudinal changes in insulin sensitivity in response to aerobic exercise training during pregnancy. Using the minimal model technique to assess glucose metabolism, the physiological response to pregnancy appears to supersede the chronic improvements in insulin sensitivity previously described in response to exercise training in nonpregnant individuals (9–11). Given that elevated maternal insulin sensitivity has previously been associated with fetal growth restriction...
the lack of a chronic exercise effect on maternal insulin sensitivity may be a reassuring finding. Our observations suggest that, during a healthy pregnancy, maternal insulin sensitivity is persistently regulated to achieve optimal fetal growth and is not sensitive to modest increases in energy expenditure through exercise. Furthermore, across the entire cohort, maternal SI obtained in mid or late gestation was not correlated with any indices of offspring size. Previous investigators have described significant inverse relationships between maternal insulin sensitivity

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| TABLE 1. Maternal characteristics and changes in size, energy intake, and aerobic fitness during pregnancy in 84 women who completed baseline (19 ± 1.1 wk) and late gestation (35 ± 0.8 wk) assessments |
|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| Control (n = 37)                              | Exercise (n = 47)                                | P values (time, group, interaction) |
| Body weight (kg)                              | Body weight (kg)                                |                                  |
| Baseline                                      | Baseline                                      | Baseline                                      |
| 71.6 ± 10.7                                    | 70.3 ± 13.1                                    | t < 0.01, g = 0.76, tg = 0.35 |
| 79.6 ± 9.8                                     | 78.5 ± 13.6                                    |                                  |
| BMI (kg/m²)                                    | BMI (kg/m²)                                    |                                  |
| Baseline                                      | Baseline                                      |                                  |
| 25.4 ± 2.9                                     | 25.5 ± 4.3                                     | t < 0.01, g = 0.94, tg = 0.40 |
| 28.3 ± 2.6                                     | 28.4 ± 4.3                                     |                                  |
| Energy intake (kcal/d)                         | Energy intake (kcal/d)                          |                                  |
| Baseline                                      | Baseline                                      |                                  |
| 2046 ± 352                                     | 1929 ± 305                                     | t = 0.21, g = 0.11, tg = 0.64 |
| 2113 ± 425                                     | 1979 ± 288                                     |                                  |
| PWC₁₅₀ time (sec)                              | PWC₁₅₀ time (sec)                              |                                  |
| Baseline                                      | Baseline                                      |                                  |
| 518 ± 150                                      | 485 ± 112                                      | t < 0.01, g = 0.85, tg < 0.01 |
| 536 ± 137                                      | 580 ± 133                                      |                                  |
| Peak VO₂ (ml/kg/min)                           | Peak VO₂ (ml/kg/min)                           |                                  |
| Baseline                                      | Baseline                                      |                                  |
| 20.3 ± 4.0                                     | 19.2 ± 3.7                                     | t = 0.08, g = 0.85, tg < 0.01 |
| 18.7 ± 3.3                                     | 20.0 ± 3.5                                     |                                  |

Values are expressed as mean ± sd. Repeated measures ANOVA were used to assess changes with pregnancy and differences between groups during pregnancy. Energy intake was assessed using 7-d diet records. Aerobic fitness was assessed using a submaximal exercise test to a heart rate of 150 beats per minute (PWC₁₅₀). PWC, Peak work capacity; t, time effect; g, group effect; tg, time-group interaction.

FIG. 2. Quantification of exercise volumes and compliance. Exercise volumes are shown during each phase of the exercise program in control (n = 37) and exercise (n = 47) participants. Data points are means, error bars are SEM. A, Exercise duration was similar between groups in the familiarization period (20–27 wk gestation); however, there was a significant difference between exercise and control for the overall duration of the program (P < 0.001). B, Exercise intensity was higher in the exercise group at all time periods, with a significant overall difference between exercise and control (P < 0.001). C, Weekly energy expenditure was significantly higher in the exercise group in all three exercise phases. This was maintained during wk 36–40, despite a reduction in weekly exercise duration. There was a significant difference between exercise and control for the entire duration of the program (P = 0.020). D, Distribution of compliance to exercise prescription within the exercise group (n = 47). Lines are means and sd.
TABLE 2. Changes to indices of maternal glucose regulation in 84 women who completed baseline (19 ± 1 wk) and late gestation (35 ± 0.8 wk) assessments

