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Heat stress of gilts around farrowing causes oxygen insufficiency in the umbilical cord and reduces piglet survival

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ABSTRACT

Late gestating sows are susceptible to high ambient temperatures, possibly causing farrowing complications and reducing piglet survival. This experiment aimed to quantify in the days leading up to farrowing the impact of sow heat stress (**HS**) on farrowing physiology and survival of the piglets. Pregnant primiparous sows (gilts) were allocated to either thermoneutral control (**CON**, n = 8; constant 20 °C) or cyclical HS conditions (n = 8; 0900 h to 1700 h, 30 °C; 1700 h to 0900 h, 28 °C) from d 110 of gestation until farrowing completion. Gilt respiration rate, skin temperature and rectal temperature were recorded daily, and farrowing duration was quantified by video analyses. Blood samples were collected from the piglet umbilical vein at birth. At 48 h of age, piglet growth was quantified by morphometric analyses. The thermal exposure model induced HS and respiratory alkalosis in the gilts, as indicated by increased respiration rate, rectal temperature, skin temperature (all $P < 0.001$), plasma cortisol ($P = 0.01$) and blood pH ($P < 0.001$). Heat-stressed gilts took longer to start expelling placentae ($P = 0.003$), although the active farrowing duration was not significantly different between treatments. Stillbirth rates were higher in the HS group ($P < 0.001$), with surviving piglets at birth having lower umbilical vein partial pressure of oxygen ($P = 0.04$), oxygen saturation rate ($P = 0.03$) and tending to have increased lactate concentrations ($P = 0.07$). At birth, piglet skin meconium staining scores were greater in the HS group ($P = 0.022$). At 48 h of age, piglets from the HS group had reduced small intestinal length ($P = 0.02$), reduced jejunal crypt depth ($P = 0.02$) and lighter absolute brain weight ($P = 0.001$). In contrast, piglet BW, growth rate, relative organ weight and small intestinal mucosal barrier function did not change between treatments. Collectively, these findings demonstrated gilt HS during late gestation caused farrowing complications and reduced the umbilical oxygen supply to the piglets at parturition, leading to increased risks of piglet stillbirth with implications on impaired neonatal survivability and development.

Implications

This experiment was conducted in the context of understanding and improving sow reproductive performance under thermal stress conditions. This experiment was the first to demonstrate that sow heat stress during late gestation and farrowing reduces umbilical oxygen supply to the newborn piglets during parturition, contributing to increased risks of stillbirth and vulnerable liveborn piglets. These data highlight the need for mitigation strategies in the farrowing shed during the hot summer months to improve sow and piglet welfare, newborn survival and maintain the production efficiency.

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Introduction

Piglet preweaning mortality, especially around parturition, is considered a major factor compromising the welfare and pig production efficiency (Muns et al., 2016a). In modern domestic sows, stillborn rates can range between 5% and 15%, with hyper-prolific sows having an even higher stillborn rate (Langendijk and Plush, 2019). Piglet stillbirth mostly occurs during parturition, highlighting the risk of farrowing complications on piglet survival (Vanderhaeghe et al., 2013). Piglet asphyxia *in utero* or during delivery, due to oxygen insufficiency, is among the leading causes of the stillbirth (Herpin et al., 1996). The underlying mechanisms responsible for stillbirth are postulated to be associated with repeated uterine contractions, compressing the placenta and even rupturing the umbilical cord, thereby disrupting the blood and oxygen delivered from the placenta to the foetus (Herpin et al., 1996). Postnatally, there is evidence that asphyxiated piglets are less viable at the neonatal stage and have impaired subsequent growth performance (Herpin et al., 1999; Langendijk et al., 2018).

Late gestating sows have a relatively cooler thermal comfort zone and are sensitive to elevated ambient temperatures (McConn et al., 2021; Robbins et al., 2021). The consequences of sow heat stress (**HS**) during gestation are numerous, including reduced farrowing rate (Plush et al., 2019; Liu et al., 2022), placental insufficiency (Zhao et al., 2020) and lower piglet birthweight (Liu et al., 2020), with long-term implications on the postnatal productivity (Johnson et al., 2020). When experiencing HS, pigs will reduce feed intake as an adaptive strategy to reduce metabolic heat production from digestive processes (Renaudeau et al., 2013). As a consequence, the low energy status of the sow, especially during the onset of farrowing, might affect farrowing kinetics and increase the incidence of stillbirth (Feyera et al., 2018). Climate-controlled studies have demonstrated that moderate heat exposure (25 °C) of sows around farrowing increased the duration of parturition (Muns et al., 2016b). Even under a temperate climate region, higher piglet stillborn rates were observed in summer than in other seasons (Wegner et al., 2014; Rangstrup-Christensen et al., 2017), especially due to elevated temperatures in the days preceding farrowing (Wegner et al., 2016). While there is evidence that summer heatwaves result in higher piglet mortality, the physiological mechanisms by which sow acute HS prepartum causes piglet mortality and reduces neonatal piglet viability remain poorly understood, making it difficult to develop evidence-based husbandry decisions. Therefore, the aims of this experiment were to identify 1) the impact of maternal heat exposure during the last week of gestation (from d 110 of gestation until farrowing) on sow stress responses and farrowing physiology, 2) whether the cumulative impacts on sows would reduce the oxygen supply to the piglets and increased the risk of stillbirth, and 3) whether maternal HS during late gestation and farrowing would cause an immediate impact on piglet neonatal survival and development over the first 48 h of life.

Material and methods

Animals and experimental design

All animal procedures were approved by the Animal Ethics Committee of the University of Melbourne (Ethics ID: 21074). The experimental protocols followed the Australian Code for the Care and Use of Animals for Scientific Purposes (8th edition; National Health and Medical Research Council, 2013).

Sixteen primiparous sows (gilts; *Large White* × *Landrace*) were selected from a commercial farm (SunPork Farms, SA, Australia) for artificial insemination (d 0) and group-housed in gestation sheds. The experiments were conducted across two replicates (n = 8 gilts per replicate). The gilts were confirmed pregnant by ultrasound scans on d 28 of gestation. Gilts were fed a wheat-based gestation diet (13.2 MJ DE/kg) at an average of 2.3 kg/d as per the standard farm practice. The environmental temperatures ranged between 6.6 °C and 18.3 °C during the gestating stage (d 0 to d 75 of pregnancy) at the farm of origin (Roseworthy, SA, Australia). Around d 75 of gestation, gilts were confirmed for pregnancy once more and had their BW and backfat thickness measured, followed by transportation to the climate-controlled facility at the University of Melbourne (Parkville, VIC, Australia). Upon arrival at the facility, gilts were randomly allocated into either treatment (n = 8 gilts) or control (n = 8 gilts) rooms and individually housed in plastic-slatted flooring pens (2.2 m × 1.5 m) for acclimation until d 110 of gestation. For the treatment group, gilts were housed in neighbouring rooms, with two gilts per room, whereas the control gilts were housed within one room. The temperature for the acclimation period was constant at 20 °C, and the relative humidity ranged between 40% and 50% for all rooms. The housing light cycle was adjusted to a 15 h light period (0600 h to 2100 h) and a 9 h dark period (2100 h to 0600 h) over the acclimation and experimental periods for all rooms. Gilts from the control and treatment rooms had similar BWs (189 ± 14.2 vs 187 ± 10.9 kg, mean ± SD; $P = 0.67$) and backfat thickness (19.7 ± 2.24 vs 19.3 ± 1.52 mm, mean ± SD; $P = 0.72$) at the beginning of the acclimation period. All gilts were fed twice daily with the same gestation diet as per the standard farm practice at an average of 2.3 kg/d and had *ad libitum* access to water over the acclimation period. On d 109 of gestation, farrowing crate divisions (2.2 m × 0.6 m) were installed into the individual pens. Additionally, gilts were auricular (ear) vein catheterised on the same day. A total of 13 gilts (n = 6 gilts from the control group; n = 7 gilts from the heat treatment group) had functional catheter insertions for subsequent blood sampling.

