

Relationships among maternal backfat depth, plasma adipokines and the birthweight of piglets

Paola Superchi^a, Roberta Saleri^a, Sven Menčik^b, Silvia Dander^a, Valeria Cavalli^a, Chiara Izzi^a, Michela Ablondi^a, Alberto Sabbioni^{a,*}

^a Department of Veterinary Science, University of Parma, Via del Taglio 10, 43126 Parma, Italy

^b Department of Animal Husbandry, Faculty of Veterinary Medicine, University of Zagreb, Vjekoslava Heinzelova 55, 10000 Zagreb, Croatia

ARTICLE INFO

Keywords:

Pregnant sows
Backfat depth
Adipokines
Piglets
Birthweight

ABSTRACT

Adipose tissue produces hormones, such as leptin and adiponectin, that are key factors in energy metabolism. The aim of this study was to assess the endocrine role of the adipose tissue in controlling intrauterine growth, so we evaluated the relationships among maternal adiposity, leptin and adiponectin-pregnancy trends and foetal growth in 48 Large White x Landrace crossbreed sows. Two groups of sows were designated based on backfat (BF) depth at the end of the lactation phase: a Low Fat group (LF, 11.60 mm; $n = 24$) and a High Fat group (HF, 18.20 mm; $n = 24$). During the subsequent pregnancies, the same level of feed was provided to both groups. The BF values of the sows were recorded, and blood samples were collected to assess the concentrations of leptin and adiponectin at mating and during gestation. The weights and temperatures of piglets were recorded at farrowing and after 24 h, and their body mass index and ponderal index values were calculated at farrowing. Before the piglets suckled colostrum, blood samples were collected, and the leptin, adiponectin and IGF-1 plasma levels were analysed. The observed differences in backfat depth between the LF and HF groups at mating persisted during pregnancy, and a decrease in adiponectin and an increase in leptin plasma levels were observed throughout gestation in both groups. Plasma adiponectin was lower in the HF group than in the LF group, but plasma leptin did not differ significantly. Compared to HF sows, LF sows gave birth to lighter piglets ($P = 0.014$). In addition, the weights of 27% of the piglets in the LF group and 14% in the HF group fell within the first 25th percentile (weight ≤ 1 kg). A positive correlation between offspring weight and maternal adiposity at mating ($r = 0.149$; $P = 0.020$) and a negative correlation between offspring weight and adiponectin-leptin ratio at mating ($r = -0.198$; $P = 0.022$) were observed. The morphometric parameters (body mass index, ponderal index) and thermoregulatory abilities of the piglets were unaffected by maternal adiposity. In terms of haematology, differences were found in the IGF-1 level, which was lower in piglets born from LF than HF sows ($P < 0.001$). The knowledge gained from this study suggested that differences in maternal adiposity, which were due to individual variability and not feeding strategies, influence the plasma concentration of adipokines, thus affecting offspring weight.

1. Introduction

Birthweight is an important indicator of postnatal performance, and foetal growth and development result from the balance between foetal demand and maternal substrate availability (Jansson and Powell, 2006). During pregnancy, the regulation of glucose metabolism varies in the sow, which leads to a state of relative insulin resistance. This regulation is affected by placental hormones, and it plays an important role in ensuring the provision of nutrients to the foetus (Père et al., 2000). The development of an insulin-resistant state

increases hepatic gluconeogenesis and reduces glucose uptake in maternal skeletal muscle and maternal adipose tissue. In addition, the insulin-resistant state, which promotes lipolysis in maternal adipose tissue, increases the availability of glucose and lipids to the foetus. This complex system is modulated by several factors, including the body condition of the mother, the utero-placental blood flow and the expression and function of trophoblast nutrient transporters (Aye et al., 2013). As a reflection of the nutritional status of the sow, maternal adiposity is one of the main factors programming nutrient partitioning and foetal growth (Amdi et al., 2014; Redmer et al., 2004). Adipose

* Corresponding author.

E-mail address: alberto.sabbioni@unipr.it (A. Sabbioni).

<https://doi.org/10.1016/j.livsci.2019.03.012>

Received 10 September 2018; Received in revised form 13 March 2019; Accepted 15 March 2019

1871-1413/ © 2019 Elsevier B.V. All rights reserved.

tissue is a specialised endocrine and paracrine organ that modulates energy metabolism via the secretion of circulating adipokines, such as leptin and adiponectin, that are involved in the regulation of body fatness and energy expenditure (Ahlsson et al., 2013). Adiponectin and leptin are key modulators of insulin action and glucose metabolism, so they can be considered potential candidates for intrauterine foetal development. Studies refer that serum leptin concentrations are positively correlated with backfat depth in sows (De Rensis et al., 2005). High leptin levels were reported from the end of mid-pregnancy to farrowing in breeding sows whose gestational hyperphagia was managed through dietary strategies (Saleri et al., 2015), but the increase in maternal leptin levels during pregnancy might also be a consequence of placental production. Indeed, the expression of the short form of the leptin receptor in the placental tissue of the sow at farrowing has been observed (Ashworth et al., 2000; Saleri et al., 2015). Conversely, the course of adiponectin in pregnant sows is not known. In pregnant women, an inverse correlation between adiponectin and fat mass and between adiponectin and the body mass index have been reported (Skvarca et al., 2013). Furthermore, it has been shown that longitudinal changes in serum adiponectin concentrations occur in pregnant women; the lowest adiponectin levels have been observed in late pregnancy when insulin levels rise (Fuglsang et al., 2005).