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 47)</th>
<th>Exercise (n = 47)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Late gestation</td>
</tr>
<tr>
<td>SI (10⁻⁰·₉5·min⁻¹·μU·ml⁻¹)</td>
<td>2.24 (1.95–2.55)</td>
<td>2.12 (1.86–2.39)</td>
</tr>
<tr>
<td>AIR (mIU/liter)</td>
<td>152 (126–179)</td>
<td>157 (131–173)</td>
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<tr>
<td>DI</td>
<td>176 (150–200)</td>
<td>202 (177–227)</td>
</tr>
<tr>
<td>SG (10⁻¹·₂·min⁻¹·μU·ml⁻¹)</td>
<td>0.90 (0.73–1.09)</td>
<td>0.93 (0.75–1.10)</td>
</tr>
<tr>
<td>FPG (mmol/liter)</td>
<td>4.30 (4.10–4.49)</td>
<td>4.35 (4.16–4.47)</td>
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</table>

All values are expressed as geometric mean (95% confidence interval). FPG and FPI were assessed from an average of three fasting measurements. All other parameters were obtained from minimal model analysis of the frequently sampled iv glucose tolerance test. SI, AIR, DI, and FPI were logarithmically transformed prior to analyses to conform to normal distribution requirements. Weight gain (kilograms) and baseline BMI (kg/m²) were controlled for in these analyses. SG, Glucose effectiveness; DI, glucose disappearance rate; FPG, fasting plasma glucose; FPI, fasting plasma insulin.

Erving muscle and skin (34). Together with intermittent redistribution of maternal cardiac output toward the exercising muscle and skin (34). Furthermore, a single bout of moderate-intensity cycling exercise in late gestation has been shown to increase insulin sensitivity for at least 30 min (18). During prolonged exercise, there is a redistribution of maternal cardiac output toward the exercising muscle and skin (34). Together with intermittent redistribuciónd of maternal cardiac output toward the exercising muscle and skin (34).

TABLE 3. Neonatal auxology at birth and at 17 ± 4 d of age in 84 offspring of control and exercise participants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 37)</th>
<th>Exercise (n = 47)</th>
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<tbody>
<tr>
<td>Birth weight SDS</td>
<td>0.23 ± 0.19</td>
<td>0.25 ± 0.20</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>0.40 ± 0.01</td>
<td>0.41 ± 0.02</td>
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</table>

All auxological measurements were obtained by a study investigator (S.A.H.) within 48 h of birth. Body composition was evaluated at mean ± SD of 17 ± 4 d using DXA. GA, Gestational age at delivery; BW, birth weight; SDS, SD score; BMD, bone mineral density.

and neonatal size and body composition (21–23). However, these studies have included women with extremes of insulin sensitivity, including those with fetal growth restriction or gestational diabetes mellitus. The results of the present study suggest that this relationship between insulin sensitivity and neonatal size is not present within the range of maternal SI occurring in nondiabetic, healthy mothers. The mechanisms underlying the effects of exercise on fetal growth remain unclear. In this study, the timing of insulin sensitivity assessments was designed to evaluate long-term adaptations in response to exercise training, as opposed to the transient residual effects of the last exercise session. Therefore, the absence of a persistent effect on insulin sensitivity, as found in our study, does not exclude an influence of regular acute changes in insulin action on the processes governing fetal growth. Indeed, previous studies have demonstrated a reduction in glucose and insulin for a sustained period after an exercise session, particularly in late pregnancy (16, 17). Furthermore, a single bout of moderate-intensity cycling exercise in late gestation has been shown to increase insulin sensitivity for at least 30 min (18). During prolonged exercise, there is a redistribution of maternal cardiac output toward the exercising muscle and skin (34). Together with intermittent
reductions in maternal glucose levels after exercise, these changes may result in as yet undefined adaptations within the placenta, leading to decreased nutrient partitioning to the fetus. Reductions in nutrient delivery to the fetus would result in lower fetal insulin concentrations and a decrease in fetal IGF-I and IGF-II that would down-regulate fetoplacental growth (35). The lower IGF-I and IGF-II concentrations in cord blood from exercising subjects supports this hypothesis. Future studies should therefore concentrate on examining the repeated acute effects of exercise training to investigate whether this is the mechanism underlying an exercise effect on fetal growth.

Previous studies examining the effects of regular aerobic exercise on fetal growth have focused primarily on birth size and have reported contrasting effects on birth weight (1, 3–5, 7). Contradictory findings may be explained by variations in exercise prescription (e.g., timing and volume) and by differences in study populations. Our findings are consistent with a small reduction in birth weight (100 g) demonstrated in a group of previously active women who performed a low volume of weight-bearing exercise in early pregnancy before trebling their exercise volume in the second half of gestation. However, ours is the first study to demonstrate a significant effect of non-weight-bearing exercise on birth weight. A previous underpowered study by Marquez-Sterling et al. (4), using a mixed exercise regimen, reported a similar reduction in birth weight (207 g) but had inadequate statistical power (n = 9) to detect modest effects on offspring birth weight. In contrast, our data differ from those of Collings et al. (5) who reported a nonsignificant increase in birth weight (243 g) in response to stationary cycling training in a small group (n = 12) of sedentary, multiparous women. However, their study design prescribed low volumes of exercise that may explain contrasting effects on fetoplacental growth. Therefore, in contrast to previous suggestions (36), our data suggest that non-weight-bearing exercise also has a significant impact on fetal growth. This is an important finding because for many women non-weight-bearing exercise may be better tolerated during pregnancy, minimizing joint and musculoskeletal stress (8). Indeed, our exercise program was achievable and acceptable for the participants involved, with good compliance and only two withdrawals (4%) from the exercise group. However, further studies will be necessary to determine whether this exercise program can be implemented in other settings.

