

## IGF-1 concentrations after weaning in young sows fed different pre-mating diets are positively associated with piglet mean birth weight at subsequent farrowing

T. Han <sup>a,\*</sup>, S. Björkman <sup>a</sup>, N.M. Soede <sup>b</sup>, C. Oliviero <sup>a</sup>, O.A.T. Peltoniemi <sup>a</sup>

<sup>a</sup> Production Animal Hospital, Department of Production Animal Medicine, Faculty of Veterinary Medicine, University of Helsinki, Finland

<sup>b</sup> Adaptation Physiology Group, Department of Animal Sciences, Wageningen University & Research, the Netherlands

### ARTICLE INFO

#### Article history:

Received 12 March 2020

Received in revised form 19 June 2020

Accepted 19 June 2020

Available online 24 January 2021

#### Keywords:

IGF

Litter uniformity

Metabolic state

Piglet birth weight

Sow reproduction

### ABSTRACT

Pre-mating diets can influence piglet birth weight and within-litter birth weight variation and thereby piglet survival and development. The major objective of this study was to evaluate the litter characteristics of young sows whose pre-mating diets received different supplementation. The supplements included a top-dressing of 200 g, consisting of either wheat (CON) or wheat plus microfibrillated cellulose, L-carnitine or L-arginine at one of two supplementation levels (low and high) in late lactation and during the weaning-to-oestrus interval (WEI). The second objective was to investigate the role of body condition loss and IGF-1 concentration during the WEI for subsequent litter characteristics. In total, sows after their first ( $N = 41$ ) and second ( $N = 15$ ) lactation were used. One week before weaning, the sows were allocated to the seven treatments based on the number of piglets and BW loss from farrowing until 1 week before weaning. Pre-mating diets did not affect litter characteristics at subsequent farrowing. However, at subsequent farrowing, sows after their first lactation had a lower total number of piglets born per litter (18.3 v. 20.3), higher mean piglet birth weight (1365 v. 1253 g), lower CV of birth weight (20.0 v. 26.1%) and lower percentage of piglets < 1000 g (11.5 v. 24.4%) than sows after their second lactation. Litter weight at second parturition was positively related to IGF-1 during the WEI after first lactation ( $P < 0.04$ ). Within parity, piglet mean birth weight was positively related to IGF-1 at oestrus ( $P < 0.02$ ). Surprisingly, within parity, a higher relative loin muscle depth loss during previous lactation was related to lower CV and SD of birth weight ( $P < 0.05$ , for both). In conclusion, pre-mating diets did not affect litter characteristics at subsequent birth. However, a higher IGF-1 concentration during the WEI was positively associated with subsequent litter weight and piglet mean birth weight. Further studies should elucidate the role of IGF-1 during the WEI for subsequent litter characteristics and dietary interventions to stimulate IGF-1.

© 2020 The Authors. Published by Elsevier Inc. on behalf of The Animal Consortium. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

### Implications

In sows with large litters, the increase in pre-weaning mortality related to low piglet birth weight is a great concern in the pig industry. We have shown that higher IGF-1 concentration in young sows before mating is related to higher subsequent litter weight and mean piglet birth weight. This suggests that optimization of sow metabolic states during lactation may improve piglet survival rate. Thus, appropriate feed strategies are needed. This is important for both productivity and animal welfare.

### Introduction

Litter size in the pig has increased in recent decades because of genetic selection, which results in a lower mean birth weight and higher

within-litter birth weight variation (Wientjes et al., 2013; Zak et al., 2017). Both are related to a higher pre-weaning mortality (Milligan et al., 2002; Wientjes et al., 2013). Pre-mating diets, such as insulin-stimulating (with increased levels of dextrose and lactose) and fibre-rich diets, have been shown to positively influence mean piglet birth weight and within-litter birth weight uniformity (Ferguson et al., 2004 and 2007; Van den Brand et al., 2006 and 2009). The mechanism by which pre-mating diets may influence litter characteristics involves plasma IGF-1, which was positively related to follicular IGF-1 (Costermans et al., 2020) and oocyte maturation (Ferguson et al., 2003; Costermans et al., 2020). Moreover, follicle and oocyte development subsequently influences embryo development (Pope et al., 1990; Zak et al., 1997) and luteal development (corpus luteum (CL) size and progesterone secretion; Soede et al., 1998; Wientjes et al., 2012b). In turn, these processes have an impact on subsequent placental and foetal development and uniformity, and thereby piglet birth weight and uniformity (Van der Lende et al., 1990; reviewed by Wientjes et al., 2013). However, direct

\* Corresponding author.

E-mail address: [taehee.han@helsinki.fi](mailto:taehee.han@helsinki.fi) (T. Han).

relations between plasma IGF-1 concentrations before ovulation and piglet characteristics at subsequent parturition have not been established.

In our companion paper (Han et al., 2020), we used L-carnitine (LC) and L-arginine (AR), expecting them to stimulate IGF-1 since these amino acids have previously been reported to increase IGF-1 concentration in sows (Doberenz et al., 2006; Zhu et al., 2017; Guo et al., 2017). Microfibrillated cellulose (MF) is processed through fibrillation of cellulose fibres and has been used as functional food ingredients for human nutrition in terms of dietary fibres (Serpa et al., 2016). It was hypothesized that MF may act as a fibre-rich diet for sows because of its high crude fibre content (57.6%, Han et al., 2020).

The sows' body condition loss during lactation may also have an impact on piglet characteristics at subsequent parturition (Wientjes et al., 2013). This is probably related to the consequences of the nutritional deficiencies on plasma IGF-1 that not only causes body reserve mobilization but also impacts follicle development during the weaning-to-oestrus interval (WEI; Van den Brand et al., 2001; Quesnel et al., 2009; Wientjes et al., 2013; Han et al., 2020). In general, sows with higher body reserve mobilization during lactation have lower plasma IGF-1 at weaning (Costermans et al., 2020; Han et al., 2020) because the somatotrophic axis becomes uncoupled during lactation (reviewed by Lucy, 2008). Costermans et al. (2020) reported that feed restriction during the last 2 weeks of lactation resulted in lower plasma IGF-1 and smaller follicles after weaning, and subsequent poor oocyte quality compared to full-fed sows. A negative consequence of lactational body condition loss on embryo development (Hoving et al., 2012) and piglet birth weight (Wientjes et al., 2013) was also reported. Nevertheless, whether or not lactation weight loss-related IGF-1 indeed has an impact on subsequent litter characteristics has not been studied.