On the basis of the endocrine role of adipose tissue, we focused our attention on the evaluation of plasma levels of the two major adipokines, leptin and adiponectin in pregnant sows with the aim of study the link between maternal adiposity and offspring growth.

2. Materials and methods

2.1. Animals

The research protocol and animal care were in accordance with EC Directive 2010/63/UE on animal husbandry and guidelines of the Italian law on animal welfare for experimental animals (Legislative Decree 26/2014).

Forty-eight multiparous Large White x Landrace crossbreed sows were randomly selected based on P2 backfat (BF) depth at the end of lactation and parity order. Backfat depth was measured by a single operator on both the left and right sides of standing sows using an ultrasound scanner (Lean-Meater, Renco Corporation, Minneapolis, Minnesota, USA), and the mean value was utilised (Maes et al., 2004). Based on the BF mean (\pm SD) values, two groups were formed: Low Fat (LF, 11.60 ± 1.51 mm; $n = 24$) and High Fat (HF, 18.20 ± 2.05 mm; $n = 24$). Mean (\pm SD) of parity order was 4.0 ± 2.1 and 3.6 ± 1.2 for the LF and HF groups, respectively. Sows were identified and moved in individual pens in the same gestation room, and at the onset of standing oestrus (mean \pm SD: 4.75 ± 0.95 days after the end of lactation), they were artificially inseminated twice, at day 0 of gestation and again 24 h later using semen pooled from five Large White x Duroc crossbreed boars. Twenty-eight days after mating, the sows were evaluated by ultrasound (Aloka SSD 500®, Hitachi Medical System SpA, Milano, Italy; 5.0-MHz linear probe) to determine the state of pregnancy. One of the sows in the LF group was not pregnant and thus removed from the study. From day 29 until day 109 of gestation, the sows were kept in a group housing system, and at day 110 of gestation, they were moved to individual farrowing pens. Parturition was induced on day 113 of gestation by deep intramuscular injection of 0.7 mL of cloprostenol sodium per head (PGF VEXX®, Veyx-Pharma GmbH, Söhreweg, Germany), so all sows gave birth at day 114 of gestation. Gestation took place in a climate-controlled room with an average temperature of 20 °C, but the room temperature was raised to 23 °C on the day of farrowing. Floor heating and an infrared lamp were used to create a microclimate for the piglets. Twenty-four h after birth, litter sizes were standardised by cross-fostering within groups. During gestation and the transition period (from day 110 of gestation to day 3 after farrowing), all sows received the same standard diets offered twice

Table 1

Ingredients and chemical analysis of diets fed to sows during pregnancy (on air dry basis).

	Gestation diet (g/kg)	Transition diet (g/kg)
Ingredients:		
Wheat bran	240	–
Barley	230	267
Corn	180	310
Unmolassed sugar-beet pulp	147	150
Sunflower meal	137	–
Soybean meal	–	135
Fish meal	–	46
Soybean protein	–	10
Soybean oil	15	20
Dextrose	–	40
Rapeseed meal	20	–
Ground limestone	15	–
Dicalcium phosphate	10	15
Sodium chloride	4	4
Lysine HCl	0.5	1
Vitamins and minerals ^a	1.5	2.0
Chemical analysis ^b :		
Dry matter, g/kg	878	872
CP, g/kg	141.2	153.6
Crude fibre, g/kg	82.2	58.4
Crude fat, g/kg	38.2	42.1
Digestible energy, MJ/kg	12.9	13.5

^a Supplied per for kg of diet: Cu: 40 mg, Zn: 80 mg Fe: 150 mg, Se: 0.2 mg, I: 0.6 mg, Mn: 50 mg, vitamin A: 12,000 IU, vitamin D3: 1000 IU, vitamin E: 100 IU, vitamin K: 20 mg, vitamin B12: 55 µg, vitamin B1: 2 mg, vitamin B2: 5 mg, vitamin B6: 1.5 mg, nicotinic acid: 12 mg, pantothenic acid: 10 mg, folic acid: 5 mg, choline chloride: 500 mg, biotin: 200 µg.

^b Proximate analyses of diets were performed according to the Commission Regulation (EC) 152/2009 laying down the methods of sampling and analysis for the official control of feed (Annex III).

Table 2

Feed intake of the sows during pregnancy (kg/day).

