Impact of sow energy status during farrowing on farrowing kinetics, frequency of stillborn piglets, and farrowing assistance[1]

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ABSTRACT: Farrowing duration is rather long in sows most likely due to selection for large litters, and we hypothesized that prolonged farrowings would compromise sow energy status during farrowing and in turn the farrowing process. Two studies were performed as follows: 1) to evaluate whether sow energy status during farrowing compromise the farrowing kinetics (**FK**, i.e., farrowing duration and birth intervals) and 2) to study the underlying mechanisms potentially affecting stillbirth rate and farrowing assistance. In study-1, parameters affecting FK were characterized based on data from a total of 166 farrowings from 7 feeding trials focused on sow colostrum production. The data were screened for associations with FK using the CORR procedure of SAS. Traits that were correlated with the FK at $P < 0.05$ were included in a multivariate regression model. Time since last meal until the onset of farrowing greatly affected the farrowing duration ($r = 0.76$; $n = 166$; $P < 0.001$) and a broken-line model was fitted to describe that relationship. According to the model, farrowing duration was constant (3.8 ± 1.5 h) if the farrowing started before the breakpoint (3.13 ± 0.34 h after the last meal), whereas farrowing duration increased to 9.3 h if the farrowing started 8 h after the last meal. Subsequently, sows were divided into 3 categories based on that trait (≤3, 3 to 6, and >6 h) to evaluate the impact on birth intervals, farrowing assistance, and stillbirth rate. Birth intervals ($P < 0.001$), odds for farrowing assistance ($P < 0.001$), and odds for stillbirth ($P = 0.02$) were low, intermediate, and high when time since last meal was ≤3, 3 to 6, and >6 h, respectively. In study-2, blood samples were collected once or twice each week in late gestation and each hour during farrowing to measure arterial concentrations and uterine extractions of plasma metabolites. Time since last meal was strongly negatively correlated with arterial glucose 1 h after the onset of farrowing ($r = -0.96$; $n = 9$; $P < 0.001$). Glucose appeared to be the key energy metabolite for oxidative metabolism of gravid uterus. In conclusion, the present study strongly suggests that a substantial proportion of sows suffer from low-energy status at the onset farrowing and that this negatively affects the farrowing process. Transferring this knowledge into practice, the results suggest that sows should be fed at least 3 daily meals in late gestation.

Key words: birth interval, break-point analysis, farrowing duration, last meal, plasma glucose, stillbirth rate

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INTRODUCTION

A successful farrowing is a condition when the stillbirth rate (**SR**) is less than 10% in the litter (Oliviero, 2010). Farrowing duration (**FD**) and birth intervals (**BI**) are the key factors influencing SR (Zaleski and Hacker, 1993; van Dijk et al., 2005), but umbilical rupture and low BW are

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also known risk factors (Dial et al., 1992; Mota-Rojas et al., 2005). Several studies have reported that litter size (**LS**) is positively correlated with FD (Fahmy and Friend, 1981; van Dijk et al., 2005) and negatively correlated with BI (Vallet et al., 2010). Giving birth to a piglet is an energy demanding process (Vallet et al., 2013). The intense uterine contractions and abdominal straining during farrowing (Assali et al., 1958) may compromise sow energy status, especially during prolonged farrowings. Most of the dietary energy is absorbed from the GI-tract of sows and pigs in the form of glucose during the first 4 to 6 h postprandially (Serena et al., 2009; Theil et al., 2011). Energy originating from fiber fermentation in the hind-gut is available for much longer period postprandially but in lower quantities (Bach Knudsen et al., 2016). However, the proportion can be increased by increasing the fiber intake (Serena et al., 2009), and recently, we reported a decreased proportion of SR in sows that were fed high-fiber diet in late gestation (Feyera et al., 2017). This finding suggests that an increased energy uptake from the hind-gut postprandially may improve the farrowing process. Thus, the impact of sow energy status during farrowing may be of importance for FD, BI, farrowing assistance (**FA**), and SR; hence, these associations need to be elucidated. Therefore, the present studies aimed to evaluate whether sow energy status during farrowing affected FD and BI, FA, and SR. Moreover, uterine extractions of plasma metabolites were performed to evaluate which dietary components are the substrate for uterine oxidation in late gestation and during farrowing.

MATERIALS AND METHODS

The present experiment complied with Danish Ministry of Justice Law number 382 (June 10, 1987), Act number 726 (9 September 1993, as amended by Act number 1081 of 20 December 1995), concerning experiments with the care of animals.

The results presented in this paper are based on data generated from 2 independent studies. In study-1, data were compiled from a total of 166 litters included in 7 independent feeding trials focusing on colostrum production performed during a 7-yr period. These recordings were used to characterize traits affecting the farrowing kinetics (**FK**; FD and BI), FA, and SR. In study-2, intensive experiment with 10 multicatheterized sows was performed to investigate the relationship between the arterial concentration of glucose during farrowing with FD and the time from last meal until the onset of farrowing (**TLMUOF**) and to generate qualitative data on uterine oxidation pattern during late gestation and farrowing.

Study-1

Study population. The data from the 7 experiments (Exp. 1 through 7) included in study-1 were obtained from Danish Landrace × Danish Yorkshire sows. In these 7 independent experiments, the effects of different dietary treatments on sows and piglets performance were investigated. The study represented a total of 166 farrowings that gave birth to 2,889 total born piglets (2,704 live-born and 185 stillborn piglets), whereas mummified piglets (n = 53) were excluded from both the LS and the statistical analyses of traits related to the farrowing. The sows were of first to fifth parity.