Thus, the main objective of this study was to evaluate the effects of different pre-mating diets (i.e. provided during the last week of lactation and the WEI) on litter characteristics in young sows. In addition, we hypothesized that the sows' high body condition loss during lactation negatively affects IGF-1 concentration during the WEI, which carries over the negative effect to follicular development before ovulation and to the subsequent litter characteristics. Therefore, we aimed to investigate if and how body condition loss during lactation, post-weaning IGF-1 concentrations and follicle development affects litter characteristics at birth.

## Material and methods

### Animals and management

This experiment was performed in 2018 on a research herd in western Finland. Sows (DanAvl, alternate cross between Landrace (L) and Yorkshire (Y), either YLY or LYL) after their first ( $N = 41$ ) and second ( $N = 15$ ) lactation were used in three consecutive batches ( $N = 20$ ,  $N = 20$  and  $N = 16$ , respectively).

Sows were crated in individual farrowing pens during farrowing and lactation. Within 2 days after farrowing, litters were equalized to 13 or 14 piglets (according to the number of functional teats). After weaning at  $26.1 \pm 0.2$  day of lactation, the sows were moved into insemination units with individual stalls. From weaning onwards, oestrus detection was performed daily at 1200 h by a farm technician using fence-line boar contact. Sows were artificially inseminated once on every day of oestrus with a commercial dose of semen (mostly for two consecutive days,  $2 \times 10^9$  sperm cells, DanAvl; Finnpig, Finland). Sows remained in the insemination unit until pregnancy diagnosis by real-time B-mode ultrasonography at 35 days after insemination. Sows were then moved to the gestation unit with a group housing system (4 to 6 sows per pen). One week prior to parturition, sows were transferred to the farrowing and lactation unit.

### Feeding

Both parity groups of sows had the same amount of gestation diet during pregnancy. In the farrowing and lactation unit, sows were fed liquid feed (1:3.35, feed to water ratio) and water *ad libitum*. Further information on feeding in this unit until insemination is described by Han et al. (2020). From days 0 to 35 of gestation (day 0 is day of first insemination), sows were fed 3.37 kg/d of commercial gestation diet 1. From days 35 to 40 of gestation, sows were fed 3.26 kg/d of commercial gestation diet 1. Gestation diet 1 was formulated to contain 9.0 MJ net energy (NE)/kg DM, 11.5% CP, 4.0% crude fat, 4.0% crude fibre and 5.5 g/kg of lysine (Tiineys Pekoni 1; Hankkija Oy, Hyvinkää, Finland). From days 40 to 84 of gestation, sows were fed 2.63 kg/d of commercial gestation diet 2. Gestation diet 2 was formulated to contain 9.1 MJ NE/kg DM, 13.0% CP, 4.2% crude fat, 4.0% crude fibre and 6.1 g/kg of lysine (Tiineys Pekoni 2; Hankkija Oy, Hyvinkää, Finland). From day 84 of gestation until transfer to farrowing unit, sows were fed 3.68 kg/d of commercial gestation diet 2. In the farrowing unit, sows were fed 2.99 kg/d of commercial lactation diet (9.2 MJ NE/kg DM, 13.8% CP, 4.4% crude fat, 6.7% crude fibre and 0.8% lysine; Imetys Pekoni 1; Hankkija Oy, Hyvinkää, Finland).

### Dietary treatments

One week before weaning, sows were assigned to one of seven dietary treatments that were given during the last week of lactation and from weaning until oestrus. Allocation to treatments was stratified based on parity, BW loss (kg) until 1 week before weaning and number of piglets at 1 week before weaning. During the treatment period, all sows received a once-daily top-dressing of 200 g consisting of either wheat (CON; control) or wheat plus MF (Betulium® Microfibrillated cellulose, Espoo, Finland), LC (Carniking™, Lonza Group, Inc., Allendale, NJ, USA) or AR (Cheiljedang, Indonesia) at one of two supplementation levels, as described in Han et al. (2020) and in Supplementary Table S1 and S2.

### Body condition of the sow

Sow BW, back fat (BF) and loin muscle depth (LM) were measured at farrowing and weaning, and those data were presented elsewhere (Han et al., 2020). Sow BW at subsequent farrowing was calculated as BW at entering the farrowing unit deducted by the sum of the weight of the foetuses, placentas and intrauterine fluid, as suggested by Bergsma et al. (2009). Sow BF and LM were measured on day 1 of lactation with ultrasound (MyLab One VET; Esaote, The Netherlands), as described by Han et al. (2020). Sow BW, BF and LM gain during gestation were determined as the difference between weaning and subsequent farrowing.

### Follicle development

Trans-rectal ultrasonography with an 8-MHz linear array probe (MyLab one VET; Esaote, The Netherlands) was performed to assess follicle diameter (mean of five largest in one ovary) on the day of weaning, 3 days after weaning, and at 12-h intervals during oestrus until ovulation, as described by Han et al. (2020). Ultrasound clips were taken from one ovary only due to bilaterally synchronized ovarian function in sows (Soede N. M., unpublished results). The clips were saved and exported in DICOM format and analyzed using the DICOM viewer Horos (Version 3.3.2, available at [www.horosproject.org](http://www.horosproject.org)). Data were presented elsewhere (Han et al., 2020).

### IGF-1

Sampling and analysis of IGF-1 were described previously (Han et al., 2020). Briefly, blood samples for IGF-1 were taken from the *vena*

coccygea 30 min before feeding at weaning, 3 days after weaning and the second day of oestrus. They were analyzed using a commercial kit (IRMA IGF-1 A15729@; Immunotech, Marseille, France) after extraction of the samples with ethanol and HCl. The sensitivity was 2 ng/ml, and intra- and inter-assay CV were 2.0% and 1.9%, respectively.