From d 110 of gestation, gilts in the control room remained at the thermoneutral conditions (CON; n = 8 gilts; constant 20 °C; 40% to 50% relative humidity) throughout the experiment, whereas gilts in the treatment rooms were exposed to cyclic heat stress conditions (HS; n = 8 gilts; 30 °C between 0900 h and 1700 h; 28 °C between 1700 h and 0900 h; 40% to 50% relative humidity) until farrowing completion. Gilts were fed with a commercial transition diet (12.9 MJ DE/kg) twice daily at 4.0 kg/d from d 110 of gestation until the day of farrowing with *ad libitum* access to water. Once the last gilt in each heat treatment room had finished farrowing (no new piglets were born naturally), with less than 24 h between farrowing of two gilts within the same room, the room temperature was downregulated and maintained at 20 °C during the postpartum period. Heating lamps were provided to all litters. Gilts were fed this same transition diet *ad libitum* postpartum.

Gilt measurements

The physiological signs of HS, including respiration rate, rectal temperature, and skin temperature, were assessed for each gilt twice daily (0900 h and 1500 h) from d 110 of gestation until the day of farrowing. The respiration rate was assessed by counting the flank movement for 20 s using a digital timer and recorded as breaths per min. The rectal temperature was measured using a digital thermometer (Surgipack; Vega Technologies Inc., Dongguan, China). Gilt skin temperature was assessed by a non-invasive laser thermometer (Digitech Inc., Zurich, Swiss). Gilt feed intake was assessed daily and was calculated as average daily feed intake. The measurement day was expressed as day relative to farrowing day.

From d 110 of gestation, a blood sample was collected once daily (around 1600 h) using a 5 ml syringe via the auricular vein

catheter until the day of farrowing. Approximately 1 ml of the blood sample was immediately loaded into a blood gas analyzer (Epoc; Alere, Waltham, MA, USA) to quantify oximetry and biochemistry in the blood. The remaining volume of the blood samples were immediately loaded into a sodium heparin vacutainer (BD Vacutainer, Macquarie Park NSW, Australia) and then centrifuged at 2 000*g* for 15 min at 4 °C. The plasma was then collected and stored at −20 °C for analysis. The patency of ear vein catheters was maintained by daily flushing with heparinised (50 000 IU/l) saline 0.9% (v/v) after each sample collection.

Farrowing physiology

Gilts farrowed naturally without induction and were monitored 24 h/d by investigators. A digital camera (GoPro; CA, USA) was placed behind and 30 cm above each farrowing crate to record the active farrowing process of each gilt. Farrowing duration (time between the natural birth of first and last piglet), birth interval (time between the birth of two consecutive piglets) and placental expulsion interval (time between the birth of first piglet and expulsion of first placenta part) were recorded and analysed. A 5 ml colostrum sample was collected from the first functional anterior teat of each gilt in the middle of the parturition process and immediately stored at −20 °C. Gilts with 1) a birth interval greater than 90 min and having received manual farrowing assistance and oxytocin administrations, or 2) a gestation length greater than d 119 were excluded from the study. Consequently, two gilts (n = 1 gilt from the CON group; n = 1 gilt from the HS group) were excluded based on these exclusion criteria. Piglets and placentae that were retained within the birth canal postpartum were excluded from the analysis.

Piglet measurements at birth

As soon as a piglet was born, if an intact umbilical cord was present, the umbilical cord was immediately double ligated with haemostatic forceps. A 15 cm long section of umbilical cord was obtained, and a 1 ml blood sample was collected from the umbilical vein (carries oxygenated blood from the placenta to the piglet) via a 23G needle (TERUMO) and a heparinised syringe and immediately load into the blood gas analyzer (Epoc; Alere, Waltham, MA, USA). In the interim, piglet variables were assessed and recorded at birth for the following: stillbirth or liveborn, birthweight, sex, rectal temperature and whether the umbilical cord was ruptured. Piglet meconium staining scores at birth were assessed using the criteria described previously (Mota-Rojas et al., 2002). Piglet birth order (first piglet to last piglet in the litter) was divided into thirds based on the total born of each litter and classified as 'early' (first 1/3), 'middle' (middle 1/3) and 'late' (last 1/3).

Piglet euthanasia and gross anatomical morphology measurements

Neonatal piglets were not cross-fostered and left to suckle their birth dams. Individual piglet BW was measured at 24 h and 48 h of age. At 48 h of age, a subset of piglets (CON, n = 39 piglets; HS, n = 34 piglets, equal sex) selected based on BWs closest to the litter average were sedated with intramuscular injections of a mixture of Xylazil-20 (20 mg/ml; 1 mg/kg live weight; Troy Laboratories Pty LTD, NSW, Australia) and Ketamine (100 mg/ml; 10 mg/kg live weight; Troy Laboratories Pty ltd, NSW, Australia) using a 21 G needle (TERUMO). Blood samples were collected from the external jugular vein using a 3 ml syringe and 21 G needle (TERUMO) and loaded into a sodium heparin vacutainer (BD Vacutainer, Macquarie Park NSW, Australia) followed by euthanasia via intracardiac barbiturate overdose (325 mg/ml; Sodium pentobarbitone; 162.5 mg/kg liveweight; Lethabarb; Virbac, NSW, Australia). The blood samples were centrifugated at 2 000*g* for 15 min at 4 °C to obtain plasma samples, which were then stored at −20 °C. Piglets (CON, n = 39 piglets; HS, n = 34 piglets) were dissected for morphometric analysis of the small intestine, liver, heart, spleen, brain, *vastus intermedius* (quadriceps) muscle and femur. A 10 cm section of proximal jejunum and distal ileum was removed and rinsed in a PBS solution (pH = 7.4) for mucosal barrier function measurements. A jejunum biopsy sample (5 cm long) was collected and fixed with 4% paraformaldehyde in 0.1 M PBS (pH = 7.4) for 24 h, then transferred to PBS/ 0.1% sodium azide and stored at 4 °C until processing for histological analysis. All gilts and the remaining piglets were euthanised subsequently.