Details of the included experiments were described for the individual investigations in Exp.1: Hansen et al. (2012), Exp. 2: Flummer et al. (2012), Exp. 3: Krogh et al. (2012), Exp. 4: Krogh et al. (2015), Exp. 5: Krogh et al. (2016), and Exp. 6: Pedersen et al. (2016), respectively. In Exp. 7, diets with a 2 × 2 factorial design, having 2 levels of energy and 2 levels of lysine, were formulated by blending 2 separate dietary components: a basal diet and a supplementary diet, and fed to the sows during late gestation on an individual basis (T. Feyera, U. Krogh, and P. K. Theil, unpublished data). Twenty-four second-parity sows (Danish Landrace × Danish Yorkshire) were included in Exp. 7 from day 102 of gestation until weaning 28 d after farrowing. All sows in late gestation (Exp. 1 through 7) were fed restrictedly (2.9 to 3.3 kg/d) with a reduced feed allowance during the last 3 d of gestation (2.6 to 2.9 kg/d). The sows were fed 2 (Exp. 1) or 3 daily meals (Exp. 2 through 7) throughout the experiments, i.e., every 12th or 8th h, respectively, for Exp. 1 and Exp. 2 through 7. However, if sows did not ingest their last meal, the time until the onset of farrowing was corrected accordingly.

Dietary treatment and ME intake. All sows included in these 7 experiments were fed standard gestation diets until approximately 1 wk before expected farrowing and then shifted to lactation diets and fed these diets until weaning 28 d after farrowing. The diets were mainly based on barley, wheat, and soybean meal as the main ingredients, even though diet composition varied among the experiments and among treatments within the experiments. Feed intake was corrected for feed refusal, whereby daily ME intake was calculated for each sow by multiplying the daily feed intake (kg/d)

with the calculated energy content of the diet (MJ ME/kg). The ME supply from days 84 to 112 of gestation ranged from 37 to 43 MJ ME/d, but was reduced to approximately 31 MJ ME/d in the last 3 d of gestation.

Management and recordings around farrowing. Approximately 1 wk before expected farrowing, sows were moved to an individual farrowing pen made of concrete and slatted floor equipped with an infrared lamp to establish a warm microclimate for the piglets. Sows were supervised daily around farrowing, video recordings were used to identify, and survey sows that approached the farrowing based on nest-building behavior and absence/presence of milk in the mammary glands. All sows farrowed naturally, that is, without inducing farrowing. FAs were given when the interval between 2 consecutive births exceeded approximately 90 min. All sows were closely monitored during farrowing starting from the birth of the first piglet to the expulsion of the placenta.

For each litter, the numbers of live-born, stillborn, and thus total born piglets were recorded along with the time of birth and birth weight for each piglet. LS was defined as the number of fully formed piglets; that is, mummified piglets were excluded. Piglets were classified as live-born if they breathed or moved physically immediately after birth. BI were calculated as the time since the last piglet was born; therefore, the first-born piglets had no BI according to this definition. When 2 piglets were born successively within less than a minute, a BI of 0.5 min was assigned to the second piglet. FD was defined as the time elapsed between the birth of the first-born and the last-born piglet in the litter. The TLMUOF was calculated as the difference between the time of last supplied meal before the actual farrowing and the recorded time when the first piglet was born. Consequently, TLMUOF was used to evaluate sow energy status during farrowing.

Statistical analysis. All statistical analyses were performed using SAS version 9.3 (SAS Inst. Inc., Cary, NC). Normality of the data was checked using the UNIVARIATE procedure of SAS. All independent traits were individually screened for association and collinearity with the dependent variables (FK) using the CORR procedure of SAS. All independent traits that were correlated with the dependent traits at $P < 0.05$ were initially included in a multivariate regression model to evaluate which traits are related to FD, mean BI, SR, and FA. SR and FA were analyzed as binary responses. From a total of 86 independent traits initially included, only 4 traits (TLMUOF, LS, mean piglet BW at birth, and FA) were identified to be significantly related to FD, mean BI, SR, and FA and final multivariate regression models were then fitted for these traits. The effect of TLMUOF on FD adjusted for average piglet body weight at birth (**BWB**) in the litter, LS, and FA was analyzed as a nonlinear mixed effects model using the NLMIXED procedure of SAS. The model was stepwise linear with a plateau until a break point and a linear regression in TLMUOF afterwards. That is, the model has 6 fixed effect parameters (intercept, break point, slope after break point, BWB, LS, and FA). In addition, the model included a random intercept of an experiment to account for unobserved differences among experiments and the implicated correlation between sows from the same experiment. The effect of TLMUOF on average BI and risk of stillbirth was modeled by, respectively, a linear mixed effects model and by a mixed effects logistic regression, i.e., a binomial generalized linear mixed effects model with logit link. For both of these models, TLMUOF was categorized into 3 levels (≤3, 3 to 6, >6 h) and included in addition to BWB, LS, and FA as fixed effects and experiment as a random component. Correspondingly, the effect of TLMUOF on the need for FA was modeled by a mixed effects logistic regression using the same parameters except FA now being the outcome. The logistic regressions were carried out using the GLIMMIX procedure of SAS and effects are shown as odds ratios using ≤3 h as a reference for TMLUOF, "no" as a reference for FA, per kg increase of BWB, and per extra piglet within the litter. Statistical difference was declared at $P < 0.05$, and $P < 0.10$ was considered a tendency.