Litter characteristics

The number of live born and stillborn piglets were assessed at subsequent farrowing. The total number of piglets born per litters was calculated by summing the number of live born and stillborn piglets. All live born and stillborn piglets were weighed individually within 12 h after birth, and SD and CV of birth weight were calculated for these piglets. The proportions of piglets weighing <1000 g and >1800 g in the same litters were calculated.

Statistical analyses

SAS 9.4 (SAS Inst. Inc., Cary, NC, USA) was used for statistical analysis of all data. Normality of the model residuals was verified with the UNIVARIATE procedure using the Shapiro–Wilk test. Normally distributed parameters were presented as least square mean, and non-normally distributed parameters were presented as means. The statistical model 1 (MIXED procedure; Supplementary Materials S1) included treatment (CON, MF1, MF2, LC1, LC2, AR1, AR2), parity (1, 2) and their interactions as fixed effects to test treatment effects on total number of piglets born per litter, litter weight at birth, mean birth weight, SD and CV birth weight, as those parameters are normally distributed. In model 2 (GLIMMIX procedure; Supplementary Materials S2), a binomial distribution with a logit link function was used to evaluate the proportions of piglets <1000 g and piglets >1800 g. Treatment (CON, MF1, MF2, LC1, LC2, AR1, AR2), parity (1, 2) and their interactions were included as fixed effect in the model, as those parameters are non-normally distributed. In both models, preliminary analyses showed that batch (1, 2 and 3) and breed (YLY and LYL) were not significant; they were thus used as a random effect to account for possible environmental and genetic variation. Tukey–Kramer corrections were used for multiple comparisons. Lactation characteristics (IGF-1 concentrations before weaning, BW loss [%], BF loss [%] or LM loss [%]) and their interactions with treatment were added to the models. The factors and interactions included in the statistical model were tested for significance and stepwise omitted from the model if they were non-significant (except for treatment, parity and their interaction). Pearson and Spearman correlations were used for detecting the relations among normally distributed

(total number of piglets born per litter, litter weight at birth, mean birth weight, SD and CV birth weight) and non-normally distributed parameters (proportions of piglets <1000 g and piglets >1800 g, respectively). Relationships between IGF-1 concentrations, follicle development and body condition losses and litter characteristics were estimated using the following model:  $Y_{ij} = \mu + PAR + \beta X_{ij} + \beta X_{ij} \times PAR + \epsilon_{ij}$ , where  $Y_{ij}$  is the litter characteristics,  $\beta$  is the regression coefficient and  $X_{ij}$  is either one of the IGF-1, follicle development or body condition losses, or litter characteristics (total number of piglets born per litter, litter weight at birth, mean birth weight, SD and CV birth weight, proportions of piglets <1000 g and piglets >1800 g; Supplementary Materials S3 and S4). The interactions were excluded from models when not significant ( $P > 0.05$ ).

Results

Data for body condition loss during lactation, IGF-1 concentration and follicle development during the WEI were presented in our companion paper (Han et al., 2020).

Gestation length and body condition changes during gestation

An overview of gestation length and body condition changes during gestation is presented in Table 1. During gestation, sows gained on average  $44.6 \pm 3.9$  kg of BW,  $2.7 \pm 0.3$  mm of BF and  $7.7 \pm 0.7$  mm of LM. No differences existed in these parameters between treatments ( $P > 0.05$ ). Sows after their first lactation gained more BW (51 v. 29 kg,  $P = 0.02$ ) and thereafter had similar BW at subsequent farrowing (238 v. 240 kg,  $P = 0.43$ ) compared with sows after their second lactation.

Effect of treatment and parity on litter characteristics

Sows farrowed on average  $19.0 \pm 0.4$  total born (range 12–25),  $17.9 \pm 0.4$  born alive (range 12–24) and  $1.1 \pm 0.2$  stillborn piglets (range 0–4). The average mean piglet birth weight was  $1336 \pm 28$  g, and SD and CV of piglet birth weight were  $285 \pm 63$  g and  $21.9 \pm 0.8\%$ , respectively. Pre-mating diets did not affect litter characteristics. At subsequent farrowing, sows after their first lactation had a lower total number of piglets born per litter (18.3 v. 20.3; Table 2), higher mean piglet birth weight (1365 v. 1253 g; Table 2), lower CV of piglet birth weight (20.0 v. 26.1%; Table 2) and lower proportions of piglets <1000 g (11.5 v. 24.4%; Table 2) compared with sows after their second lactation. This was still the case when piglet birth weight was corrected for litter size (data not shown).

**Table 1** Gestation length, body condition at farrowing and body condition gain during gestation of sows treated a top-dressing (200 g) of either wheat (CON) or wheat plus microfibrillated cellulose (MF), L-carnitine (LC) or L-arginine (AR) at one of two supplementation levels (1,2) during 1 week before weaning and the weaning-to-oestrus interval.

Items	TRT								PAR		P-values <sup>1</sup>		
	CON (N = 4)	MF1 (N = 8)	MF2 (N = 11)	LC1 (N = 8)	LC2 (N = 10)	AR1 (N = 8)	AR2 (N = 7)	RMSE	1 (N = 41)	2 (N = 15)	RMSE	TRT	PAR
Gestation length (day)	116.3	117.3	117.0	117.6	117.1	117.2	117.3	0.3	117.0	117.2	0.3	0.24	0.45
BW													
Gestation gain (kg)	45	32	31	47	50	27	44	13	51 <sup>x</sup>	29 <sup>y</sup>	10	0.42	0.02
At farrowing (kg)	245	228	235	240	256	236	246	16	238	240	14	0.29	0.43
Backfat													
Gestation gain (mm)	3.8	1.9	2.1	3.7	3.4	3.2	2.3	1.1	2.7	3.1	0.8	0.60	0.67
At farrowing (mm)	14.4	13.7	13.1	14.9	16.8	13.3	14.9	1.3	13.7	15.2	1.1	0.05	0.08
Loin muscle depth													
Gestation gain (mm)	6.4	7.0	8.5	7.0	8.0	6.0	7.2	2.0	7.9	6.3	1.2	0.97	0.32
At farrowing (mm)	53.9	54.9	55.3	51.3	55.5	53.0	54.2	2.4	54.1	53.6	1.9	0.60	0.61

RMSE = root mean square error; TRT = treatment; PAR = parity at treatment.