Piglet small intestine mucosal barrier function and histology assessment

As soon as the small intestine tissues were collected, the mucosal barrier function was assessed via transepithelial electrical resistance (**TER**) using methods previously described (Cottrell et al., 2020). Briefly, the proximal jejunum and distal ileum segments were opened along the mesenteric border, and the muscular layer from the serosal side was removed. The remaining tissue was pinned on a round aperture slider (0.3 cm^2), which was then mounted into a Ussing chamber system (EasyMount Diffusion Chambers, Physiologic Instruments, San Diego, CA, USA). Following the tissue equilibration for 20 min in the Krebs mannitol-glucose solutions, the tissues were clamped to the voltage of 0 V and administrated five pulses of 2 mV for a duration of 5 min. Changes in voltage (**V**) and current (**I**) were recorded for each pulse over the 5 min period. The TER was calculated by Ohm's Law (R = V/I) multiplied by the surface area of the slider. Fixed jejunum biopsy samples were paraffin-embedded and cut via the cross-sectional area at the thickness of 5 μm using a rotary microtome (Leica Biosystems, Victoria, Australia). The slides were then stained with haematoxylin and eosin (**H&E**). A total of eight images (four images per section) were obtained from each sample using a digital microscope (Zeiss, Oberkochen, Germany). Only intact (full finger-shaped) and well-orientated villus was chosen for the measurements. Intestinal villus height and crypt depth were measured using ImageJ software (NIH, USA) with the sample ID blinded. The villus height to crypt depth ratio was calculated.

Biochemical analysis

Piglet plasma and colostrum immunoglobulin G (**IgG**) concentrations were analysed using a commercially available porcine IgG ELISA basic kit (Cat # 3151-1HD-6; Mabtech, Nacka Strand, Sweden), as per the manufacturer's instructions. The intra- and inter-assay CVs were 5.1% and 7.1%, respectively. Total protein concentrations for colostrum and piglet plasma were analysed using the Pierce BCA assay kit (Cat # 23227; Thermo Fisher, Waltham, MA). The intra- and inter-assay CVs were 2.6% and 2.1%, respectively. Gilt and piglet plasma cortisol concentrations were determined via radioimmunoassay methods described in a previous study (Lee et al., 2014). Each sample was assayed in duplicate, and the intra-assay CV was 3.1% and the assay sensitivity was 0.17 ng/ml.

Statistical analysis

Data were analysed in Genstat (18th ed, VSN International, Hemel Hempstead, UK). Data normality was verified using Shapiro–Wilk's test. Log transformation was performed for parameters that were not normalised, and back-transformed means were reported. Each pregnant gilt was considered an experimental unit. For the repeated measurements of gilt thermal stress, data were

analysed by linear mixed models (**REML**) with temperature treatment, day, time, and their interaction being fixed factors and gilt's ID and replicate being random factors. Sow venous blood data were analysed with temperature treatment and day as fixed factors and gilt's ID and replicate being random factors. Gilt reproductive performance data were analysed by two-way ANOVA. Piglet stillborn rate (stillbirth number / total born) and umbilical cord ruptured rate (ruptured umbilical cord number / total born) were analysed using Fisher's exact test. For piglet umbilical vein blood parameters at birth, data were analysed by REML. The statistical model included temperature treatment, sex and birth order as fixed effects with gilt's ID as a random factor. Other piglet data were analysed with temperature treatment, sex and their interaction being fixed effects and gilt's ID as a random factor. Birth order was removed as its effect was not significant. Attributable risk analysis was performed to evaluate the risk of being stillborn if piglets were born to a heat-stressed gilt and if the umbilical cord was ruptured. Pearson's correlation coefficient analysis was performed between appropriate continuous variables. A P-value ≤ 0.05 was considered significant, and a P-value ≤ 0.1 was considered a trend. The estimates were expressed as predicted means ± SEM.

Results

Thermal stress of the gilts

Heat stress increased average gilt respiration rates across the experimental period (CON = 32 ± 4.1 vs HS = 104 ± 4.1 breaths per min, $P < 0.001$; Fig. 1A). Respiration rates were higher at 1500 h than 0900 h (72 ± 3.4 vs 64 ± 3.4 breaths per min, $P < 0.001$; data not shown in the Fig.). No main effect of day on respiration rates ($P = 0.49$) was observed, but there was a significant interaction ($P = 0.032$) between temperature treatment and day for respiration rates, such that gilts under HS conditions had a lower respiration rate on the day of farrowing (77 ± 8.1 breaths per min) than other days, whereas gilts from the CON group had a consistent respiration rate over the experimental period. Gilts exposed to HS had higher rectal (CON = 38.1 ± 0.19 vs HS = 39.5 ± 0.19 °C, $P < 0.001$; Fig. 1B) and skin temperatures (CON = 34.0 ± 0.26 vs HS = 38.1 ± 0.26 °C, $P < 0.01$; Fig. 1C) than gilts from the CON group across the experimental period. Gilt rectal temperatures (39.0 ± 0.14 vs 38.6 ± 0.14 °C, $P < 0.001$) and skin temperatures (36.4 ± 0.20 vs 35.7 ± 0.19 °C, $P < 0.001$) were higher at 1500 h than 0900 h (data not shown on the Fig.). Furthermore, there was an interaction ($P = 0.006$) between temperature treatment and day for rectal temperatures as gilts under CON conditions had higher rectal temperatures when approaching the due day, whereas heat-stressed gilts showed the opposite trend (Fig. 1B). The effect of day on skin temperatures was significant ($P < 0.001$), with the highest being observed on d −1 and the lowest being observed on d −6 relative to the farrowing day. A temperature treatment by day interaction for skin temperatures was also significant ($P < 0.001$), such that gilts from the CON group had increased skin temperatures as gestation advanced, whereas heat-stressed gilts had consistent skin temperatures over the experimental period (Fig. 1C).