Several aspects of our study design should be considered when interpreting the results of this study. First, due to withdrawals, this study was underpowered to detect differential effects of exercise training on maternal insulin sensitivity. However, given the absence of any measurable effect on insulin sensitivity, it is unlikely that these findings were affected by the smaller study numbers. Second, the increased withdrawals from the control group may introduce experimental bias, particularly affecting the results if these women differed from those completing the study. However, comparison of the final study population with the women who did not complete the study did not identify any differences between groups. Finally, the minimal model, like all current methods to determine insulin sensitivity, does not account for non-insulin-mediated glucose transport to the fetus via the placenta. It is likely therefore that insulin sensitivity was overestimated during pregnancy. Despite this limitation, the longitudinal, controlled study design should negate these inaccuracies by providing intraindividual as well as between-group controls.

There is now a large body of evidence demonstrating the influence of the in utero environment on growth trajectory in postnatal life. Increased size at birth is associated with greater risk for the development of overweight and obesity in childhood (37). In this study, the reduction in birth weight and IGF concentrations in exercise offspring suggests that maternal exercise had an impact on nutrient stimulation of fetal growth. This could be viewed as a normalization, rather than reduction, of nutrient supply given that our control offspring displayed newborn size parameters consistently above the mean for our reference population. Therefore, the modest reduction in birth weight in this study may lead to a long-term reduction in the risk for obesity in offspring of women who exercised in pregnancy. Alternatively, the potential exists for negative long-term sequelae as a result of reduced birth weight and IGF-I levels in exercise offspring, emphasizing the need for detailed long-term follow-up of these children.

### TABLE 4. Concentrations of growth-related peptides in umbilical cord serum obtained at delivery of offspring of control and exercise participants

<table>
<thead>
<tr>
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<th>Control (n = 33)</th>
<th>Exercise (n = 40)</th>
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<tr>
<td><strong>Plasma glucose</strong> (mmol/liter)</td>
<td>4.30 (3.82–4.85)</td>
<td>4.37 (3.97–4.81)</td>
</tr>
<tr>
<td><strong>Plasma insulin</strong> (µU/ml)</td>
<td>3.73 (2.84–4.90)</td>
<td>3.45 (2.76–4.31)</td>
</tr>
<tr>
<td><strong>IGF-I (ng/ml)</strong></td>
<td>45 (36–55)</td>
<td>32 (26–40)</td>
</tr>
<tr>
<td><strong>IGF-II (ng/ml)</strong></td>
<td>421 (386–458)</td>
<td>372 (343–403)</td>
</tr>
<tr>
<td><strong>IGFBP-1 (ng/ml)</strong></td>
<td>98 (71–134)</td>
<td>116 (92–145)</td>
</tr>
<tr>
<td><strong>IGFBP-3 (ng/ml)</strong></td>
<td>1336 (1247–1432)</td>
<td>1276 (1178–1381)</td>
</tr>
<tr>
<td><strong>Leptin (ng/ml)</strong></td>
<td>10.3 (7.7–13.8)</td>
<td>7.7 (5.5–10.9)</td>
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Umbilical cord samples were obtained at delivery. Serum samples were frozen and stored at −20 C before batch analysis using commercially available ELISA kits. All outcomes except plasma glucose were logarithmically transformed prior to analyses to conform to normal distribution requirements. Values are expressed as geometric mean (95% confidence interval).

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*a* P < 0.05 for group comparison using independent samples t test.
Longitudinal growth assessments are continuing in this cohort to determine whether the reduction in birth weight in the offspring of exercising mothers persists into postnatal life and whether this is associated with an improved metabolic profile. Future studies should investigate the impact of exercise in overweight and obese mothers during pregnancy to determine whether exercise-related alterations in fetal growth occur in a population with increased risk of macrosomia.

In conclusion, regular moderate-intensity, non-weight-bearing exercise training during the second half of pregnancy was associated with reduced concentrations of fetal IGFs and lower offspring birth weight but had no measurable effect on aspects of maternal glucose metabolism. Further studies are required to validate these findings in other populations and to address the future recommendations that have developed as a result of the experimental observations in this study.

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References


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