All data were presented as least square (LS) means.

<sup>x,y</sup> Means within a row without a common superscript are different (PAR effect;  $P \leq 0.05$ ).

<sup>1</sup> The interactions between treatment and parity were not significant ( $P > 0.05$ ) and are therefore not presented.

**Table 2**

Litter characteristics at subsequent birth of sows treated a top-dressing (200 g) of either wheat (CON) or wheat plus microfibrillated cellulose (MF), L-carnitine (LC) or L-arginine (AR) at one of two supplementation levels (1,2) during 1 week before weaning and the weaning to oestrus interval.

Items	TRT								PAR			P-values <sup>1</sup>	
	CON (N = 4)	MF1 (N = 8)	MF2 (N = 11)	LC1 (N = 8)	LC2 (N = 10)	AR1 (N = 8)	AR2 (N = 7)	RMSE	1 (N = 41)	2 (N = 15)	RMSE	TRT	PAR
Total born <sup>2</sup> , n	18.5	21.0	20.7	18.8	18.8	19.5	17.8	1.5	18.3 <sup>x</sup>	20.3 <sup>y</sup>	1.1	0.22	0.02
Litter weight at birth, kg	25.4	23.7	26.0	24.5	24.6	24.60	24.2	2.2	24.1	22.0	1.8	0.83	0.43
Mean birth weight, g	1364	1234	1324	1291	1357	1266	1330	83	1365 <sup>x</sup>	1253 <sup>y</sup>	55	0.10	<0.01
SD of birth weight, g	303	296	313	267	282	313	276	24	275	311	13	0.65	0.07
CV of birth weight, %	21.8	24.7	25.8	21.2	21.8	25.7	20.5	2.0	20.0 <sup>y</sup>	26.1 <sup>x</sup>	1.1	0.17	<0.01
Piglets <1000 g, % <sup>3</sup>	8.7	25.3	26.6	17.1	19.7	21.7	8.5	5.4	11.5 <sup>y</sup>	24.4 <sup>x</sup>	3.8	0.13	<0.01
Piglets >1800 g, % <sup>3</sup>	7.0	2.2	2.5	3.3	12.5	2.5	5.2	4.1	7.9	2.8	2.9	0.22	0.09

RMSE = root mean square error; TRT = treatment; PAR = parity at treatment.

All data were presented as least square (LS) means, unless otherwise stated.

<sup>x,y</sup> Means within a row without a common superscript are different (PAR effect; P ≤ 0.05).

<sup>1</sup> The interactions between treatment and parity were only significant for mean birth weight. LC2-par1 had higher birth weight (1561 g) than LC2-par2 (1566 g) and MF2-par2 (1018 g).

<sup>2</sup> Total number of piglets born per litter.

<sup>3</sup> Data presented as means.

**Relationships among litter characteristics**

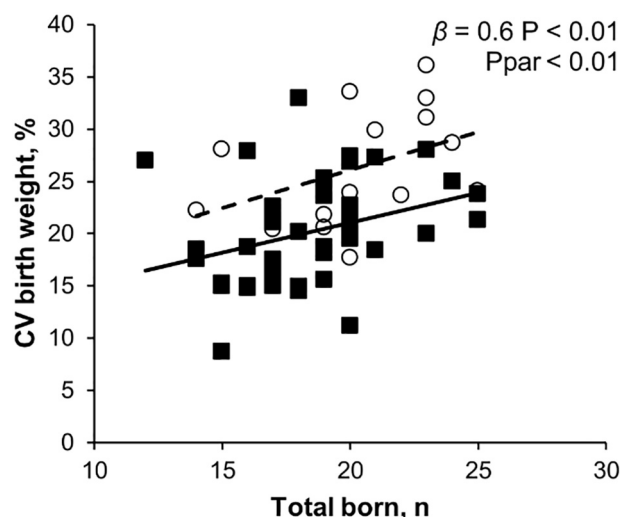
Relationships among litter characteristics as shown below were similar for sows after their first and second lactation, as described below. As the total number of piglets born per litter increased by one, mean birth weight decreased by 37 g (P < 0.001), proportions of piglets > 1800 g decreased by 2% (P < 0.01; Table 3), CV of birth weight increased by 0.6% (P < 0.01; Fig. 1; Table 3) and proportions of piglets < 1000 g increased by 2% (P < 0.001; Table 3). CV of birth weight was positively related to proportions of piglets < 1000 g (P < 0.001; Table 3) but was negatively related to mean birth weight (P < 0.001; Table 3).

**Relationships between body condition loss during previous lactation and litter characteristics**

No interactions between parity and body condition loss characteristics were observed (P > 0.05). BW loss and BF loss were not related to any litter characteristics, but higher relative LM loss during previous lactation was related to lower CV and SD of birth weight (β = -0.1%/%, P < 0.05 and β = -1.7 g/%, P = 0.04, respectively; Fig. 2).

**Relationships between IGF-1 and litter characteristics**

Sow IGF-1 concentration did not relate to total number of piglets born per litter (P > 0.05). Higher IGF-1 concentrations during the WEI were related to a higher litter weight at birth (β ≥ 0.02 kg per ng/ml, P ≤ 0.02; Fig. 3a, b, c) only in sows after their first lactation at subsequent parturition. IGF-1 concentration at 3 days after weaning in sows after their first lactation was also positively related to mean piglet birth



**Fig. 1.** Relationship between total number of piglets born per litter (total born) and CV of birth weight at subsequent farrowing in sows after their first (■) and second lactation (○). β = regression coefficient, Ppar = P-value for parity. No interactions between parities were found.

weight at second parturition (β = 1.1 g per ng/ml, P < 0.02; Fig. 3e). Within parity, higher IGF-1 concentrations at oestrus were related to a higher mean piglet birth weight (β = 1.0 g per ng/ml, P = 0.03; Fig. 3f); this relationship was changed after correction for the number of