Study-2

Animal model and experimental design. Ten third- to fifth-parity sows (Danish Landrace × Danish Yorkshire) were used to measure arterial concentrations and uterine extractions of plasma metabolites and blood gases during late gestation and farrowing. Sows were stratified for BW (276 ± 18 kg, mean ± SD), and parity at day 75 ± 2 of gestation and surgically implanted with permanent indwelling catheters in the femoral artery and uterine vein in the right uterine horn. Two other catheters were also inserted into the mammary gland to measure mammary uptake of nutrients during the colostrum period (to be published elsewhere). For catheterization of an arterial catheter, incision of 5 to 7 cm was made in the inguinal

region, the arterial branch was freed from the connective tissue, and then the catheter was inserted using a guide wire (THSF-25–260, Cook Danmark, Bjaeverskov, Denmark). For catheterization of the uterus, the right uterine horn along with 1 to 2 fetuses was gently exteriorized by mid-ventral laparotomy of 15 to 18 cm incision and kept in cotton cloth wetted in a 0.9% saline solution during the procedure. At approximately one-third of the length of the uterine horn from the proximal end of the uterus, a 10-cm long catheter was inserted into the uterine vein using a guide wire (THSF-25–260, Cook Danmark, Bjaeverskov, Denmark). The position was verified using autopsies at the end of the experiment. After insertion of the catheter, the uterine horn along with the fetuses was again carefully placed in the abdominal cavity. Thus, most of the piglets from the right uterine horn passed the part of the uterus during expelling, where the catheter was placed. Catheters were tunneled subcutaneously to the exteriorization point in the right lumbar region using long stainless needles. The functionality of the catheters was checked and then flushed with approximately 20 mL of saline containing heparin (100 IU/mL, Heparin LEO, LEO Pharma A/S, Ballerup, Denmark). Finally, the catheters were filled with saline containing heparin (100 IU/mL, Heparin LEO; LEO Pharma A/S, Ballerup, Denmark), benzyl alcohol (0.1%; benzyl alcohol + 99%; Sigma-Aldrich, St. Louis, MO), and benzyl penicillin (0.2%; benzylpenicillin; Panpharma, NordMedica A/S, Copenhagen, Denmark). Detailed description of the surgical procedures and postsurgery medications was described by Krogh et al. (2016). After recovery and until weaning 28 d after farrowing, sows were individually housed in a farrowing pen (2.7 × 2.1 m) made of concrete and slatted floor equipped with an infrared lamp to establish a warm microclimate for the piglets. Sows were fed either a low- or a high-fiber experimental diet in late gestation similar to the 2 diets used in Feyera et al. (2017). Unfortunately, the impact of diets on uterine extraction of nutrients during farrowing could not be tested, because 5 out of 10 uterine vein catheters and 1 arterial catheter stopped functioning shortly before farrowing. The uterine extraction form the remaining 5 sows was therefore performed to study whether uterine extraction of nutrients was positive or negative. The sows were fed 3 equal daily meals at 8-h intervals during the experiment.

Blood sampling. Arterial and uterine vein blood samples were collected on d −28, −21, −14, −10, −7, and −3 relative to the expected date of farrowing in late gestation, and at 1, 2, 3, 4, 5, 6, 7, 8 and 24 h relative to the birth of the first-born piglet during farrowing. At each sampling time, 3 to 4 mL of the blood was initially drawn and discarded before blood sampling to ensure collection of representative samples. The blood samples from the arterial and venous catheters were collected simultaneously in heparinized 1-mL RAPIDLyte syringes (Siemens Healthcare Diagnostic Inc., Tarrytown, USA) for immediate measurements of O_2 and CO_2 using RapidPoint 500 system Gas Analyzers (Siemens Healthcare Diagnostics Ltd., UK). Moreover, 2- × 9-mL blood samples were drawn from arterial and venous catheters and transferred to heparinized vacutainer tubes (Greiner BioOne GmbH, Kremsmuenster, Austria), mixed, and stored on ice until centrifugation at 1,558 × *g* for 10 min at 4 °C. Plasma was harvested and stored at −20 °C pending analysis.

Analytical procedures. Plasma glucose, lactate, and triglycerides were determined according to standard procedures (Siemens Diagnostics Clinical Methods for ADVIA 1800) using an autoanalyzer, ADVIA 1800 Chemistry System (Siemens Medical Solutions, Tarrytown, NY 10591, USA). Nonesterified fatty acids were determined using the Wako, NEFA C ACS-ACOD assay method using an autoanalyzer, ADVIA 1800 Chemistry System (Siemens Medical Solutions, Tarrytown, NY 10591, USA). Plasma concentrations of short chain fatty acids were determined by gas chromatography as described by Brighenti (1998) with the modification that 2-ethyl butyrate (FLUKA no. 03190; Sigma-Aldrich) was used as an internal standard instead of isovalerate.

Statistical analysis. All statistical analyses were performed using SAS version 9.3 (SAS Inst. Inc., Cary, NC). For extraction of plasma metabolites and blood gases during farrowing, blood samples collected during the first 24 h after the birth of the first piglet were grouped into 2 categories. Accordingly, samples collected while the sows were farrowing were categorized as "farrowing" and samples collected after the sows completed farrowing were categorized as "postfarrowing." Uterine extractions of plasma metabolites and blood gases were calculated as the uptake or release divided by the arterial concentrations and reported as a percentage. Sow energy status during farrowing was evaluated by the TLMUOF and arterial concentration of glucose.

The impact of stage of gestation (d −28, −21, −14, −10, −7, and −3 relative to date of farrowing) and farrowing status (farrowing and postfarrowing)

on arterial concentrations and uterine extractions of plasma metabolites and blood gases were analyzed using the MIXED procedure of SAS. The stage of gestation and farrowing status were included as fixed effects, whereas sow was included as a random component in the model. Pearson correlation coefficient of arterial concentration of plasma glucose with TLMUOF and FD was analyzed using the CORR procedure of SAS. A statistical difference was declared at $P < 0.05$, whereas $P < 0.10$ was considered a tendency.

RESULTS

Study-1

LS at birth ranged from 9 to 27 with a mean of 17.5 ± 3.8 piglets. The mean live-born and stillborn piglets were 16.3 ± 3 and 1.1 ± 1.2, respectively. The percentage of stillborn piglets ranged from 2.8% to 10.0% of total born on an individual experiment basis with an overall percentage of 6.4%. The mean piglet and litter birth weight were 1.28 ± 0.22 and 21.9 ± 3.8 kg, respectively, and the birth weight of individual piglets ranged from 0.32 to 2.36 kg and litter birth weight ranged from 11.7 to 31.6 kg. The overall mean for TLMUOF was 4.6 ± 2.2 h and it ranged from 0.5 to 10.3 h. The mean FD was 5.8 ± 2.7 h, and on an individual basis, it ranged from 1.5 to 14.3 h. The mean BI was 21.6 ± 9.9 min, whereas on individual sow level it ranged from 7.2 to 60.2 min. Of the total 166 farrowings, 24% of the sows received assistance during farrowing at least once.