Gilt feed intake and venous blood parameters

Heat stress decreased gilt average daily feed intake (CON = 3.5 ± 0.24 vs HS = 1.4 ± 0.25 kg/d, $P < 0.001$) across the experimental period. The effects of HS on gilt venous blood parameters are presented in Table 1. Heat stress increased gilt plasma cortisol concentrations ($P = 0.01$). Gilts from the HS group had higher whole blood

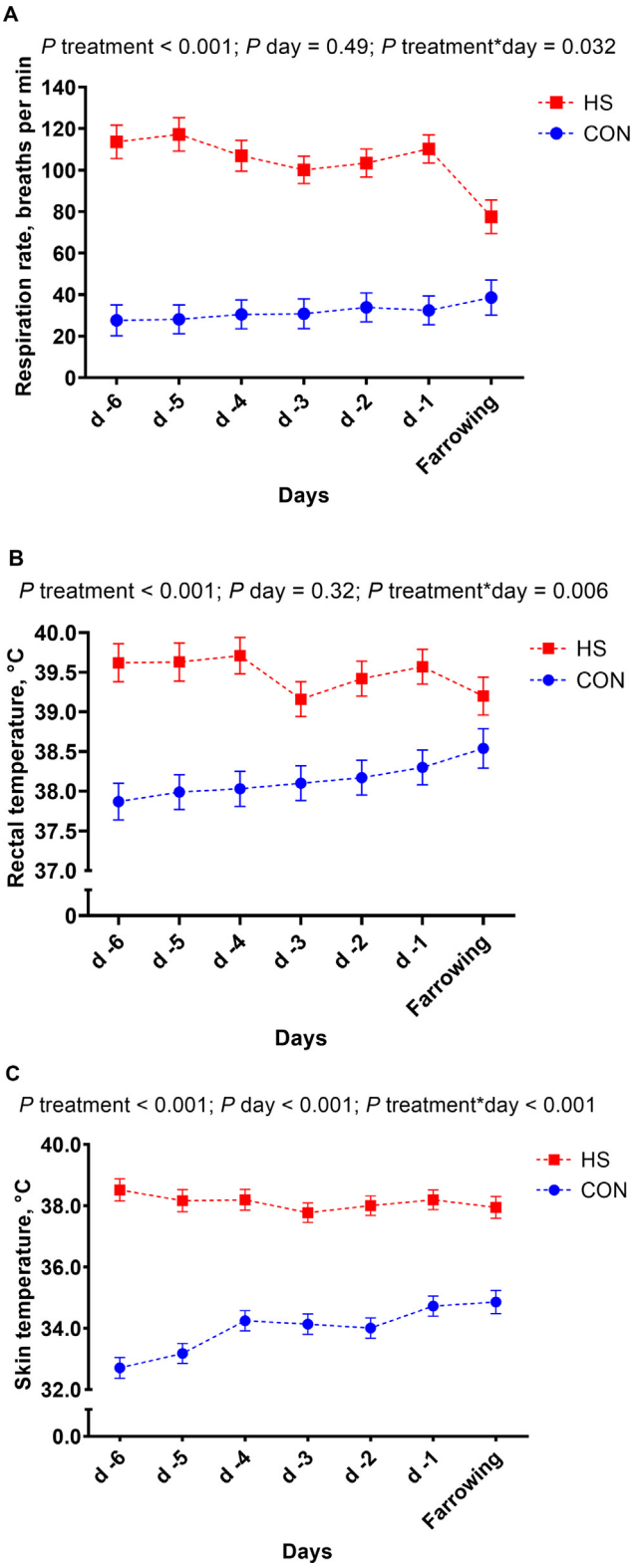

Fig. 1. Predicted means (±SEM) for respiration rate (A), rectal temperature (B) and skin temperature (C) of pregnant gilts exposed to control (CON, n = 8 gilts) or cyclical heat stress (HS, n = 8 gilts) conditions.

pH ($P < 0.001$), creatinine ($P = 0.02$), while having lower partial pressure of carbon dioxide (pCO_2, $P = 0.002$), bicarbonate ($cHCO_3$, $P = 0.02$), and calcium ($P = 0.04$). Heat stress tended to increase oxygen saturation rate ($P = 0.06$) and tended to decrease sodium ($P = 0.09$) and base excess ($P = 0.07$) in the gilt venous blood.

Table 1
Predicted means (±pooled SEM) for blood parameters of gilts exposed to control (CON) or heat stress (HS) conditions between d 110 of gestation until farrowing completion.

Variable	Treatment[1]		SEM	*P*-value
	CON	HS		
Glucose, mmol/l	5.40	5.12	0.195	0.35
Cortisol[2], ng/ml	1.32	1.60	0.062	0.01
	(20.9)	(39.8)	–	–
pH	7.47	7.53	0.008	<0.001
Partial pressure of CO_2, mmHg	43.9	32.7	1.79	0.002
Partial pressure of O_2, mmHg	35.5	37.4	1.50	0.50
Sodium, mmol/l	144	142	0.80	0.09
Potassium, mmol/l	4.26	4.07	0.075	0.11
Calcium, mmol/l	1.28	1.21	0.022	0.04
Lactate, mmol/l	1.20	1.20	0.115	0.90
Creatinine, mg/dl	2.87	3.50	0.170	0.02
Haematocrit, %	33.7	34.7	1.14	0.57
Haemoglobin, g/dl	11.4	11.8	0.39	0.50
Bicarbonate, mmol/l	31.4	27.6	1.02	0.02
Base excess, mmol/l	7.75	4.95	0.971	0.07
Oxygen saturation, %	67.8	77.4	2.91	0.06

[1] Treatment: CON = control (n = 6 gilts; constant 20 °C); HS = cyclic heat stress (n = 7 gilts, 0900 h to 1700 h, 30 °C; 1700 h to 0900 h, 28 °C).
[2] Cortisol was analysed from the plasma while other parameters were analysed from the whole blood. Log transformation was performed before analysis, and figures in parentheses are back-transformed means.

Gilt farrowing performance

The gestation length was similar between the treatment groups ($P = 0.70$; Table 2). A total of 88 piglets were born to gilts in the CON group, of which two male piglets were stillborn. A total of 93 piglets were born to gilts in the HS group, of which 31 piglets (n = 13 females; n = 18 males) were stillborn. Thus, the overall stillborn rate was significantly higher in the HS group than the CON group (CON = 2.3% vs HS = 33.3%, $P < 0.001$). It is important to note that one gilt from the HS group farrowed nine piglets that were all stillborn. Gilts from the HS group tended to farrow less liveborn piglets ($P = 0.09$) than the CON group (Table 2). Heat-stressed gilts took longer to start expelling placentae ($P = 0.003$), although the active farrowing duration was not statistically significant ($P = 0.21$; Table 2). There was a positive correlation between farrowing duration and placental expulsion interval (r = 0.60, $P = 0.02$). Piglet birth interval was not different between the treatment groups ($P = 0.16$; Table 2). Irrespective of treatments, there was an effect of birth order on piglet birth interval ($P < 0.001$) as piglets born late in the litter had a greater birth interval compared to the early and middle groups (early = 14.3 ± 3.22, middle = 12.3 ± 2.98 and late = 21.1 ± 3.03 min; data not shown in the Table). The total born was similar between the treatment groups (Table 2). Liveborn litter weights were reduced by HS ($P = 0.02$), although total litter weights (incl. stillbirth) were similar between treatments (Table 2). The odd for a piglet to be born with a ruptured umbilical cord was higher in the HS group than in the CON group ($P < 0.001$; Table 2). Among the 31 stillborn piglets in the HS group, 16 piglets were born with a ruptured umbilical cord. The attributable risk analysis revealed that cord rupture explained 55% of the stillbirth. The association between birth order and stillbirth was significant ($P = 0.01$), such that the odd for stillbirth increased with birth order (early = 11.5%, middle = 13.8% and late = 30.5%), regardless of temperature treatments. Risk analysis revealed that the relative risk factor of stillbirth associated with HS was 14.7, meaning that gilts in the HS group were almost 15 times more likely as gilts in the CON group to farrow stillborn piglets. In addition, attributable risk analysis indicated that 93% of stillbirth observed in the current study could be attributed to HS. Of note, two gilts from the HS group had three piglets and their associated placentae retained at the birth canal, which were found on d 3 postpartum (piglets were not included for birth interval and farrowing duration analyses). In contrast, retained piglets or placentae did not occur in gilts from the CON group.