**Table 3**

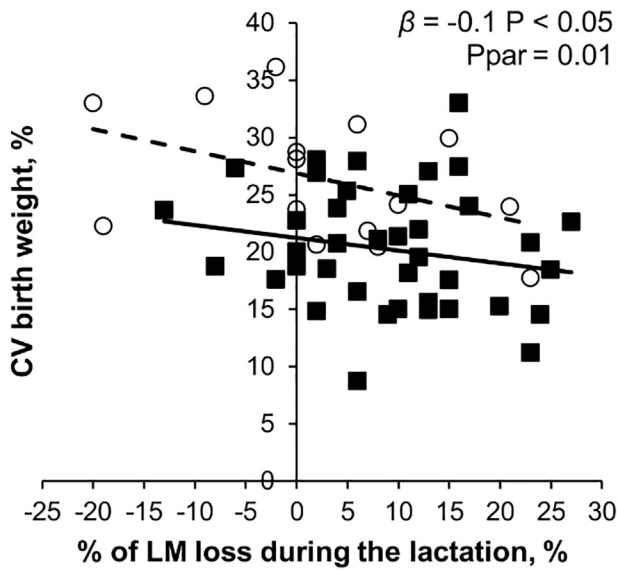
Regression coefficients (β) among litter characteristics in sows.

Litter characteristics <sup>1</sup>	Litter characteristics <sup>1</sup>						
	Total born <sup>2</sup> , n	Litter weight at birth, kg	Mean birth weight, g	SD of birth weight, g	CV of birth weight, %	Piglets <1000 g, %	Piglets >1800 g, %
Total born <sup>2</sup> , n	-	-	-	-	-	-	-
Litter weight at birth, kg	0.6***	-	-	-	-	-	-
Mean birth weight, g	-37***	23**	-	-	-	-	-
SD of birth weight, g	1.2	3.5	0.04	-	-	-	-
CV of birth weight, %	0.6**	-0.09	-0.01***	0.07***	-	-	-
Piglets <1000 g, %	2***	-1.3**	-0.05***	0.03	1.4***	-	-
Piglets >1800 g, %	-2**	1.5**	0.06***	0.08*	-0.3	-0.45**	-

\* <0.05; \*\* <0.01; \*\*\* <0.001.

<sup>1</sup> The interactions between treatment and parity were not significant (P > 0.05).

<sup>2</sup> Total number of piglets born per litter.



**Fig. 2.** Relationship between loin muscle depth (LM) loss during previous lactation and CV birth weight at subsequent farrowing in sows after their first (■) and second lactation (○).  $\beta$  = regression coefficient,  $P_{par}$  =  $P$ -value for parity. No interactions between parity were found.

piglets born per litter (mean piglet birth weight (g) =  $1848.9 + 0.8 \times$  IGF-1 at oestrus (ng/ml;  $P = 0.02$ ) -  $38.8 \times$  litter size ( $P < 0.0001$ ).

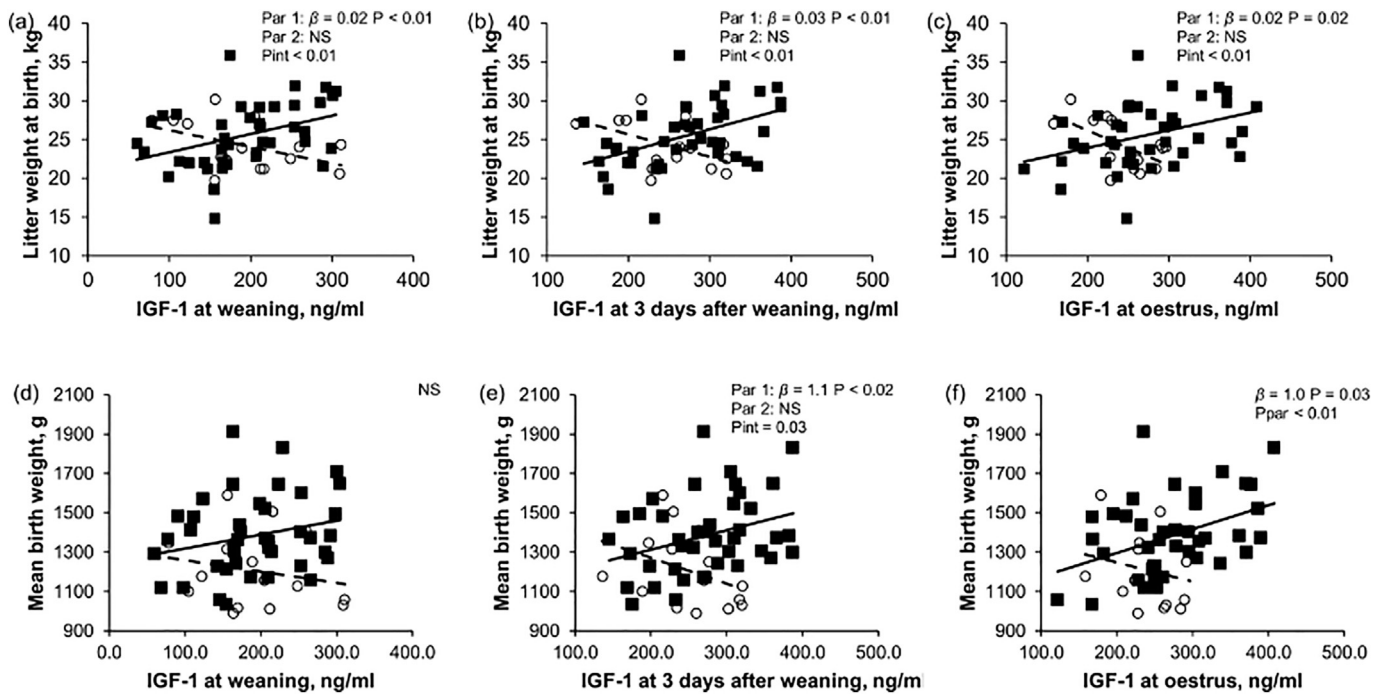
*Relationships between follicle development during the WEI and litter characteristics*

No interactions between parity and follicle development characteristics were observed ( $P > 0.05$ ). Follicle diameters during the WEI were not related to litter characteristics at birth.

