Title: Using objective behavioral measurements to build robust producer tools for detecting, scoring and treating lameness in sows – **NPB #09-251**

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Industry summary

Lameness associated with painful joint lesions has been identified as a welfare challenge for confined sows. It has been ranked as the number 3 reason for culling sows; comprising 15% of the culls marketed in the U.S. Producers in the U.S. currently treat sow lameness using husbandry tools, for example housing sows individually to provide easy access to key resources and rubber mats. Currently, producers assess sow lameness using subjective scoring systems, which have been shown to be variable in their application. Objective tools to measure sow lameness on farm are required. The objective of this study was to validate a list of potential objective tools to determine which could discriminate between sows in a painful and non-painful lameness state. ***Cortisol*** was elevated on most lame days compared to sound and resolved days. For the ***Prototype Embedded Microcomputer-based force plate system*** weight placed on the injected hoof decreased on the most lame day. *GAITFour ® pressure mat gait analysis walkway system*; **Stride Time** increased on most lame day for all hooves. **Stride Length** decreased on most lame day compared to baseline levels. **Maximum Pressure** placed on the induced hoof decreased on the most lame day compared to baseline levels. **Stance time** increased for all sound hooves between sound and most lame day. ***Mechanical Nociception Threshold*** test pressure tolerated by the lame hoof decreased for every landmark when comparing sound and most lame days. The sound hoof tolerated more pressure on most lame and resolved than on baseline sound day. ***Thermal Nociception Threshold*** test tolerated by the sound hoof did not change over the 3 treatment days. However, the sows tolerated less heat stimulation on their lame hoof on most lame day compared to baseline levels. Therefore, in conclusion, the physiology, kinematics and pain sensitivity tests all detected changes when sows were sound and in acute lameness states and show promise for on farm application.

Keywords

Behavior, Lame, Sound, Sow Productive Lifetime

Scientific Abstract:

The objective of this study was to develop validated, objective tools able to discriminate between sows in a painful and non-painful lameness state. Tools assessed included plasma cortisol, embedded microcomputer force plate system, GaitFour® walkway system, Mechanical Nociception Threshold (MNT) and Thermal Nociception Threshold (TNT) tests. A total of 24 mixed parity sows (220.15 ± 21.23 kg) were individually housed. All sows served as their own control and treatment. On D0, sows were induced lame using a chemical synovitis model. After completion of the first round, sows were given a 7d rest period and then the trial was repeated with the other rear hoof being induced lame. Three treatment days were compared (1) ***sound*** (day before induction: D-1), (2) ***most lame*** and (3) ***resolved*** (first and sixth day after injection of amphotericin B). ***Cortisol*** was elevated on most lame days compared to sound and resolved days. For the ***Prototype Embedded Microcomputer-based force plate system*** weight placed on the injected hoof decreased on the most lame day ($P < 0.05$). *GAITFour ® pressure mat gait analysis walkway system*; **Stride Time** increased on most lame day for all hooves ($P < 0.05$) and returned to baseline levels by the resolved day. **Stride Length** decreased on most lame day compared to baseline levels ($P < 0.05$). All hooves (except RF when RH induced lame) returned to baseline levels by resolved day (Table 6). **Maximum Pressure** placed on the induced hoof decreased on the most lame day compared to baseline levels ($P < 0.05$). **Stance time** increased for all sound hooves between sound and most lame day (P < 0.05). ***Mechanical Nociception Threshold test*** *p*ressure tolerated by the lame hoof decreased for every landmark ($P < 0.05$) when comparing sound and most lame days. The sound hoof tolerated more pressure on most lame and resolved than on baseline sound day ($P < 0.05$). ***Thermal Nociception Threshold test*** tolerated by the sound hoof did not change over the 3 treatment days ($P > 0.05$). However, the sows tolerated less heat stimulation on their lame hoof on most lame day compared to baseline levels. Therefore, in conclusion, the physiology, kinematics and pain sensitivity tests all detected changes when sows were sound and in acute lameness states and show promise for on farm application.

Introduction: An overview of the researchable question and its importance to producers.

Lameness associated with painful joint lesions has been identified as a welfare challenge for confined sows (Stalder et al., 2004; Elmore et al., 2010). It has been ranked as the number 3 reason for culling sows, comprising 15% of the culls marketed in the U.S. (Schenk et al., 2010). In addition, sow lameness has been associated with several variables that result in poor reproductive performance including decreased litter size, poor farrowing performance, and decreased sow longevity (Anil et al., 2009; Engblom et al., 2008; Fitzgerald et al., 2012). Producers in the U.S. currently treat sow lameness using husbandry tools, for example housing sows individually to provide easy access to key resources and rubber mats. However, there are no analgesic drugs approved for use in swine by the United States Food and Drug Administration (US-FDA). The lack of drug approval is due to no objective assessment tools for pain which are a requirement according to FDA Guidance Document 123. Developing objective assessment tools requires populations of known status, specifically painful and non-painful. To reduce intra-animal variation, it is optimal that individuals serve as their own control (non-painful) and treated (painful) experimental unit. This addresses the "3 R's" that can reduce the number of animals required to detect significant differences, thereby addressing a key animal welfare concern (Karriker et al., 2012). Successful lameness induction models using amphotericin B have demonstrated a predictable, acute synovitis in cattle (Kotschwar et al., 2009 and Schulz et al. 2011), horses (Bowman et al., 1983) and sows (Karriker et al., 2012) with no long term residual effects observed. Kinematics, pain and physiology are potential tools that can be used on farm to identify sows that are in varying stages of lameness.