Table 2
Predicted means (±pooled SEM) for reproductive performance of gilts exposed to control (CON) or heat stress (HS) conditions between d 110 of gestation until farrowing completion.

Variable	Treatment[1]		SEM	*P*-value
	CON	HS		
Gestation length, d	115.6	116.0	0.66	0.70
Farrowing duration[2], min	2.21	2.32	0.061	0.21
	(162)	(209)	–	–
Birth interval[2], min	1.09	1.23	0.086	0.16
	(12.3)	(17.0)	–	–
Placental expulsion interval[2], min	2.11	2.25	0.026	0.003
	(129)	(178)	–	–
Total born, n	13.3	13.8	1.07	0.76
Liveborn piglet, n	12.6	8.6	1.51	0.09
Stillbirth, %	2.3	33.3	–	< 0.001
Umbilical cord ruptured, %	10.2	30.6	–	< 0.001
Mummified foetus, %	8.3	4.1	–	0.18
Litter weight (incl. stillborn), kg	16.7	16.5	1.63	0.96
Litter weight (liveborn), kg	16.5	10.1	1.61	0.02
Coefficient of variation for piglet birth weight	0.16	0.18	0.023	0.37

[1] Treatment: CON = control (n = 7 gilts; constant 20 °C); HS = cyclic heat stress (n = 7 gilts, 0900 h to 1700 h, 30 °C; 1700 h to 0900 h, 28 °C).
[2] Log transformation was performed before analysis, and figures in parentheses are back-transformed means.

Piglet umbilical vein parameters and meconium staining at birth

Piglets born to heat-stressed gilts had lower birth umbilical vein partial pressure of oxygen (pO_2, P = 0.04), oxygen saturation rate (P = 0.03), base excess (P = 0.02) and pCO_2 (P = 0.01) than piglets from the CON group (Fig. 2). Piglets from the HS group tended to have higher lactate (P = 0.07) and lower bicarbonate (P = 0.07) in the umbilical vein (Fig. 2). Other umbilical blood variables, such as pH and haematocrit, were not significantly different between temperature treatments (Fig. 2). Piglets born late in the litter had lower umbilical vein pH (P = 0.05), base excess (P = 0.02) and higher lactate levels (P = 0.002) than piglets born earlier in the litter. In addition, piglets born early in litter had higher sodium (P = 0.02), calcium (P = 0.005), but lower potassium ion concentrations (P = 0.005) than piglets born late in the litter, regardless of temperature treatments. There were no main effects of sex on any of the cord blood parameters. At birth, piglets born to heat-stressed gilts had greater skin meconium staining scores (CON = -1.09 ± 0.424 (back-transformed mean, 0.47) vs HS = 0.06 ± 0.424 (back-transformed mean, 1.04), P = 0.022).

Neonatal piglet development and morphology

The incidence of liveborn mortality within 48 h of age showed a trend to be higher in the HS group (CON = 2.3% vs HS = 8.1%, P = 0.10). The impacts of maternal HS on piglet morphology are presented in Table 3. There were no differences between the CON and the HS groups for average piglet BW at birth (P = 0.37), 24 h (P = 0.29) and 48 h of age (P = 0.29; Table 3). Piglet 24-h and 48-h average growth rates were not significantly different between treatment groups (Table 3). Piglet rectal temperature at birth tended to be higher in the HS group (CON = 37.6 ± 0.33 vs HS = 38.5 ± 0.37 °C, P = 0.09), but was not different between treatment groups at 48 h of age (CON = 38.5 ± 0.18 vs HS = 38.4 ± 0.18 °C, P = 0.83) (data not shown in the Table). At 48 h of age, piglets born to gilts exposed to HS had a shorter small intestine than piglets born to CON gilts (P = 0.02; Table 3). However, the small intestine weight relative to length remained similar between treatment groups (Table 3). The absolute brain weight was lower in piglets from the HS group (P = 0.001). However, relative brain weight was not different between treatment groups (P = 0.83). There was an interaction (P = 0.02) between treatment and sex for relative muscle weight, such that the weight percentage was higher in females than males in the HS group (female = 0.26 ± 0.009 vs male = 0.24 ± 0.009%) but was similar between sexes (female = 0.25 ± 0.009 vs male = 0.25 ± 0.008%) in the CON group (data not shown in the Table). The effect of temperature treatments on other absolute or relative organ weights was not significant (Table 3). Regardless of temperature treatments, male piglets had heavier absolute spleen (P = 0.03) and brain (P = 0.004) weights but had