**Discussion**

The average litter size was 19.0 total born piglets, and litter size was negatively related to piglet birth weight and positively related to within-litter birth weight variation (i.e. litter uniformity), which corroborates with previous studies (Milligan et al., 2002; Quesnel et al., 2008; Wientjes et al., 2012a). Not only low birth weight (Rutherford et al., 2013), but also huge within-litter birth weight variation (high SD or CV of birth weight; Wientjes et al., 2012a) are associated with higher mortality during lactation. We also found an increased proportion of low birth weight piglets in large litters ( $\beta = 2\%$ ). Small piglets are more vulnerable as they are less capable to compete for colostrum and have greater risk of chilling (reviewed by Rutherford et al., 2013). Thus, piglet mean birth weight and litter uniformity should be improved, particularly in large litters.

One possibility to improve litter characteristics is through a nutritional approach (i.e. composition of pre-mating diets). This study, however, failed to show an effect of the pre-mating diets used (i.e. LC, AR and MF in late lactation and during the WEI) on litter characteristics at subsequent birth. In our companion paper (Han et al., 2020), we reported that the used pre-mating diets did not affect plasma IGF-1 or follicle development during the WEI in these sows, and the current paper reports a lack of effect on subsequent litter characteristics. It needs to be stressed, however, that a small sample size per treatment was used in this study and therefore further study with larger sample size will be needed to further investigate the effects of these pre-mating diets on post-weaning IGF-1 concentrations and subsequent litter characteristics. Interestingly, MF sows had a numerically larger litter size in this study (21.0 and 20.7, for MF1 and MF2, respectively, compared to from 17.8 to 19.5 for the other treatment groups). This seems to correspond with the findings of Ferguson et al. (2004 and 2007) that higher levels of dietary fibre in the pre-mating diet resulted in increased litter size and improved oocyte quality and embryo survival in sows and gilts. They attributed these effects to higher gonadotropin levels before ovulation (Ferguson et al. (2007)). Thus, it may be worth further



**Fig. 3.** Relationship between plasma IGF-1 during the weaning-to-oestrus interval (WEI) and (a, b, c) litter weight at subsequent farrowing and (d, e, f) mean birth weight in sows after their first (■) and second lactation (○). Interactions with parity are indicated where significant.  $\beta$  = regression coefficient, Par 1 = first-parity, Par 2 = second-parity, Pint =  $P$ -value for interaction.

investigating effects of MF- and fibre-supplemented pre-mating on sow reproductive processes and performance.

In this study, sow BW gain during gestation following treatments was different between the two parities when the feeding level was the same. This is consistent with Young et al. (2005) who reported that sows after their first lactation had higher BW gain during gestation than sows after their second lactation. In general, primiparous sows still need to grow during gestation so that they reach mature size similar to multiparous sows (Young et al., 2005; Hoving et al., 2012), which might be the reason why younger sows are more sensitive to body condition losses during lactation.

Similarly, in the present study, litter size at second farrowing sows was lower than that at the third farrowing, as seen before (Thaker and Bilkei, 2005; Quesnel et al., 2008). A lower second litter size compared to the first litter size has been attributed to a limited feed intake capacity during first lactation, resulting in high lactational weight losses (Hoving et al., 2012). In our study, sows during their first and second lactation had similar relative body condition losses (i.e. BW, BF and LM loss; Supplementary Table S3), for example, a 13.3 vs 12.2% BW loss, which are both levels that are considered indicative for reduced reproductive performance (Thaker and Bilkei, 2005). However, sows in their first lactation seem more susceptible to the impact of body condition losses on subsequent reproductive performance as their body reserve is limited and energy for body growth after weaning is higher than in older parity sows (Hoving et al., 2012). Therefore, it can be concluded that primiparous sows were vulnerable to body condition loss during lactation and had a lower litter size at subsequent farrowing. On the other hand, although our experimental sows had large litter size at subsequent farrowing, a better reproductive performance, such as higher litter size and mean birth weight, can be expected if body condition losses are minimized.

An association between IGF-1 during WEI and subsequent litter size was not observed in this study. On the other hand, we found a positive relationship between IGF-1 during WEI and piglet mean birth weight. Besides, a higher plasma IGF-1 concentration at oestrus was related to larger piglet birth weight and higher proportion of heavy piglets in both parities (data not shown). These effects might be due to the effects of IGF-1 on follicle development. First of all, in the study of Costermans et al. (2020), plasma IGF-1 concentration was highly correlated with IGF-1 in follicular fluid and the percentage of better quality cumulus-oocyte complexes (COCs). This higher percentage of better quality COC resulted in a higher fertilization rate (Costermans et al., 2020) and may also affect embryo quality. Related to this, a higher IGF-1 concentration during the WEI seems to be related to a larger follicle diameter (Costermans et al., 2020; Han et al., 2020). This larger follicle before ovulation seems to become a larger CL (Soede et al., 1998; Wientjes et al., 2012b), which may be beneficial for embryo development during the early stage, as the average diameter of CL during early gestation was positively related to mean piglet birth weight (Da Silva et al., 2017b). Additionally, Langendijk et al. (2008) reported that IGF-1 at weaning was related to the increment of progesterone in early pregnancy. Thus, higher IGF-1 during the WEI seems to improve follicle and oocyte quality, and CL function, which further support embryo development and finally increase piglet mean birth weight, as litter characteristics were determined by early embryo developmental stage (van der Lende et al., 1990). Van den Brand et al. (2009) support this positive impact of pre-mating IGF-1 on piglet mean birth weight as they found that IGF-1-stimulating diet (dextrose plus lactose) group sows tended to have higher piglet mean birth weight compared to control group sows (1483 vs. 1569 g,  $P = 0.07$ ). Therefore, for young sows, increasing IGF-1 concentration before ovulation seems to result in increased piglet weight at subsequent birth.