Objectives

To objective of this project was to validate a list of potential objective tools to determine which could discriminate between sows in a painful and non-painful lameness state.

Materials & Methods

Animals, housing, and husbandry

The project was approved by the Iowa State University Animal Use and Care Committee. The experiments were conducted from July 25 to November 16, 2011. The laboratory was at the A-wing of the College of Veterinary Medicine, Ames, IA. A total of 24 (220.15 ± 21.23 kg) non-bred clinically normal, mixed-parity, crossbred sows were purchased from a producer in Iowa. To avoid confounding injury due to aggression, each sow was housed in an individual pen. Each pen measured 3.7 m length x 1.4 m width x 1.2 m height and had a solid concrete floor. A rubber mat (2.4 m length x 2 cm height x 1.4 m width) was provided for comfort. Pigs had *ad libitum* access to water via one nipple waterer (Trojan Specialty Products Model 65, Dodge City, KS) that was positioned over a grate. Pigs were hand-fed 2.3 kg in the morning. This ration was given on the embedded force plate when on trial to keep the sows still and any remaining ration not given on the embedded force plate w given to the sows in their home pen. When not on trial all sows received their morning ration on the raised concrete step. In the afternoon, sows were given 0.46 kg at 1600 onto a raised concrete step (55 cm length x 55 cm in width x 24 cm depth). Feed was a custom mixed pelleted diet composed of corn, soybean meal, and soy hulls. Feed mix was specifically designed to meet the energy requirements of gestating sows and was formulated to meet requirements (NRC, 1998).A total of 6.8 ml (15 mg) of Matrix (Intervet/Schering-

Plough, Milsboro, DE) was added to 0.45 kg of diet daily to prevent initiation of estrus cycle. Metal fences (1.2 m height x 76 cm width) were affixed at the end of each home pen and lights were on a 12:12 light dark cycle (light hours [0600 and 1800]). All sows were checked at 0730 and 1530 daily. Three data loggers (Hobo Pro series, Hobo, Janesville, WI) were placed in the alley of the home pens, next to the embedded force plate and gait analysis pressure mat. Each logger was approximately 1-m from the floor. Relative humidity (%) and temperature (^{o}C) were recorded every 10-minutes and average temperature and relative humidity over the trial was 22.1 ^{o}C and 59% respectively.

Treatment descriptions

All sows were acclimated for ~8 d prior to study commencement. Each pig served as her own control and treatment. This experimental design provides robust control of intra- and inter-animal variations in behavioral responses and limited the number of animals required. The experimental design was a 3(days) x 2(hoof) factorial arrangement of treatments and home pen containing the sow was the experimental unit. Sows were blocked by body weight and randomly allocated to one hoof for the first induction of lameness. **Hoof** was defined as left rear vs. right rear hoof injected. Three treatment **days** were compared, ***sound*** defined as the day before lameness induction occurred (2) ***most lame*** defined as 24 hours post amphotericin B injection and ***resolved*** defined as 6-days post amphotericin B injection. **Trial** was defined as either 1 or 2 with trial 1 including sows 1-12 and trial 2 including sows 13-24. **Round** was defined as 1 or 2, as first or second induction of lameness. The time periods for sound, most lame and resolution had been previously determined by Karriker et al. (2012).

Inducement of lameness

Humane endpoint criteria were established because at the onset of the experiment, lameness severity and duration resulting from injecting amphotericin B into the distal inter-phalangeal joints in swine was unknown. The investigators established humane endpoint criteria so that any sow which progressed to non-weight bearing lameness for 48 hours or was unable to access water for greater than 12 hours or feed for greater than 24 hours was removed from the study and humanely euthanized (this did not apply to any sows in this study). All sows were restrained in a standing position using a humane pig snare and then anesthetized (accomplished using Xylazine (4.4 mg/kg; Anased®, Lloyd Laboratories, Shenandoah, IA, USA), Ketamine HCl (2.2 mg/kg; Ketaset®, Fort Dodge Animal Health, Wyeth, Madison, NJ, USA), and Tiletamine HCl (4.4 mg/kg; Telazol®, Fort Dodge Animal Health, Wyeth, Madison, NJ, USA) administered intramuscularly). Dosages were based on recommendations by Jean and Anderson (2006). Palpebral reflex was tested to confirm insensibility following anesthesia administration. After insensibility was established, the assigned claws were washed with water to remove obvious fecal contamination, scrubbed for 3 minutes with iodine based surgical scrub (Operand®, Aplicare Inc., Branford, CT, USA) using 10 x 10 cm sterile gauze pad, and rinsed with 70% isopropyl alcohol until no evidence of the surgical scrub remains. After cleaning, ten mg of amphotericin B (X-gen Pharmaceuticals, Inc., Big Flats, NY, USA) were injected in the intraarticular space of the medial, distal inter-phalangeal joint (Karriker et al., 2012). Throughout anesthesia, respiratory rate (chest elevations resulting from inspiratory effort for 15 seconds), and rectal temperature were monitored every 15 minutes until sows returned to a standing position unaided.