	Gestation diet	Transition diet
From mating to day 10	1.5	–
From day 11 to day 28	2.0	–
From day 29 to day 109	2.5	–
From day 110 to day 114	–	2.5

a day at 0800 h and 1600 h, and water was available *ad libitum*. The ingredients and chemical composition of the diets are shown in the Table 1, and the daily feed intake of the sows is presented in Table 2.

2.2. Measurements

The BF of the sows was evaluated at days 0, 28, 85 and 113 of gestation, and blood samples from all sows were collected before the morning meal at the same time-points by jugular venepuncture in 10-mL vacutainer tubes with lithium heparin. Samples were immediately centrifuged ($1327 \times g$ for 10 min), and plasma was collected and stored at -20 °C until analysis.

The total number of piglets born, born alive, and born dead within the first 24 h of life as well as their genders were recorded. Piglets were individually weighed (electronic dynamometer; Wunder Sa. Bi. srl, Trezzo sull'Adda, MI, Italy) within the first 2 h of life (BW0) and at 24 h after the birth of the first-born piglet (BW24). The body mass index (BMI) and ponderal index (PI) of all piglets were calculated from the crown-rump length and birthweight (Baxter et al., 2008), and body temperature was assessed at birth and at 24 h using an infrared ear thermometer with accuracy of 0.2 °C (GIMA, Gessate, MI, Italy). Before they began suckling colostrum, the first six piglets born alive from each litter, half males and half females were chosen, held in dorsal

recumbency, and 5 mL of blood was collected from the external jugular vein into vacutainer tubes with lithium heparin. Mean body weight (\pm SD) of the chosen newborn piglets was 1183 ± 180 g and 1290 ± 136 g for the LF and HF groups, respectively. The blood samples were processed in the same way as mentioned above for sows.

2.3. Blood hormone assays

The adiponectin plasma concentration was determined using a species-specific commercial kit (Porcine Adiponectin ELISA, BioVendor, Brno, Czech Republic). The sensitivity of the method was 0.03 ng/mL, and the intra- and inter-assay CVs were 6.7% and 8.2%, respectively. The leptin plasma concentration was assessed using a commercial kit (Multispecies Leptin RIA, Linco Research, St. Louis, MO, USA). The sensitivity of the method was 100 pg/mL, and the intra- and inter-assay CVs were 4.7% and 9.1%, respectively. Plasma IGF-1 content was evaluated using a multispecies IGF-1 ELISA (Alpco Diagnostic, Salem NH, USA), according to the manufacturer's instructions. The intra- and inter-assay CVs were 7.8% and 5.3%, respectively, and the minimal detection limit was 30 pg/mL. All samples were analysed in duplicate.

2.4. Statistical analyses of results

Litter size data were analysed by one-way ANOVA using the GLM procedure in SAS® software version 9.4 (SAS Institute, Inc., Cary, NC, US) according to a model including the sow group (LF, HF) as a fixed factor and the parity order as a covariate. Similarly, piglet data were processed via ANOVA according to a model that corrected for the following fixed factors: sow group (LF, HF) and piglet sex (M, F), and the random factor of sow within the group. The sow data were analysed according to a repeated measures model using the GLM procedure in SAS software and including the group (LF, HF) as a fixed factor and the parity order as a covariate. Time was added to the model, and the interaction between time and group was considered. A Pearson correlation analysis was performed among maternal adiposity and adipokines and offspring weight. Residuals were checked for normality by the UNIVARIATE procedure in SAS software, and when not normally distributed, the data were log transformed. Based on birthweight, piglets were divided into percentile classes using the UNIVARIATE procedure in SAS software as follows: 0–25th percentile, 0.55–1.05 kg; 25th–50th percentile, 1.06–1.30 kg; 50th–75th percentile, 1.31–1.50 kg; and 75th–100th percentile, 1.51–2.00 kg. The chi-square test was applied to the observed and expected frequencies of piglets in the percentile body weight classes relative to the adiposity of the sows. Mortality, assessed per group before the litter size was standardised, was evaluated by the chi-square test. The significance level was set at $P \leq 0.05$.

3. Results

3.1. Sow parameters

The observed differences in backfat depth between the LF and HF groups at mating ($P < 0.001$) persisted during the entire pregnancy (28 d: $P = 0.003$; 85 d: $P = 0.013$; 113 d: $P < 0.001$), and no differences in backfat depth gain ($P = 0.358$) were observed between the two BF groups (Table 3). The concentration of adiponectin decreased from 0 to 113 days of gestation ($P = 0.008$): at these point times, the mean values (\pm SD) were 195.85 ± 21.5 and 61.67 ± 7.4 μ g/mL for the LF group and 98.19 ± 10.5 and 19.87 ± 2.4 μ g/mL for the HF group, respectively (Fig. 1A). Plasma adiponectin was lower in the HF group than the LF group at the following time-points: mating ($P = 0.044$), day 85 of gestation ($P = 0.027$) and farrowing ($P = 0.048$). After the first month of gestation, plasma leptin increased in both groups (Fig. 1A) to reach the highest concentration at farrowing ($P = 0.004$). No differences in plasma leptin were observed between groups throughout gestation ($P > 0.05$). At conception, at 85 and 113 days of gestation, the

Table 3

Changes in backfat depth during pregnancy in sows considered Low Fat or High Fat at the end of the previous lactation and litter size (least squares mean values \pm SEM).