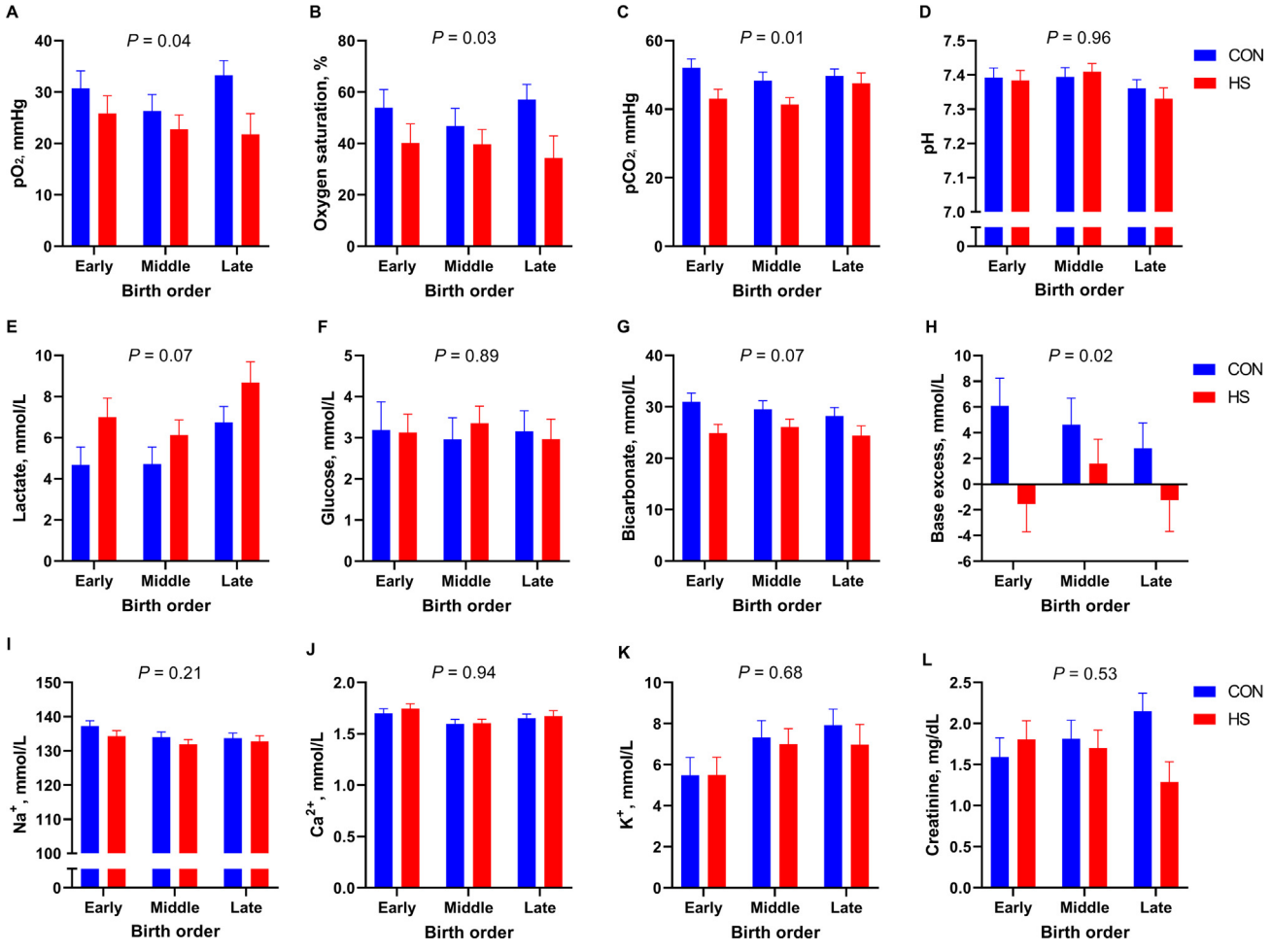

Fig. 2. Predicted means (±SEM) for piglet umbilical vein parameters (A-L) from control (CON, n = 33 umbilical blood samples) or heat stress (HS, n = 28 umbilical blood samples) groups. Piglet birth order (first piglet to last piglet in the litter) was divided into thirds based on the total litter size of each gilt and classified as 'early' (first 1/3), 'middle' (middle1/3) and 'late' (last 1/3). *P*-values represent the statistical significance of the main effect of temperature treatment from the linear mixed model.

Table 3
Predicted means (±pooled SEM) for piglet BW and gross morphology.

Variable	Treatment[1]		SEM	Sex		SEM	*P*-value	
	CON	HS		Female	Male		Treatment	Sex
Piglet BW and growth rate								
Birth (incl. stillborn), kg	1.29	1.22	0.065	1.24	1.27	0.048	0.50	0.33
Birth (liveborn), kg	1.29	1.20	0.068	1.24	1.25	0.052	0.37	0.69
24 h, kg	1.41	1.29	0.074	1.35	1.36	0.057	0.29	0.94
48 h, kg	1.54	1.41	0.076	1.44	1.51	0.059	0.29	0.13
24-h growth rate, g/d	103	89	30.8	93	99	22.4	0.77	0.55
48-h growth rate, g/d	113	94	23.3	95	113	17.5	0.63	0.12
Piglet gross morphology at 48 h of age								
Small intestine								
Length, cm	393.6	351.7	10.84	364.4	381.0	8.48	0.02	0.03
Weight, g	66.8	56.4	4.94	61.5	61.7	3.67	0.17	0.95
Weight/length, g/cm	0.171	0.159	0.012	0.168	0.163	0.009	0.50	0.31
Length/BW, cm/kg	255.4	256.9	11.44	255.1	257.1	8.67	0.93	0.78
Weight/BW, %	4.39	3.98	0.176	4.27	4.11	0.141	0.13	0.21
Organ absolute weight & length								
Liver weight, g	57.6	50.2	4.95	53.4	54.4	3.61	0.32	0.50
Brain weight, g	31.8	28.3	0.57	29.1	31.0	0.51	0.001	0.004
Muscle weight, g	3.90	3.48	0.313	3.66	3.72	0.232	0.38	0.55
Heart weight, g	13.8	12.2	0.65	13.2	12.8	0.55	0.12	0.53
Spleen weight, g	2.61	2.33	0.226	2.32	2.63	0.174	0.41	0.03
Femur weight, g	3.95	3.36	0.251	3.62	3.71	0.191	0.12	0.61
Femur length, cm	4.15	3.99	0.077	4.06	4.08	0.061	0.18	0.63
Relative weight								
Femur weight/length, g/cm	0.947	0.827	0.048	0.876	0.899	0.038	0.10	0.53
Brain/liver weight, g/g	0.576	0.620	0.061	0.596	0.600	0.045	0.62	0.85
Muscle/femur weight, g/g	0.99	1.05	0.058	1.03	1.02	0.043	0.53	0.92
Muscle/BW, %	0.249	0.250	0.008	0.254	0.246	0.006	0.91	0.20
Liver/BW, %	3.74	3.56	0.170	3.68	3.62	0.134	0.45	0.60
Brain/BW, %	2.12	2.09	0.119	2.09	2.11	0.093	0.83	0.78
Heart/BW, %	0.904	0.869	0.031	0.924	0.849	0.028	0.43	0.04
Spleen/BW, %	0.165	0.165	0.007	0.158	0.172	0.006	0.96	0.06
Femur/BW, %	0.258	0.238	0.009	0.252	0.244	0.008	0.13	0.32

[1] Treatment: CON = control (constant 20 °C); HS = cyclic heat stress (0900 h to 1700 h, 30 °C; 1700 h to 0900 h, 28 °C). Piglet BWs were assessed for all newborn piglets, whereas morphology data were obtained from a subset of piglets (CON, n = 39 piglets; HS, n = 34 piglets) at 48 h of age.

lighter relative heart weight ($P = 0.04$) than female piglets (Table 3). In addition, the male piglets had a longer small intestine than females ($P = 0.03$; Table 3).

Piglet small intestinal barrier function and histology

At 48 h of age, there were no differences in piglet jejunal ($P = 0.56$; Fig. 3A) or ileal ($P = 0.30$; Fig. 3B) TER between treatment groups. The jejunal villus height was similar between treatments ($P = 0.26$; Fig. 3C). Jejunal crypt depth was lower in piglets from the HS group compared to the CON group ($P = 0.02$; Fig. 3D). The villus height to crypt depth ratio was similar between treatment groups ($P = 0.89$; Fig. 3E). None of those variables were affected by piglet sex or treatment by sex interaction.