The correlation analysis (Table 1) indicated that both FD and BI were positively correlated with TLMUOF, mean piglet BW at birth, and FA. FD was also positively correlated with LS, whereas BI were not correlated with LS. Both FA and SR were positively correlated with TLMUOF and LS, and furthermore, the SR was also positively correlated with FA and negatively correlated with mean piglet birth weight.

Analysis of FD revealed that it was constantly low (3.8 ± 1.5 h) if farrowing was onset prior to the breakpoint (3.13 ± 0.34 h). The FD increased by 1.14 ± 0.10 h for each hour the farrowing started later than the breakpoint. Initially, different break points from the individual experiments (Exp. 1 through 7) were tested and ranged from 3.11 to 3.64 h ($P = 0.72$), and different slopes were tested and found within the range of 1.12 to 1.19 ($P = 0.99$), respectively, and consequently a model with a common breakpoint and a common slope was chosen (Figure 1; Table 2). The model also revealed that the FD was increased by 0.21 ± 0.04 h for each extra piglet within the litter, by 2.72 h for each increase in average BW at birth and farrowing lasted 0.72 ± 0.32 h longer when FA was required. Increasing the average piglet BW with 1 kg increased BI by 11.5 min ($P = 0.002$), but decreased the odds for stillbirth to 0.25 ($P = 0.005$; Table 3), whereas LS did not affect these traits statistically. BI ($P < 0.001$), odds for FA (Figure 2A; $P < 0.001$), and odds for stillbirth (Figure 2B; $P = 0.02$) were low, intermediate, and high when time since last meal was ≤3, 3 to 6, and >6 h, respectively. When farrowings were assisted, BI and odds of stillbirth increased by 3.62 min ($P = 0.02$) and 1.76-fold ($P = 0.03$), respectively.

Study-2

Maintaining the functionality of the uterine vein catheters was observed being a challenge with the progress of gestation. During the first weeks postsurgery, no problems were observed when drawing blood but at days 101, 108, and 115 of gestation, 2, 3 and 5 out of the 10 uterine vein catheters, respectively, did not allow blood samples to be drawn. In contrast, problems were only experienced with the arterial catheter in 1 sow. Autopsies at weaning revealed that the tip of several catheters in the uterine veins was kinked and consequently prevented blood samples to be drawn. Thus, focus on effect of dietary treatments in study 2 was reduced to a minimum and data

Table 1. Pearson correlation coefficient between the dependent traits and the independent traits in 166 farrowings (study-1)

Item[1]	Farrowing duration		Birth interval		Farrowing assistance		Stillbirth	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value	*r*	*P*-value
TLMUOF	0.76	< 0.001	0.63	< 0.001	0.28	< 0.001	0.28	< 0.001
Litter size	0.30	< 0.001	−0.07	0.34	0.21	< 0.007	0.44	< 0.001
BWB	0.10	0.03	0.24	0.002	−0.12	< 0.13	−0.37	< 0.001
FA	0.35	< 0.001	0.25	0.001			0.29	< 0.001

[1]TLMUOF = time from last meal until the onset of farrowing in hour; BWB = mean piglet BW at birth in kg; FA = farrowing assistance.

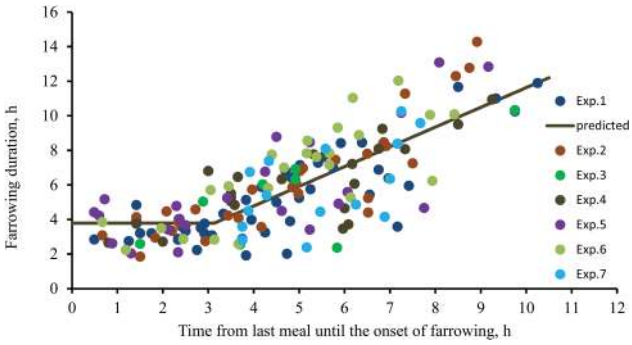

Figure 1. The relation between time from last meal until the onset of farrowing and farrowing duration. In Exp. 1, sows received 2 daily meals and in Exp. 2 through 7, sows received 3 daily meals. The solid circles with different colors indicate individual sows studied in 7 previous experiments, whereas the solid line indicate predicted values (data from study-1).

Table 2. Effect of time from last meal until the onset of farrowing (TLMUOF) on farrowing duration adjusted for litter size, mean piglet BW at birth (BWB), and farrowing assistance

Items	Estimate	SEM	*P*-value	LCL[1]	UCL[1]
Intercept[2]	−3.60	1.54	0.06	−7.34	0.16
Break point	3.13	0.34	< 0.001	2.30	3.97
TLMUOF[3]	1.14	0.10	< 0.001	0.90	1.38
Litter size	0.21	0.04	0.003	0.10	0.32
BWB	2.72	0.74	0.01	0.91	4.54
Farrowing assistance[4]	0.72	0.32	0.06	−0.05	1.50

[1]LCL = lower confidence limit and UCL= upper confidence limit.

[2]The mean farrowing duration before the break point (shown in Figure 1) is 3.8 h and can be derived as follows: −3.60 + 0.21 × average litter size + 2.72 × average BWB + 0.24 × 0.72 (see footnote 4).

[3]The estimate of 1.14 indicates the slope after the breakpoint (shown in Figure 1).

[4]Twenty-four percent of the farrowings received farrowing assistance, and this estimate shows that farrowing duration on average was prolonged 0.72 h when farrowing assistance was required.

from the 2 dietary treatments were pooled to investigate the correlations between arterial concentration of plasma glucose during farrowing and TLMUOF and FK, and the impact of stages on uterine extractions of plasma metabolites and blood gases.