Parameters	Groups		SEM	P-values
	LF	HF		
BF depth				
day of mating, mm	11.9	17.1	1.69	<0.001
day 28 of gestation, mm	12.4	17.3	1.77	0.003
day 85 of gestation, mm	13.9	18.9	1.47	0.013
day 113 of gestation, mm	14.6	19.7	1.47	<0.001
Δ BF (mating – day 113 of gestation), mm	2.7	2.5	0.48	0.358
Total born, <i>n</i>	17.2	15.7	3.16	0.327
Born alive, <i>n</i>	15.1	14.1	1.94	0.182

LF (Low Fat, 11.6 ± 1.5 mm; $n = 24$) and HF (High Fat, 18.2 ± 2.0 mm; $n = 24$) indicate the backfat depth (mean \pm SD) of sows recorded at the end of the previous lactation. One of the sows in the LF group was not pregnant and thus removed from the study; BF = backfat.

adiponectin-leptin ratio (Fig. 1B) was lower in the HF than LF group ($P = 0.025$, 0.036 , 0.044 , respectively). The adiponectin-leptin ratio was negatively correlated with offspring weight at mating ($r = -0.198$, $P = 0.022$), at 85 ($r = -0.189$, $P = 0.028$) and at 113 days of gestation ($r = -0.178$, $P = 0.040$). The total number of piglets born ($P = 0.327$) and born alive ($P = 0.424$) (Table 3) were the same for both groups.

3.2. Newborn piglets performance and hormone plasma levels

The body mass index ($P = 0.384$) and ponderal index ($P = 0.599$) (Table 4) were not affected by maternal BF depth. In the first 24 h of life, thermoregulatory ability was the same in both groups ($P = 0.608$). Conversely, maternal adiposity affected foetal growth; piglets born from HF sows showed a higher BW0 (+7%; $P = 0.014$) and BW24 (+4%; $P < 0.001$) than those from LF sows. A positive correlation between offspring weight and maternal adiposity at mating ($r = 0.149$; $P = 0.020$) was observed. In addition, significant differences were observed in percentile weight grouping (Table 5); 26.8% of piglets in the LF and 14.4% in the HF group exhibited weights that fell in the first 25th percentile (weight ≤ 1 kg; $P = 0.030$); 20.5% of piglets in the LF and 33.6% in the HF group exhibited weights that fell between 50th and 75th percentiles (weight from 1.31 to 1.50 kg; $P = 0.037$). Piglet mortality from 0 to 24 h of life was 9.6% and 2.5% for the LF and HF groups, respectively ($P = 0.035$). Plasma adiponectin ($P = 0.339$) and leptin levels ($P = 0.096$) were not affected by maternal adiposity, but higher IGF-1 plasma levels ($P < 0.001$) were recorded in piglets born from HF sows than from LF sows (Table 6).

4. Discussion

Foetal development is the result of the interaction among different factors, including the maternal nutrition status, the foetal nutrients supply and the metabolic hormone activity (Aye et al., 2013). We focused on the endocrine role of maternal adipose tissue during pregnancy with the aim of investigate how different adiposity at mating influence the course of pregnancy, both in terms of maternal hormone levels and the weight and size of the newborn piglets.

4.1. Maternal backfat depth and its relationship with piglet birthweight

Pregnancy is a dynamic anabolic state during which nutritional needs increase due to both the foetal growth and the development of associated maternal tissues. In sows, as in other species, the changes in body weight and fat deposition during gestation are physiological events of maternal adaptation and they are linked to metabolic hormonal changes, i.e., progesterone, leptin, prolactin and cortisol (Saleri et al., 2015). Maternal backfat depth at mating has a greater