Piglet plasma and colostrum biochemistry

Maternal HS did not change piglet plasma cortisol (CON = 1.75 ± 0.059 (back-transformed mean, 56.2) vs HS = 1.83 ± 0.063 (back-transformed mean, 67.6) ng/ml, $P = 0.39$), IgG (CON = 21.9 ± 3.02 vs HS = 18.7 ± 3.17 mg/ml, $P = 0.50$) or total protein (CON = 47.5 ± 2.81 vs HS = 47.5 ± 2.99 mg/ml, $P = 0.99$) concentrations at 48 h of age. Gilts had similar colostrum IgG (CON = 41.4 ± 5.04 vs HS = 43.4 ± 5.82 mg/ml, $P = 0.80$) and total protein (CON = 174.8 ± 8.62 vs HS = 170.3 ± 9.95 mg/ml, $P = 0.77$) concentrations between treatments. There was a positive correlation between IgG and total protein concentration in piglet plasma at 48 h of age ($r = 0.66$, $P = 0.002$). However, there was no significant correlation between IgG and total protein concentration in the colostrum ($r = 0.27$, $P = 0.35$).

Discussion

The principal findings of this study were that heat exposure of pregnant gilts during the last week of gestation and farrowing upregulated maternal stress responses and altered farrowing physiology, leading to reduced umbilical oxygen supply from the placenta to the piglet. These cumulative effects contributed to increased perinatal mortality of piglets. To the best of our knowledge, this is the first study to demonstrate that maternal HS during late gestation and farrowing negatively affects oxygen supply through the umbilical cord in pigs. These findings emphasise the detrimental effects of sow HS in the farrowing shed on sow welfare and piglet survival.

Data from the current study demonstrated that gilts were heat-stressed under the thermal regime (cyclic 28 to 30 °C). This is evidenced by higher plasma cortisol concentrations and upregulated thermoregulatory responses in gilts. Recent studies reported that late gestating sows had a lower environmental thermal preference (between 12.6 and 15.6 °C) (Robbins et al., 2021) and were more sensitive to thermal stress than mid- or non-gestating sows (McConn et al., 2021). Therefore, the thermal condition applied in the current study implied the gilts were under excessive heat loads and stress. Increased plasma cortisol concentrations were reported in late gestating sows exposed to HS (He et al., 2019) or other stressors (Terry et al., 2021). The change in gilt physiology and metabolism caused farrowing problems, as evidenced by the observations of increased risk of stillborn piglets, increased incidence of piglets born with a ruptured umbilical cord, retained piglets and placentae at the birth canal postpartum, and that gilts from the HS group took longer to start expelling placentae. These findings are consistent with that higher stillbirth rates were

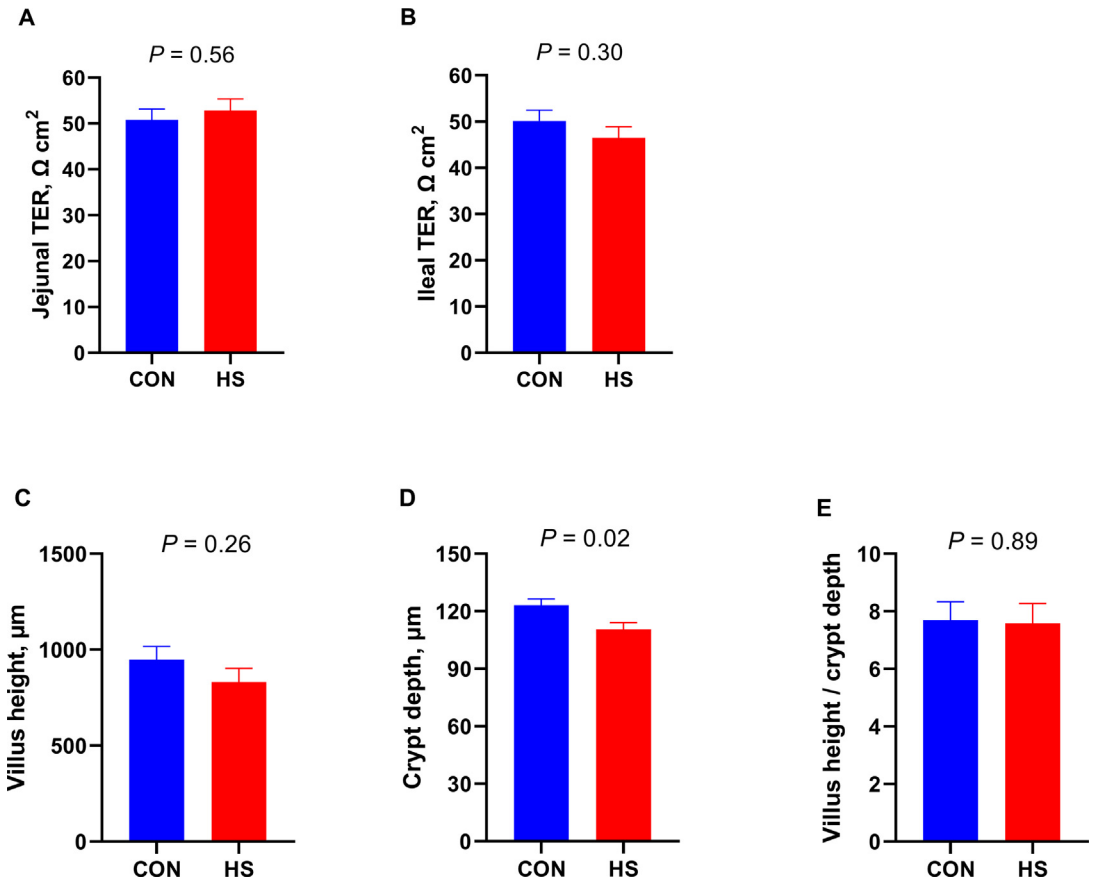

Fig. 3. Predicted means (±SEM) for jejunal transepithelial electrical resistance (TER) (A), ileal TER (B), jejunal villus height (C), jejunal crypt depth (D) and villus height to crypt depth ratio (E) of piglets from control (CON, n = 39 piglets) or heat stress (HS, n = 34 piglets) groups.

observed in sows when they were heat-stressed in the farrowing house from other studies (Odehnalová et al., 2008; Wegner et al., 2016). However, we did not detect significant differences between treatments for piglet birth interval or farrowing duration, whereas other studies reported that sow HS during late gestation had prolonged farrowing duration (Muns et al., 2016b; He et al., 2019). The non-significant difference observed in the current study could be possibly due to the limited number of observations and the biological variation of farrowing duration among gilts.