Correlation of arterial concentration of plasma glucose with TLMUOF and FK. The arterial concentration of plasma glucose during farrowing was remarkably constant during the first 8 h after the birth of the first piglet, whereas the level of plasma glucose was clearly dependent on whether farrowing was onset ≤3, 3 to 6, or >6 h after the last meal was ingested (Figure 3). The arterial concentration of plasma glucose at 1 h after the birth of the first piglet was negatively correlated with TLMUOF ($r = -0.90$; $P < 0.001$; Figure 4A) and the arterial glucose concentration was numerically higher (+0.37 mM; $P = 0.27$; Figure 4B) in sows fed high-fiber diet. Moreover, arterial glucose concentration at 1 h after birth of the first piglet was negatively correlated with FD ($r = -0.96$; $P < 0.001$; Figure 4C) and BI ($r = -0.82$; $P < 0.01$; data not shown).

Arterial concentrations and uterine extractions of plasma metabolites during late gestation and farrowing. The arterial concentration of acetate was elevated during the last week of gestation ($P < 0.02$; Table 4) because half of the sows were fed a high-fiber diet. Other measured plasma metabolites and blood gases were not affected by the stage of gestation. Farrowing sows had greater arterial concentrations of O_2 ($P < 0.01$), lactate ($P < 0.001$), triglycerides ($P < 0.001$), and NEFA ($P < 0.001$) than postfarrowing sows. In contrast, arterial concentrations of CO_2 ($P < 0.01$) and glucose ($P < 0.001$) were lower in farrowing sows than in postfarrowing sows.

The uterus extracted glucose at all stages and uterine glucose extraction increased with the progress of gestation ($P < 0.001$). However, the stage of gestation had no impact on the extractions of other plasma metabolites or blood gases. Uterine extraction of O_2 was greater than the extraction of all other measured metabolites at all stages except at d −3, where extraction of butyrate was slightly higher than that of O_2. Butyrate and NEFA were extracted by the uterus in late gestation, whereas these 2 metabolites were released during farrowing. In contrast, the uterus extracted triglycerides during farrowing, whereas these extraction rates did not differ from zero before or after farrowing.

DISCUSSION

Impact of Sow and Piglet-Related Traits on FK

Farrowing is a complex process driven by several interacting factors that influence the FK (van Rens and van der Lende, 2004; Oliviero, 2010). Prolonged farrowing and longer BI are among the key factors associated with increased SR (Zaleski and Hacker, 1993; Oliviero et al., 2010). Therefore, insight into the underlying mechanisms of the FK is of prime importance in an attempt to reduce SR. Previous studies, which attempted to investigate factors affecting the FK, focused mainly on those traits related to sow and piglet characteristics such as parity, gestation length, and piglet birth weight (Fahmy and Friend, 1981; van Rens and van der Lende, 2004; van Dijk et al., 2005). The findings that FD increased with LS and heavier piglets at birth are in agreement with previous studies (Holm et al.,

Table 3. Effect of litter size, mean piglet BW at birth (BWB), time from last meal until the onset of farrowing (TMLUOF), and absence/presence of farrowing assistance (FA) on birth intervals, the need for farrowing assistance, and the incidence of stillbirth

	Birth intervals			Odds ratio of farrowing assistance[1]				Odds ratio of stillbirth			
Item	Estimate	SEM	*P*-value	Estimate	LCL	UCL	*P*-value	Estimate	LCL	UCL	*P*-value
Intercept	4.06	7.42	0.59								
Litter size	−0.29	0.22	0.18	1.00	0.92	1.09	0.94	1.01	0.96	1.07	0.63
BWB	11.5	3.61	0.002	0.60	0.13	2.73	0.51	0.25	0.10	0.65	0.005
TMLUOF[2]											
≤3 h (Ref)	0.00			1.00				1.00			
3 to 6 h	6.37	1.53	< 0.001	5.27	1.56	17.8	0.008	1.11	0.69	1.77	0.67
> 6 h	15.7	1.75	< 0.001	9.17	2.71	31.1	< 0.001	1.76	1.09	2.86	0.02
FA											
No (Ref)	0.00							1.00			
Yes	3.62	1.49	0.02					1.46	1.03	2.08	0.03

[1]LCL = lower confidence limit; UCL = upper confidence limit.

[2]TLMUOF was categorized into 3 classes based on the observed break point for the farrowing length; Ref. is the reference value for comparison with the rest of the classes.

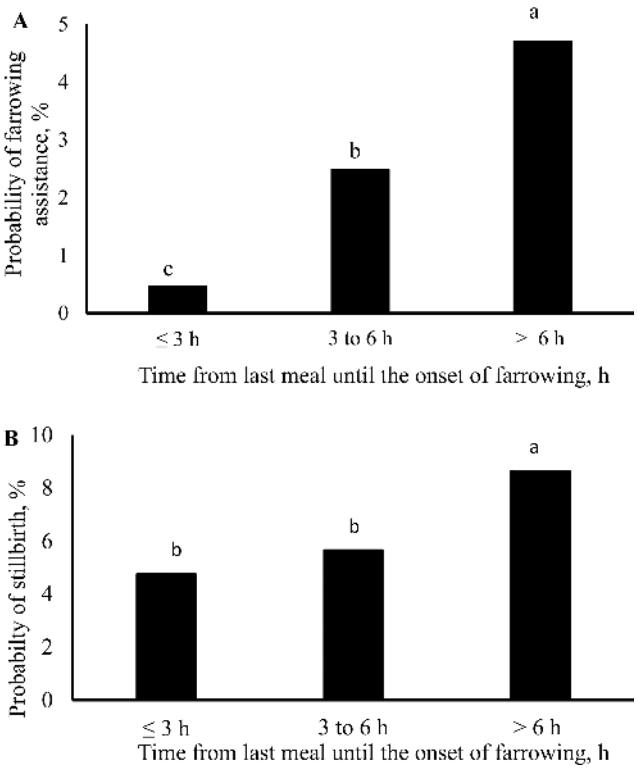

Figure 2. The impact of time from last meal until the onset of farrowing on (A) the probability of farrowing assistance and (B) the probability of stillbirth rate. Time from last meal until the onset of farrowing was grouped into 3 categories as ≤3, 3 to 6, and >6 h, and statistical analysis was performed using the GLMMIX procedure. [a–c]Means with different litters differ ($P < 0.05$).