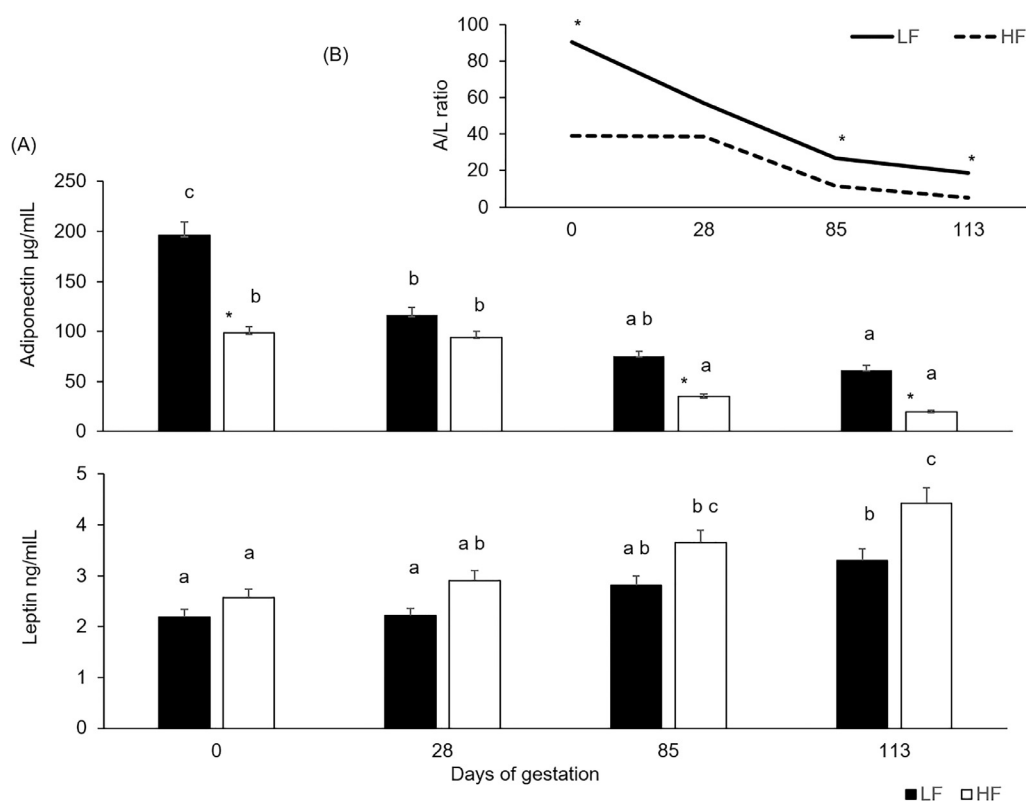


Fig. 1. The trend in adiponectin and leptin (A) and the adiponectin/leptin ratio (B) during gestation relative to the backfat depth of sows at mating (mean \pm SD of LF: Low Fat, 11.6 ± 1.5 mm; $n = 24$ and of HF: High Fat, 18.2 ± 2.0 mm; $n = 24$). One of the sows in the LF group was not pregnant and thus removed from the study. The blood sampling period started at the day of mating (0) and ended at day 113 of gestation. Error bars indicate the standard deviation. Significant differences between groups within each sampling time are labelled * ($P < 0.05$), and significant differences among sampling times within groups are labelled a, b, and c ($P < 0.05$).

Table 4

Effects of maternal backfat depth on the growth performance, morphometric parameters and body temperature of piglets (least squares mean values \pm SEM).

Parameters	Groups LF	HF	SEM	P-values
Piglets, n	347	339		
BMI, kg/m ²	20.9	20.6	2.09	0.384
PI, kg/m ³	84.0	84.4	6.74	0.599
Body temperature, °C				
at birth	37.9	37.8	0.95	0.267
at 24 h	38.8	39.0	0.50	0.608
BW0, g	1 244	1 334	278	0.014
BW24, g	1 310	1 360	85	<0.001

LF (Low Fat, 11.6 ± 1.5 mm; $n = 24$) and HF (High Fat, 18.2 ± 2.0 mm; $n = 24$) indicate the backfat depth (mean \pm SD) of sows recorded at the end of the previous lactation. One of the sows in the LF group was not pregnant and thus removed from the study; BMI = body mass index; PI = ponderal index; BW0 = birthweight; BW24 = body weight at 24 h of life.

influence on offspring growth than the amount of feed during gestation (Amdt et al., 2014). In our study, overall, the increase in maternal fat stores during pregnancy was the same, but LF sows gave birth to lighter piglets. In addition, the percentage of piglets with a birthweight lower than 1 kg in the LF group was almost double compared to the HF group. Recently, a positive correlation among maternal body condition, uterine artery pulsatility and foetal growth was found (Caradeux et al., 2016). In fact, the uterine artery pulsatility modulates the placental efficiency and therefore the ability to transfer resources to foetus. The foetus itself can use in a different manner the nutrients in function of environmental conditions. Poor maternal body condition at conception or in early pregnancy is signalled to the foetus. As a consequence, the foetus promotes peripheral glucose utilisation, which is essential for brain and heart development, and reduces the demand for amino acids to maintain a sufficient energy supply at the expense of growth (Bloomfield et al., 2013). This might be understood as a result of

Table 5

Distribution in percentile classes of piglet birthweight and mortality at 24 h after birth.

Parameters		Groups LF	HF	χ^2	P-values
Percentile weight classes					
0–25th	%	26.8	14.4	4.71	0.030
25th–50th	%	26.8	22.6	0.47	0.496
50th–75th	%	20.5	33.6	4.37	0.037
75th–100th	%	25.9	29.4	0.29	0.588
Mortality	%	9.6	2.5	4.43	0.035

LF (Low Fat, 11.6 ± 1.5 mm; $n = 24$) and HF (High Fat, 18.2 ± 2.0 mm; $n = 24$) indicate the backfat depth (mean \pm SD) of sows recorded at the end of the previous lactation. One of the sows in the LF group was not pregnant and thus removed from the study; 0–25th percentile, 0.55–1.05 kg; 25th–50th percentile, 1.06–1.30 kg; 50th–75th percentile, 1.31–1.50 kg; 75th–100th percentile, 1.51–2.00 kg.