The causes of piglet stillbirth are multi-faceted, but are largely associated with oxygen insufficiency at parturition (Herpin et al., 1996). In the current study, we further demonstrated that maternal HS decreased oxygen supply from the placenta to the newborn piglet, as evidenced by lower pO_2 and oxygen saturation rate in the umbilical vein at birth. The causes of umbilical oxygen insufficiency in the heat-stressed pigs remain unknown, but are possibly associated with placental hypoxia, as we observed higher umbilical vein lactate concentrations in the HS group. Under normal conditions, lactate can be released from the placenta and act as an energy source for foetal pigs (Fowden et al., 1997). Increased umbilical lactate levels imply accelerated anaerobic glycolysis in the placenta, possibly due to the lack of uterine oxygen supply (Kay et al., 2007). The average values of the blood parameters, such as lactate recorded in the current study, were in agreement with those obtained from the piglet umbilical vein reported in a previous study (Rootwelt et al., 2012). Reduced oxygen supply in the umbilical cord might have implications for foetal oxygenation, possibly leading to intrapartum stress in the piglets. In favour of this hypothesis is the observation of a greater degree of skin meconium staining, assessed for all piglets at birth, in the HS group compared to the CON group. Greater meconium staining of the skin is an indicator of piglet intrapartum anoxia (Mota-Rojas et al., 2002). Thus, although due to practical reasons cord blood samples were only obtained from liveborn piglets with an intact umbilical cord, data could be extrapolated to those stillborn piglets or liveborn with a broken umbilical cord, highlighting that reduced umbilical oxygen supply is a major consequence of maternal HS.

While intrapartum deaths (type II stillbirth) account for the majority of stillbirth in the pig (Vanderhaeghe et al., 2013), we could not exclude the possibility of piglet mortality before the end of gestation (type I stillbirth), associated with the thermal stress applied in the current study. We, therefore, speculate from studies in pigs and other domestic species that HS-related pathogenetic mechanisms, such as maternal oxidative stress (Wang et al., 2019), reduced placental effectiveness (Borges et al., 2005; Baxter et al., 2008) and reduced uterine blood flow (Bell et al., 1987), might all partially contribute to the relatively high stillbirth rates in heat-stressed gilts. We have previously demonstrated that heat-stressed gilts had impaired placental capacity for nutrient transport, suggesting placental insufficiency (Zhao et al., 2021). Studies in pregnant ewes showed that late gestational HS (30 °C to 40 °C) reduced uterine and umbilical blood flows by 39% and 48%, respectively, with subsequent impacts on foetal oxygenation (Bell et al., 1987), although the reductions in uterine and umbilical blood flow are yet to be verified in heat-stressed gestating sows. As oxygen is a flow-limited molecule and is transported by simple diffusion, it could be hypothesised that in the current study, the reduction in oxygen levels in the umbilical cord might be associated with reduced uteroplacental blood flow.

We demonstrated reduced jejunal crypt depth in neonatal piglets born to heat-stressed gilts, which is known to be indicative of reduced rates of enterocyte production and cell turnover in the crypt (Pluske et al., 1996). How maternal HS affects intestinal crypt depth remains unclear, but this might be related to a compensatory response to maintain villus cells and their function, as reduced crypt depth is associated with improved digestive and absorptive activity in the piglet small intestine (Pluske et al. 1996). We did not find a significant difference between HS and CON piglets for other major growth traits at 48 h of age, including BW, growth rate, small intestinal mucosal barrier function and piglet plasma IgG concentration. We speculate that the absence of growth differences observed in this study might be explained by several factors. First, the liveborn piglet numbers in the litter might affect neonatal piglet growth (Rutherford et al., 2013). On average, gilts exposed to HS farrowed four fewer liveborn piglets in the litter than the CON group. This means piglets in the HS group had fewer competitors and higher chances to access teats, possibly leading to enhanced colostrum and milk consumption to compensate for the negative impacts caused during parturition. Second, the loss of the most vulnerable, and generally smaller, piglets during parturition might confound our observations. This was supported by the observations that one third of the born-light piglets (BW less than 1.1 kg) were stillborn and a tendency of increased liveborn mortality in the HS group. These data suggest that the least viable piglets suffering from maternal HS might have already died before the measurement point at 48 h of age. Furthermore, the non-significant differences in BW and piglet growth rate might be partially explained by the survivorship bias. A further investigation into the growth performance of the liveborn piglets beyond the 48-h perinatal period is beyond the scope of the current study. Nevertheless, other studies reported that significant growth retardation of piglets due to sow HS during late gestation was not detectable until d 10 (He et al., 2019) or d 21 (Muns et al., 2016b) of postnatal life. Future studies are needed to verify the long-term impact on the growth performance of the liveborn piglets exposed to maternal HS during late gestation.

It is noted that this study was not a paired feeding experimental design. Thus, impacts on gilt physiology may be partially explained by HS-induced feed intake reductions. Reduced feed intake might have an impact on energy status for the onset of farrowing as it is an energy-demanding process (Feyera et al., 2018). However, a recent study reported that reducing gilt feed intake from 3.75 kg/d to 1.75 kg/d during the last week of gestation, similar to the feed intake levels recorded in the current study, only resulted in a non-significant increase in stillborn rates (Feyera et al., 2021). Similar stillborn rates were found in gestating sows fed low vs high energy diets from d 90 of gestation until farrowing (Che et al., 2019). These findings suggest that the reduction in feed intake alone does not explain the much higher stillborn rates in heat-stressed gilts observed in the current study. Thus, the current findings highlight the direct impact of maternal HS on piglet mortality. Furthermore, findings from the current study suggest that nutritional strategies to alleviate sow HS and reduce piglet stillborn rates need to be carefully justified if the loss of sow appetite occurs. Alternative approaches, such as in water supplementation and the use of cooling equipment in the farrowing house (Johnson et al., 2021; Zhu et al., 2021), might be considered in such a case.

Conclusion

The current data demonstrated that pregnant gilts were susceptible to elevated temperatures in the last week leading up to and during farrowing, as evidenced by higher body temperatures, a marked reduction in feed intake, increased plasma cortisol concentrations and poor farrowing outcomes. Gilts exposed to HS farrowed more stillborn piglets and fewer liveborn piglets. Maternal HS reduced oxygen supply from the placenta to the piglet through the umbilical cord, explaining the increased stillborn rates recorded. However, the causes of HS-induced umbilical oxygen insufficiency remain complicated but seem to be linked to placental hypoxia. In those liveborn piglets, maternal HS had an immediate impact on the length and crypt depth of piglet small intestine, although changes in other phenotypes were less evidenced within the first 48 h of postnatal life. Findings from the current study underscore the need for mitigation strategies in the farrowing shed during the hot summer months to improve piglet survival and improve the production efficiency.

Ethics approval

All animal procedures were approved by the Animal Ethics Committee of the University of Melbourne (Ethics ID: 21074).

Data and model availability statement

None of the data were deposited in an official repository. The datasets generated during the current study are available upon reasonable request.

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Declaration of interest

None.

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