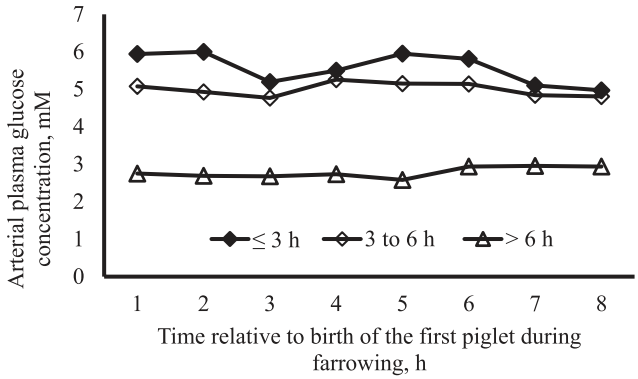

Figure 3. Arterial concentration of glucose in samples collected at hourly interval for 8 h after birth of the first piglet. Sows were divided into 3 categories representing sows with time from last meal until the onset of farrowing ≤ 3, 3 to 6, and >6 h.

2004; van Dijk et al., 2005; Canario et al., 2006). Moreover, the present study indicated that heavier piglets at birth were associated with increased BI as reported by van Dijk et al. (2005). Also, our study indicated that heavier piglets had decreased odds of being stillborn, and this is in line with that reported by Pedersen et al. (2011). The linear relationship between piglets' birth weight and BI observed in the present study could partly be explained by the premises that heavier piglets are more difficult to expel through the birth canal during farrowing compared with lighter piglets. Unlike the impact on FD, an increase in LS was not observed to affect BI statistically, which is in contrast with previous findings (Canario et al., 2006; Vallet et al., 2010). However, Vallet et al. (2011) indicated that the effect of LS on BI is not explained by LS-induced reduction in average birth weight of the litter.

Impact of Energy Status During Farrowing on the FK, FA, and SR

The present study revealed that sows which initiated and completed farrowings within a reasonable time (3.13 h) after receiving their last meal

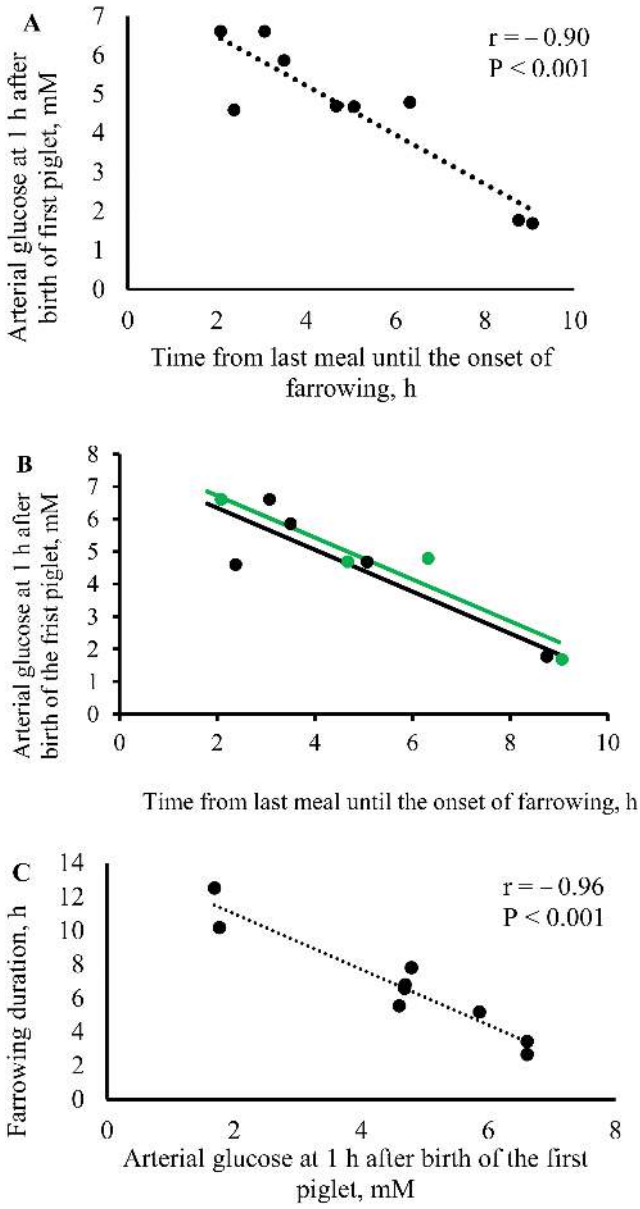

Figure 4. (A) The correlation between time from last meal until the onset of farrowing and arterial glucose concentration at 1 h after birth of the first piglet, (B) same data as in (A) but data are here presented according to dietary treatment of the sow (green and black represent high fiber and control diets, respectively, and lines represent the fitted decrease in glucose depending on dietary treatment, and (C) the correlation between arterial glucose concentration at 1 h after birth of the first piglet and the farrowing duration.