Table 6

Plasma adiponectin, leptin and IGF-I in newborn piglets in relation to the backfat depth of sows (least squares mean values \pm SEM). Each sample was analysed in duplicate.

Parameters	Groups LF	HF	SEM	P-values
Piglets, n	138	144		
Adiponectin, µg/mL	14.3	14.9	1.66	0.339
Leptin, ng/mL	3.0	3.3	0.57	0.096
IGF-I, pg/mL	4.4	5.6	1.00	<0.001

LF (Low Fat, 11.6 ± 1.5 mm; $n = 24$) and HF (High Fat, 18.2 ± 2.0 mm; $n = 24$) indicate the backfat depth (mean \pm SD) of sows recorded at the end of the previous lactation. One of the sows in the LF group was not pregnant and thus removed from the study.

intrauterine growth restriction in piglets born from LF sows. However, we think that birthweight differences are not enough to claim the presence of intrauterine growth restriction in piglets. As reported by Amdi et al. (2013), other parameters (BMI, PI), based on head morphology, must be abnormal to call for intrauterine growth restriction. We found that BMI and PI of both piglet's groups are consistent with values of normal subjects (Amdi et al., 2013). These findings lead us to believe that maternal adiposity is an important, yet not the only factor affecting foetal growth.

4.2. Hormone release as an indicator of piglet birthweight

Foetal growth is mediated via the foetal glucose/insulin/insulin-like growth factor axis. Insulin is a moderate regulator of foetal growth, dependent upon substrate supply, IGFs are thought to be the main system involved in the foetal growth. In foetal, IGFs play a paracrine and autocrine role at local level to ensure the availability of a nutrient supply and to promote the functional differentiation of the different tissues and organs (Bloomfield et al., 2013). Although IGF-2 has some effect on foetal and placental development, IGF-1 showed a predominant role in foetal growth (Hellström et al., 2016). The IGF-1 production is growth hormone (GH) independent in utero life. We found that the lighter piglets born from LF sows showed lower IGF-1 values at birth compared to the heavier ones born from HF group. Low birthweight of piglets is primarily associated with a reduced number of secondary muscle fibres (Oksbjerg et al., 2013). It is known that IGF-1 induces myogenin expression, thus it is important for muscle cell differentiation (Theil et al., 2006). Therefore, we assume that the presence of low IGF-1 levels in LF piglets contributed to the birth of light subjects. The low number of muscle fibres is an important aspect in pig production since it restricts the potential of postnatal lean growth and have a long-term impact on the production efficiency and quality of meat (Rehfeldt et al., 2008).

The energy balance of the foetus is also modulated by maternal adipose tissue hormones, i.e., adipokines, which regulate insulin sensitivity, appetite and lipid metabolism (Ahlsson et al., 2013). In both groups of sows, the concentrations of the most abundant adipokines, leptin and adiponectin, showed an inverse trend during pregnancy. Placenta contribute to the increase in leptin in pregnant sows (Ashworth et al., 2000). The high levels of leptin during pregnancy are consistent with a resistance mechanism to central leptin action as previously reported in swine (Saleri et al., 2015), humans and mice (Trujillo et al., 2011). However, the extent to which maternal leptin *per se* mediates the foetal growth and developmental remains to be clarified. In this study, we did not observe an association between maternal leptin concentration and piglet's birthweight. This finding agrees with what has been observed in humans where the differences in infant birthweight were not significantly associated with the magnitude of maternal serum leptin level (Misra et al., 2013). It is highly likely that leptin's role in foetal growth is only permissive as no major abnormalities in foetal growth were observed in leptin deficient humans (Christou et al., 2002). To clarify the role of leptin during pregnancy, it is important to also consider the role of adiponectin. The plasma adiponectin to leptin ratio (A/L ratio) has been proposed as a better marker of insulin resistance than leptin or adiponectin alone (Skvarca et al., 2013). Our study showed a lower A/L ratio in the HF than the LF sows. The lower adiponectin levels detected in the HF than the LF sows matched the higher offspring birthweight, so adiponectin might play a role in the mechanism by which maternal energy is stored in the fat mass, influencing the pattern of foetal growth (Zhang et al., 2016). Since we detected the same trend in the release of adiponectin in both groups of sows, we hypothesised that adiponectin in pregnant animals is involved in the management of the mother energy resources regardless of backfat depth. For its role on energy balance, adiponectin is connected not only to growth but also to immunity (Morelli et al., 2015). One of the most important aspect for successful of pregnancy is

the maternal immune tolerance of the foetus. The presence of adiponectin and its receptors in the porcine uteri, conceptuses, and trophoblasts during early pregnancy was detected (Smolinska et al., 2014). *In vitro* studies have shown that adiponectin arouses pro-inflammatory cytokine production in human trophoblasts (i.e., IL-1 β and IL-8) and placenta (i.e., IL-1 β , IL-6 and TNF α), so it might be detrimental to the initiation and progression of pregnancy (Lappas et al., 2005; McDonald and Wolfe, 2011). Further studies will investigate the adiponectin role on maternal immune response in swine to further unravel this complex phenomenon.