We found a negative relationship between lactational LM loss and subsequent SD and CV of birth weight in both parities. Thus, higher loin muscle losses during lactation resulted in less within-litter

variation in birth weight at subsequent farrowing. This was surprising as Wientjes et al. (2013) found a positive relationship between BW loss (both absolute and relative) and BF loss during lactation and subsequent SD and CV (only for BF loss) of piglet birth weight in sows, indicating an increase in within-litter variation. Wientjes et al. (2013), however, used mixed parity (on average 3.2) sows with a lower litter size (on average 14.0) compared to our study (parity on average 1.3, litter size on average 19.0). Presumably, different parity and litter size are the reasons for the different relationships between body condition losses and litter characteristics between two studies. One possible explanation for the impact of LM loss on litter uniformity might be their impact on follicle diameter. In our companion paper (Han et al., 2020), we showed that a higher LM loss was related to a smaller follicle size at weaning ( $r = -0.28$ ,  $P \leq 0.05$ ), and this smaller follicle size at weaning was related to a longer weaning-to-ovulation interval. Longer WEI might be connected to fewer LH pulses and lower ovulation rate (Van den Brand et al., 2000; Bracken et al., 2003). As the number of ovulations decrease, fewer and more uniform embryos may attach to the uterus (Da Silva et al., 2017a). Also, Hoving et al. (2012) found that sows with higher lactational LM loss had a lower number of embryos and implantation sites and reduced embryo survival on day 35 of pregnancy. This lower number of embryos and possibly associated lower variation in embryo weight may result in a lower within-litter birth weight variation as litter characteristics are largely determined during early pregnancy (Vallet et al., 2011). However, such a relationship between LM loss and litter characteristics has not been documented. Also, Wientjes et al. (2013) did not investigate the LM loss but BW loss and BF loss during lactation. Thus, the impact of LM loss during the previous lactation on subsequent litter characteristics will be needed to be studied in the future.

In summary, pre-mating diets (LC, AR and MF) did not affect litter characteristics in this study. Our present results suggested that a higher pre-mating IGF-1 concentration, which can result from optimizing sow body condition during lactation, may be one possibility for increasing piglet mean birth weight at subsequent farrowing, especially for sows in their first lactation.

### Supplementary materials

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.animal.2020.100029>.

### Ethics approval

Experimental procedures were reviewed and approved by the Animal Experiment Board (ELLA; ESAVI/2325/04.10.07/2017) in Finland.

### Data and model availability statement

None of the data were deposited in an official repository.

### Author ORCIDs

T. Han: 0000-0003-0801-4442

### Author contributions

Taehee Han: Conceptualization, Methodology, Data curation, Writing- Original draft preparation Stefan Björkman: Methodology, Writing -Reviewing and Editing Nicoline Soede: Methodology, Writing -Reviewing and Editing Claudio Oliviero: Methodology, Writing -Reviewing and Editing Olli Peltoniemi: Methodology, Writing -Reviewing and Editing, Supervision Both of these were provided in the latest proof stage.

## Declaration of interest

The authors declare that there are no conflicts of interest.

## Financial support statement

This study was funded by the Finnish Ministry of Agriculture (grant decision 1487/03.01.02/2016), the Mercedes-Zacharias Research Foundation, Hankkija, Vetcare, Figen, Atria, and the Finnish Foundation of Veterinary Research.