before the onset of farrowing had shorter FD and minimal need for FA, and eventually had a minimal incidence of the SR of 4.75%. In contrast, sows that started to farrow quite late (>6 h) after the last meal had substantially extended FDs with more frequent FA, and the SR increased by 1.76-fold. The negative association between the prolonged farrowing and SR is well established (Holm et al., 2004; Canario et al., 2006; Oliviero et al., 2010; Vallet et al., 2010), but the underlying mechanism has not been elucidated up to now. Moreover, giving birth to a piglet is highly energy demanding (Vallet et al., 2013). The present study indicated that sows initiating their farrowings within the first 3 h after eating their last meal were not exposed to low plasma glucose at the onset of farrowing, and it resulted in short FD, no need for FA, and a low SR. We speculate whether sows are depleting their glycogen depots during the preceding period with intense physical activity, i.e., when they perform nest-building activity. Nest building is intense during the last 6 to 12 h before the onset of farrowing (Vestergaard and Hansen, 1984; Jensen, 1993) and costs energy, although it is not known how much (Feyera and Theil, 2017), and the present study suggests that nest building may have fatal consequences for piglets when being born. A previous study suggested that stress during nest building may have negative consequences for the farrowing progress due to lowered plasma levels of oxytocin (Oliviero et al., 2008) and late introduction to crates (day 114) can considerably increase SR (Pedersen and Jensen, 2008). Within the first 4 to 6 h after meal consumption, glucose is known to be net absorbed from the GI-tract in sows and pigs (Serena et al., 2009; Theil et al., 2011), but glucose is also rapidly taken up to various tissues due to insulin secretion, and therefore, part of the net absorbed glucose is not available for the strenuous uterus. Indeed, the broken-line model in the present study strongly suggests that sows should initiate the farrowing before plasma glucose becomes a limiting factor for the farrowing process. Therefore, the time from last meal until the onset of farrowing is vital for farrowing sows and the importance is emphasized by its clear impact on the arterial concentration of glucose during farrowing, and consequently on the FK, the incidence of stillbirth, and the need for FA.

Several nutritional studies have been reported in an attempt to improve the farrowing process and thereby reducing the SR. But hitherto, nutritional interventions have not reduced the SR effectively. Creatine supplementation to sows to maintain ATP supply during strenuous activities in the last 5 d of gestation had no effect on SR (Vallet et al., 2013). Supplementation of essential fatty acids and zinc during the last 35 d of gestation had no impact on SR, whereas zinc supplementation decreased the SR only during prolonged farrowings (Vallet et al., 2014). Likewise, supplementing sows with *n*-3 long chain polyunsaturated fatty acids from day 60 (Smit et al., 2013) or 107 (Smits et al., 2011) of gestation until farrowing did not affect the SR. The present study implied that dietary supplementation of energy might improve the farrowing process and

Table 4. Arterial concentrations and uterine extractions of blood gases and energy metabolites during late gestation and farrowing (study-2)

	Stage of gestation[1]								Farrowing status[2]			
Item	d 28	d 21	d 14	d 10	d 7	d 3	SEM	*P*-value	Farrowing	Postfarrowing	SEM	*P*-value
Arterial concentration												
O_2, mM	6.6	6.5	6.5	6.4	6.3	6.3	0.2	0.60	6.2[a]	5.9[b]	0.1	< 0.01
CO_2, mM	30.6	31.0	29.7	30.3	30.4	31.2	0.6	0.42	30.2[b]	31.2[a]	0.2	< 0.01
Glucose, mM	5.2	5.4	5.1	5.1	5.5	5.0	0.2	0.40	3.9[b]	4.8[a]	0.2	< 0.001
Lactate, mM	0.8	0.9	0.9	0.9	0.9	0.8	0.1	0.73	1.5[a]	1.1[b]	0.1	< 0.001
Triglycerides, µM	436	443	455	500	529	469	62	0.85	283[a]	221[b]	0.01	< 0.001
NEFA, µM	54	81	105	93	106	100	22	0.27	829[a]	543[b]	52	< 0.001
Acetate, µM	239[b]	258[b]	261[b]	278[ab]	318[a]	329[a]	22	0.02	176	182	6.3	0.42
Propionate, µM	3.1	3.3	3.5	3.6	3.4	3.6	0.2	0.48	4.3	4.6	0.3	0.45
Butyrate, µM	4.3	4.8	5.1	5.4	5.1	4.7	0.5	0.59	2.4[b]	3.6[a]	0.3	< 0.01
Uterine extraction, %												
O_2	12.6	16.9	16.0	16.2	17.9	17.8	1.9	0.37	10.9	10.7	4.2	0.98
CO_2	−4.5	−3.4	−6.3	−3.4	−6.3	−3.9	1.8	0.30	−4.7	−2.6	1.7	0.07
Glucose	3.3[c]	4.0[b]	4.5[b]	5.6[ab]	5.4[ab]	6.1[a]	0.4	<0.001	3.0	2.2	0.7	0.29
Lactate	0.6	0.5	0.6	0.7	0.8	0.5	0.8	0.99	−3.1[a]	-8.5[b]	2.3	< 0.01
Triglycerides	−4.6	−1.5	−5.0	−2.2	−1.9	−2.8	4.1	0.97	7.2	1.2	5.9	0.11
NEFA	2.0	3.7	3.8	8.3	11.2	11.1	4.9	0.46	−0.2	−5.3	5.9	0.41
Acetate	−6.4	−3.9	−2.8	0.4	8.5	5.1	4.6	0.08	−14.1	−13.3	8.1	0.25
Propionate	−27.1	−21.2	−17.4	−16.2	−2.8	−9.3	9.3	0.34	−34.3	−40.1	5.3	0.22
Butyrate	8.4	14.1	10.3	9.0	12.2	18.6	3.4	0.17	−14.1[b]	15.9[a]	9.0	< 0.05

[a,b]Means within a row with different superscripts differ ($P < 0.05$).

[1]Samples were collected relative to the expected date of farrowing.

[2]Blood samples collected during farrowing were grouped into 2 categories: farrowing (samples collected while the sows were farrowing) and postfarrowing (samples collected after the sows completed farrowings within 24 h after birth of first piglet).

consequently reduce the SR, and sows should probably be fed strategically shortly before farrowing. In line with this, orally administered readily available energy supplement immediately preceding farrowing was shown to reduce the number of stillborn piglets per litter by 0.44 compared with a control group without energy supplementation (van Kempen, 2007).