5. Conclusions

In conclusion, the results reported in this study suggest an involvement of adipose tissue during the different stages of pregnancy. We confirmed that the role of leptin in foetal growth is only permissive regardless of a sow's adiposity. In contrast, maternal adiponectin plasma concentration seems negatively associated with maternal fat mass and birthweight of piglets. Thus, the adiposity at mating might be used as an effective indicator to optimise the performance of sows. However, further studies are needed to deepen our understanding of the relationship between the endocrinology of maternal adipose tissue and foetal growth.

Conflict of interest

The authors declare no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgement

The authors would like to thank Dr. P. Benaglia for technical assistance.

References

- Ahlsson, F., Diderholm, B., Ewald, U., Jonsson, B., Forslund, A., Stridsberg, M., Gustafsson, J., 2013. Adipokines and their relation to maternal energy substrate production, insulin resistance and fetal size. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 168, 26–29. <https://doi.org/10.1016/j.ejogrb.2012.12.009>.
- Amdi, C., Giblin, L., Ryan, T., Stickland, N.C., Lawlor, P.G., 2014. Maternal backfat depth in gestating sows has a greater influence on offspring growth and carcass lean yield than maternal feed allocation during gestation. *Animal* 8, 236–244. <https://doi.org/10.1017/S1751731113002073>.
- Amdi, C., Krogh, U., Flummer, C., Oksbjerg, N., Hansen, C.F., Theil, P.K., 2013. Intrauterine growth restricted piglets defined by their head shape ingest insufficient amounts of colostrum. *J. Anim. Sci.* 91, 5605–5613. <https://doi.org/10.2527/jas.2013-6824>.
- Ashworth, C.J., Hoggard, N., Thomas, L., Mercer, J.G., Wallace, J.M., Lea, R.G., 2000. Placenta leptin. *Rev. Reprod.* 5, 18–24. <https://doi.org/10.1530/ror.0.0050018>.
- Aye, L.L.M.H., Powell, T.L., Jansson, T., 2013. Review: adiponectin – The missing link between maternal adiposity, placental transport and fetal growth? *Placenta* 34, S40–S45. <https://doi.org/10.1016/j.placenta.2012.11.024>.
- Baxter, E.M., Jarvis, S., D'Eath, R.B., Ross, D.W., Robson, S.K., Farish, M., Nevison, I.M., Lawrence, A.B., Edwards, S.A., 2008. Investigating the behavioural and physiological indicators of neonatal survival in pigs. *Theriogenology* 69, 773–783. <https://doi.org/10.1016/j.theriogenology.2007.12.007>.
- Bloomfield, F.H., Spiroski, A.-M., Harding, J.E., 2013. Fetal growth factors and fetal nutrition. *Semin. Fetal Neonatal Med.* 18, 118–123. <https://doi.org/10.1016/j.siny.2013.03.003>.
- Caradeux, J., Serra, R., Palmeiro, Y., Correa, P.J., Valenzuela, I., Olguin, J., Montenegro, L., Nien, J.K., Osorio, E., Illanes, S., 2016. Correlation between maternal characteristics during early pregnancy, fetal growth rate and newborn weight in healthy pregnancies. *Gynecol. Obstet. Invest.* 81, 202–206. <https://doi.org/10.1159/000441786>.
- Christou, H., Serdy, S., Mantzoros, C.S., 2002. Leptin in relation to growth and developmental processes in the fetus. *Semin. Reprod. Med.* 20, 123–130. <https://doi.org/10.1055/s-2002-32503>.
- De Renzis, F., Gherpelli, M., Superchi, P., Kirkwood, R.N., 2005. Relationships between backfat depth and plasma leptin during lactation and sow reproductive performance after weaning. *Anim. Reprod. Sci.* 90, 95–100. <https://doi.org/10.1016/j.anireprosci.2005.01.017>.
- Fuglsang, J., Skjaerbaek, C., Frystyk, J., Flyvbjerg, A., Ovesen, P., 2005. Short