## References

- Bergsma, R., Kanis, E., Verstegen, M.W.A., CMC, Van der Peet-Schwering, Knol, E.F., 2009. Lactation efficiency as a result of body composition dynamics and feed intake in sows. *Livestock Science* 125, 208–222.
- Bracken, C.J., Lamberson, W.R., Safranski, T.J., Lucy, M.C., 2003. Factors affecting follicular populations on Day 3 postweaning and interval to ovulation in a commercial sow herd. *Theriogenology* 60, 11–20.
- Costermans, N.G.J., Teerds, K.J., Middelkoop, A., Roelen, B.A.J., Schoevers, E.J., van Tol, H.T.A., Laurensen, B., Koopmanschap, R.E., Zhao, Y., Blokland, M., van Tricht, F., Zak, L., Keijer, J., Kemp, B., Soede, N.M., 2020. Consequences of negative energy balance on follicular development and oocyte quality in primiparous sows. *Biology of Reproduction* 102, 388–398.
- Da Silva, C.L., Broekhuijse, M.L., Laurensen, B.F., Mulder, H.A., Knol, E.F., Kemp, B., Soede, N.M., 2017a. Relationship between ovulation rate and embryonic characteristics in gilts at 35 d of pregnancy. *Journal of Animal Science* 95, 3160–3172.
- Da Silva, C.L., Laurensen, B.F., Knol, E.F., Kemp, B., Soede, N.M., 2017b. Validation of transectal ultrasonography for assessment of corpora lutea characteristics in pregnant sows and its relationship with litter characteristics at birth. *Translational Animal Science* 1, 507–517.
- Doberenz, J., Birkenfeld, C., Kluge, H., Eder, K., 2006. Effects of L-carnitine supplementation in pregnant sows on plasma concentrations of insulin-like growth factors, various hormones and metabolites and chorion characteristics. *Journal of Animal Physiology and Animal Nutrition* 90, 487–499.
- Ferguson, E.M., Ashworth, C.J., Edwards, S.A., Hawkins, N., Hepburn, N., Hunter, M.G., 2003. Effect of different nutritional regimens before ovulation on plasma concentrations of metabolic and reproductive hormones and oocyte maturation in gilts. *Reproduction* 126, 61–71.
- Ferguson, E.M., Ashworth, C.J., Hunter, M.G., Penny, P., Slevin, J., Edwards, S.A., 2004. The effect of feeding a high fibre diet from mid lactation until breeding on subsequent litter size of sows. *BSAP Occasional Publication* 31, 175–179.
- Ferguson, E.M., Slevin, J., Hunter, M.G., Edwards, S.A., Ashworth, C.J., 2007. Beneficial effects of a high fibre diet on oocyte maturity and embryo survival in gilts. *Reproduction* 133, 433–439.
- Guo, P., Jiang, Z.Y., Gao, K.G., Wang, L., Yang, X.F., Hu, Y.J., Ma, X.Y., 2017. Low-level arginine supplementation (0.1%) of wheat-based diets in pregnancy increases the total and live-born litter sizes in gilts. *Animal Production Science* 57, 1091–1096.
- Han, T., Björkman, S., Soede, N.M., Oliviero, C., Peltoniemi, O.A.T., 2020. IGF-1 concentration patterns and their relationship with follicle development after weaning in young sows fed different pre-mating diets. *Animal* 14, 1493–1501.
- Hoving, L.L., Soede, N.M., Feitsma, H., Kemp, B., 2012. Lactation weight loss in primiparous sows: consequences for embryo survival and progesterone and relations with metabolic profiles. *Reproduction in Domestic Animals* 47, 1009–1016.
- Langendijk, P., Van Den Brand, H., Gerritsen, R., Quesnel, H., Soede, N.M., Kemp, B., 2008. Porcine luteal function in relation to IGF-1 levels following ovulation during lactation or after weaning. *Reproduction in Domestic Animals* 43, 131–136.
- Lucy, M.C., 2008. Functional differences in the growth hormone and insulin-like growth factor axis in cattle and pigs: implications for post-partum nutrition and reproduction. *Reproduction in Domestic Animals* 43, 31–39.
- Milligan, B.N., Fraser, D., Kramer, D.L., 2002. Within-litter birth weight variation in the domestic pig and its relation to pre-weaning survival, weight gain, and variation in weaning weights. *Livestock Production Science* 76, 181–191.
- Pope, W.F., Xie, S., Broeremann, D.M., Nephew, K.P., 1990. Causes and consequences of early embryonic diversity in pigs. *Journal of Reproduction and Fertility* 40 (suppl), 251–260.
- Quesnel, H., Brossard, L., Valancogne, A., Quiniou, N., 2008. Influence of some sow characteristics on within-litter variation of piglet birth weight. *Animal* 2, 1842–1849.
- Quesnel, H., Meunier-Salaun, M.C., Hamard, A., Guillemet, R., Etienne, M., Farmer, C., Dourmad, J.Y., Pèrè, M.C., 2009. Dietary fibre for pregnant sows: influence on sow physiology and performance during lactation. *Journal of Animal Science* 87, 532–543.
- Rutherford, K.M.D., Baxter, E.M., D'earth, R.B., Turner, S.P., Arnott, G., Roehe, R., Ask, B., Sandøe, P., Moustsen, V.A., Thorup, F., Edwards, S.A., 2013. The welfare implications of large litter size in the domestic pig I: biological factors. *Animal Welfare* 22, 199–218.
- Serpa, A., Velásquez-Cock, J., Gañán, P., Castro, C., Vélez, L., Zuluaga, R., 2016. Vegetable nanocellulose in food science: A review. *Food Hydrocolloids* 57, 178–186.
- Soede, N.M., Hazeleger, W., Kemp, B., 1998. Follicle size and the process of ovulation in sows as studied with ultrasound. *Reproduction in Domestic Animals* 33, 239–244.
- Thaker, M.Y.C., Bilkei, G., 2005. Lactation weight loss influences subsequent reproductive performance of sows. *Animal Reproduction Science* 88, 309–318.
- Vallet, J.L., Freking, B.A., Miles, J.R., 2011. Effect of empty uterine space on birth intervals and fetal and placental development in pigs. *Animal Reproduction Science* 125, 158–164.
- Van den Brand, H., Dieleman, S.J., Soede, N.M., Kemp, B., 2000. Dietary energy source at two feeding levels during lactation of primiparous sows: I. Effects on glucose, insulin, and luteinizing hormone and on follicle development, weaning-to-estrus interval, and ovulation rate. *Journal of Animal Science* 78, 396–404.
- Van den Brand, H., Prunier, A., Soede, N.M., Kemp, B., 2001. In primiparous sows, plasma insulin-like growth factor-I can be affected by lactational feed intake and dietary energy source and is associated with luteinizing hormone. *Reproduction Nutrition Development* 41, 27–39.
- Van den Brand, H., Soede, N.M., Kemp, B., 2006. Supplementation of dextrose to the diet during the weaning to estrus interval affects subsequent variation in within-litter piglet birth weight. *Animal Reproduction Science* 91, 353–358.
- Van den Brand, H., Van Enckevort, L.C.M., Van der Hoeven, E.M., Kemp, B., 2009. Effects of dextrose plus lactose in the sows diet on subsequent reproductive performance and within litter birth weight variation. *Reproduction in Domestic Animals* 44, 884–888.
- Van der Lende, T., Hazeleger, W., De Jager, D., 1990. Weight distribution within litters at the early foetal stage and at birth in relation to embryonic mortality in the pig. *Livestock Production Science* 26, 53–65.
- Wientjes, J.G.M., Soede, N.M., Van der Peet-Schwering, C.M.C., Van den Brand, H., Kemp, B., 2012a. Piglet uniformity and mortality in large organic litters: effects of parity and pre-mating diet composition. *Livestock Science* 144, 218–229.
- Wientjes, J.G.M., Soede, N.M., Van den Brand, H., Kemp, B., 2012b. Nutritionally induced relationships between insulin levels during the weaning-to-ovulation interval and reproductive characteristics in multiparous sows: II. Luteal development, progesterone and conceptus development and uniformity. *Reproduction in Domestic Animals* 47, 62–68.
- Wientjes, J.G.M., Soede, N.M., Knol, E.F., Van den Brand, H., Kemp, B., 2013. Piglet birth weight and litter uniformity: effects of weaning-to-pregnancy interval and body condition changes in sows of different parities and crossbred lines. *Journal of Animal Science* 91, 2099–2107.
- Young, M.G., Tokach, M.D., Aherne, F.X., Main, R.G., Dritz, S.S., Goodband, R.D., Nelssen, J.L., 2005. Effect of sow parity and weight at service on target maternal weight and energy for gain in gestation. *Journal of Animal Science* 83, 255–261.
- Zak, L.J., Xu, X., Hardin, R.T., Foxcroft, G.R., 1997. Impact of different patterns of feed intake during lactation in the primiparous sow on follicular development and oocyte maturation. *Reproduction* 110, 99–106.
- Zak, L.J., Gaustad, A.H., Bolarin, A., Broekhuijse, M.L., Walling, G.A., Knol, E.F., 2017. Genetic control of complex traits, with a focus on reproduction in pigs. *Molecular Reproduction and Development* 84, 1004–1011.
- Zhu, C., Guo, C.Y., Gao, K.G., Wang, L., Chen, Z., Jiang, Z.Y., 2017. Dietary arginine supplementation in multiparous sows during lactation improves the weight gain of suckling piglets. *Journal of Integrative Agriculture* 16, 648–655.