Sows seem to be depleted of energy shortly before the onset of farrowing, and it may be due to high energetic demands (i.e., glucose uptake) due to colostrum production, fetal growth, uterine contractions (prior to parturition), and physical activity related to nest-building behavior. Probably mammary gland (i.e., colostrum production) and fetal growth are responsible for the drop in arterial glucose because these compartments have glucose transporters (Glut1 and Glut3) with low Km values, and because these transporters are active irrespective of plasma insulin levels (Theil et al., 2012). Low energy status during farrowing could be speculated to slow down the uterine contractions, which are crucial for successful farrowing. Therefore, unlike in most mammalian species which give birth to either 1 or 2 offspring, maintaining an adequate energy status during farrowing is highly important for litter-bearing animals like sows to give birth to live-born offspring.

Two or 3 daily meals, as applied in the present study, were not sufficient to avoid lack of energy during farrowing. Therefore, this study raises the question whether the sows should be fed 3 or more daily meals shortly before farrowing. The broken-line model with the breakpoint being 3.13 h indicated that sows might benefit from receiving up to as much as 8 daily meals shortly before farrowing, although this will likely never be applied in practice. At the same time, it is important to emphasise that sows do not normally eat during farrowing; thus, sows are prevented from ingesting additional energy for an extended period of time. Indeed, if sows start to farrow 8 h after the last meal, FD will be expected to be 9.3 h as predicted by our broken-line model, and these sows have not eaten for 17.3 h when farrowing is completed. It may be logical to suggest that energy depletion before and during farrowing may partly explain why many newborn piglets are being crushed by their mother shortly after farrowing, as reported by, e.g., Pedersen et al. (2011). This study indicates that it is crucial to ensure a

high-energy status of the sows during farrowing. Including fiber in the diets for late gestating sows may likely help us to improve sows' energy status during farrowing because energy uptake from the hind-gut is elevated even 24 h after last meal is consumed (Serena et al., 2009). In support of that, sows fed fiber in the present study had numerical higher plasma glucose than sows fed the control diet, and in line with this, we recently reported a considerably reduced SR (Feyera et al., 2017) in sows that were fed similar dietary treatments as in the present study. Moreover, short-chain fatty acids released from fiber fermentation have been reported to stabilize interprandial glucose level for several hours after feeding in sows (de Leeuw et al., 2004). In line with this, the result of the present study, in combination with earlier studies, emphasized the importance of feeding at least 3 daily meals before farrowing to reduce the risk of the increased SR in modern hyperprolific sows.

Uterine Extractions of Plasma Metabolites and Blood Gases during Late Gestation and Farrowing

The uterine extraction of glucose observed in the present study at days 94 (4.0%) and 108 (5.4%) of gestation is consistent with 4.1% and 5.5% reported by Pere and Etienne (2018) during the same stage of gestation. Moreover, Père (1995) reported glucose extraction of 5% at day 103 of gestation in sows, which is within the ranges of values determined in the present study. The increased extraction of glucose observed with the progress of gestation in the present study suggests that glucose is the key energy metabolite for oxidative purpose in the gravid uterus. In line with this, Pere and Etienne (2018) stated that glucose is the main substrate for fetal oxidative metabolism. Moreover, Reynolds et al. (1985) reported that about 79% of gravid uterine and 38% of fetal energy expenditure could be met by net absorbed glucose, assuming that glucose carbon is not used for other purposes. Lindsay (1975) stated that gravid uterus relies largely on carbohydrates for oxidative purpose compared with other substrates, which was supported by the present findings. Nevertheless, catabolism of other plasma metabolites such as fatty acids and short-chain fatty acids was reported to contribute to fetal energy expenditure (Reynolds et al., 1985). In line with this, extractions of NEFA, acetate, and butyrate were observed during late gestation in the present study. This suggests that the uterus probably meets part of the energy demand by oxidizing ketogenic substrates (acetate and butyrate) and suggests that dietary fiber somehow is beneficial for late pregnant sows, although acetate and butyrate appeared not to be extracted by the uterus during farrowing.

The uterus apparently extracted triglycerides and glucose as the only energy substrates during farrowing. Extractions of glucose and triglycerides were 1.4- and 6.0-fold greater, respectively, during farrowing than postfarrowing, indicating that energy derived from triglycerides contributed considerably during intense labor. The uterus released lactate during farrowing, which may suggest that O_2 supply was inadequate to cover the huge demand for aerobic metabolism. Surprisingly, the extractions of O_2 during farrowing was lower than in late gestation. However, this result does not explicitly explain whether the differences emerged from the actual difference in workload or due to an increased uterine blood flow during farrowing which then depressed the extraction rate of the nutrients and O_2. Ferrell and Ford (1980) and Hard and Anderson (1982) elucidated that blood flow is the primary determinant of nutrient availability rather than the concentration differences across the organ. Therefore, in the absence of blood flow like in the present study, conclusive remark on metabolism or nutrient utilization of the gravid uterus could not be drawn.

CONCLUSIONS AND IMPLICATIONS

Energy status, evaluated as the arterial concentration of glucose and the time from last meal until the onset of farrowing, showed the clear and remarkable impact on the FK and odds of FA and stillbirth. Adequate energy status at the onset of farrowing allows the sows to complete the farrowing within <4 h with minimal need for FA and with the low SR. However, FD increased if the farrowing was not onset within 3.13 h after feeding and consequently the FD could be prolonged up to 14 h with increased odds of FA and stillbirth. Arterial concentration of glucose was remarkably constant during farrowing, but the level at 1 h after the onset of farrowing depends on the time since last meal. The present study suggests that allocation of at least 3 daily meals may improve energy status of the sow during farrowing and ameliorate the farrowing process and thereby reduce the number of stillborn piglets.

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