- communication: a longitudinal study of serum adiponectin during normal pregnancy. *BJOG* 113, 110–113. <https://doi.org/10.1111/j.1471-0528.2005.00792.x>.
- Hellström, A., Ley, D., Hansen-Pupp, I., Hallberg, B., Löfqvist, C., van Marter, L., van Weissenbruch, M., Ramenghi, L.A., Beardsall, K., Dunger, D., Hård, A.L., Smith, L.E.H., 2016. Insulin-like growth factor 1 has multisystem effects on foetal and pre-term infant development. *Acta Paediatr* 105, 576–586. <https://doi.org/10.1111/apa.13350>.
- Jansson, T., Powell, T., 2006. Human placental transport in altered fetal growth: does the placenta function as a nutrient sensor? – A review. *Placenta* 27, 91–97. <https://doi.org/10.1016/j.placenta.2005.11.010>.
- Lappas, M., Permezel, M., Rice, G.E., 2005. Leptin and adiponectin stimulate the release of proinflammatory cytokines and prostaglandins from human placenta and maternal adipose tissue via nuclear factor- κ B, peroxisomal proliferator-activated receptor- γ and extracellularly regulated kinase 1/2. *Endocrinology* 146, 3334–3342. <https://doi.org/10.1210/en.2005-0406>.
- Maes, D.G.D., Janssens, G.P.J., Delpitte, P., Lammertyn, A., de Kruif, A., 2004. Back fat measurements in sows from three commercial pig herds: relationship with reproductive efficiency and correlation with visual body condition scores. *Livest. Prod. Sci.* 91, 57–67. <https://doi.org/10.1016/j.livprodsci.2004.06.015>.
- McDonald, E.A., Wolfe, M.W., 2011. The pro-inflammatory role of adiponectin at the maternal-fetal interface. *Am. J. Reprod. Immunol.* 66, 128–136. <https://doi.org/10.1111/j.1600-0897.2010.00971.x>.
- Misra, V.K., Straughen, J.K., Trudeau, S., 2013. Maternal serum leptin during pregnancy and infant birth weight: the influence of maternal overweight and obesity. *Obesity* 21, 1064–1069. <https://doi.org/10.1002/oby.20128>.
- Morelli, S., Mandal, M., Goldsmith, L.T., Kashani, B.N., Ponzio, N.M., 2015. The maternal immune system during pregnancy and its influence on fetal development. *Res. Rep. Biol.* 171–189. <https://doi.org/10.2147/RRB.S80652>.
- Oksbjerg, N., Nissen, P.M., Therkildsen, M., Møller, H.S., Larsen, L.B., Andersen, M., Young, J.F., 2013. In utero nutrition related to fetal development, postnatal performance, and meat quality of pork. *J. Anim. Sci.* 91, 1443–1453. <https://doi.org/10.2527/jas2012-5849>.
- Père, M.C., Etienne, M., Dourmad, J.Y., 2000. Adaptations of glucose metabolism in multiparous sows: effects of pregnancy and feeding level. *J. Anim. Sci.* 78, 2933–2941. <https://doi.org/10.2527/2000.78112933x>.
- Redmer, D.A., Wallace, J.M., Reynolds, L.P., 2004. Effect of nutrient intake during pregnancy on fetal and placental growth and vascular development. *Domest. Anim. Endocrinol.* 27, 199–217. <https://doi.org/10.1016/j.domaniend.2004.06.006>.
- Rehfeldt, C., Tuchscherer, A., Hartung, M., Kuhn, G., 2008. A second look at the influence of birth weight on carcass and meat quality in pigs. *Meat Sci* 78, 170–175. <https://doi.org/10.1016/j.meatsci.2007.05.029>.
- Saleri, R., Sabbioni, A., Cavalli, V., Superchi, P., 2015. Monitoring blood plasma leptin and lactogenic hormones in pregnant sows. *Animal* 9, 629–634. <https://doi.org/10.1017/S1751731114003085>.
- Skvarca, A., Tomazic, M., Blagus, R., Krhin, B., Janez, A., 2013. Adiponectin/leptin ratio and insulin resistance in pregnancy. *J. Int. Med. Res.* 41, 123–128. <https://doi.org/10.1177/0300060513476409>.
- Smolinska, N., Maleszka, A., Dobrzyn, K., Kiezun, M., Szeszko, K., Kaminski, T., 2014. Expression of adiponectin and adiponectin receptors 1 and 2 in the porcine uterus, conceptus, and trophoblast during early pregnancy. *Theriogenology* 82, 951–965. <https://doi.org/10.1016/j.theriogenology.2014.07.018>.
- Theil, P.K., Sørensen, I.L., Nissen, P.M., Oksbjerg, N., 2006. Temporal expression of growth factor genes of primary porcine satellite cells during myogenesis. *Animal Sci. J.* 77, 330–337. <https://doi.org/10.1111/j.1740-0929.2006.00356.x>.
- Trujillo, M.L., Spuch, C., Carro, E., Sejaris, R., 2011. Hyperphagia and Central Mechanisms for Leptin Resistance during Pregnancy. *Endocrinology* 152, 1355–1365. <https://doi.org/10.1210/en.2010-0975>.
- Zhang, Z., Lu, Q., Huang, J., Jiao, C., Huang, S., Mao, L., 2016. Maternal and cord blood adiponectin levels in relation to post-natal body size in infants in the first year of life: a prospective study. *BMC Pregnancy Childbirth* 16, 189. <https://doi.org/10.1186/s12884-016-0978-9>.