Objective tools tested to measure transient lameness in sows

Cortisol

Sows were restrained in a standing position using a humane pig snare. Blood was collected from the jugular vein between the hours 1500 and 1700 on D-1, D +1 and D +6, respectively. A total of 10 ml of blood was collected using a 16-gauge needle, collected into a 20 mL syringe and immediately placed into two glass vacutainer plain serum blood collection red top tube (5ml/tube), centrifuged at 1,500xg for 15 minutes at 10ºC. After centrifugation, plasma was removed and stored at -80ºC prior to analysis. Cortisol sample analysis was completed with the IMMULITE® 1000 cortisol assay. The IMMULITE assay is a solid phase, competitive chemiluminescent enzyme immunoassay.

Prototype Embedded Microcomputer-based force plate system

The embedded microcomputer based force plate system measures 1.5 m x .57 cm x .11 cm (length x width x height) with 6.4-mm thick aluminum plating comprising the top and bottom plate. It has four separate load cells measuring .76 cm x .28 m (length x width), these cells quantify the pressure the sow exerts on each hoof while standing (Sun et al., 2011; Figure 1). A separation bar divides the area in half to limit the sow from placing more than one hoof per load cell. It is coated with non-slip epoxy and is accurate to 0.45 kg. The embedded force plate system was calibrated for accuracy prior to the beginning of the study using 68 kg weights. The Prototype Embedded Microcomputer-based force plate system fits standard gestation - and farrowing stalls (Sun et al., 2011). Weight distribution on each of the 4 limbs was collected twice per second for a total of 15 minutes over the 3 treatment days. Sows had free access to feed during this data collection (Figure 2).

GAITFour® pressure mat gait analysis walkway system

Sows were assessed using a GAITFour® gait analysis walkway system and associated hardware. Sows were walked in a continuous closed loop across the pressure mat (4.3 m with 13,824 sensors) to acclimate the animals to the desired speed and pattern of movement needed for footfall analysis. Gait analysis measures collected were ***maximum pressure*** (defined as the greatest amount of weight placed on a single hoof), ***stride length*** (defined as the distance in cm between 2 sequential footfalls from the same hoof), ***stride time*** (defined as the time in seconds between 2 successive footfalls by the same hoof) and ***stance time*** (defined as the duration of time (seconds) the sensors were activated by a hoof in a single stride). Each pig was required to complete three quality readings each day of data collection. A reading was considered acceptable if the pig did not hesitate, stop, or run across the walkway and if at least two complete footfall cycles (all four hooves) registered in the software. The quality footfall data was saved to the GaitFour® software program for later analysis and validation (Figures 3a, b).

Mechanical Nociception Threshold (MNT) test

A hand-held pressure algometer (Wagner Force Ten™ FDX 50 Compact Digital Force Gage, Wagner Instruments, CT, USA) with a 1 cm^2 flat rubber tip was used to quantify mechanical nociceptive thresholds (MNTs) in kilograms of force (kgf) (Figure 4a). The application rate for all sows on all landmarks was approximately 1 kgf/second. The maximum force applied was 10 kgf for a 10 second period. Pressure was applied perpendicularly to three landmarks in a randomized sequence for each sow: 1) 1 cm above the coronary band on the lateral hind claw (Outer), 2) 1 cm above the coronary band on the medial hind claw (Inner) and 3) middle of cannon on the hind limb (Cannon; Figure 4b). The randomized landmark sequence was repeated in triplicate on the right hind limb followed by the same sequence repeated in triplicate on the left hind limb. When a hoof-lift response was observed, pressure was immediately removed, and the peak pressure representing the MNT was recorded.

Thermal Nociception Threshold (TNT) test

The TNT test immediately followed the MNT test and measured the latency for a sow to withdraw her hind hoof in response to precise, focused radiant heat stimulation. The analgesia meter (IITC Plantar Analgesia Meter, IITC Life Science Inc., Woodland Hills, CA, USA) was set at a constant 80 % beam intensity; emitting 200°C. Thermal measurements were taken in triplicate 1 cm above the coronary band on the lateral side of the right hind hoof, followed by the left hind hoof. Once the machine was 7.62 cm from the landmark the thermal stimulus was activated. The latency for the sow to withdraw her hoof in response to the stimulus was recorded. To prevent tissue damage, a 20 second maximum duration was set, after which the stimulus automatically turned off (Figure 5).

Statistical analysis

For all tools, the PROC MIXED procedure in SAS for parametric data was used. For all models a PDIFF was used to determine differences. A *P* value of < 0.05 was considered significant. PROC UNIVARIATE was applied to all of the tools. All tools except TNT and MNT test were found to be normal, therefore were assigned to PROC MIXED. The TNT and MNT test were tested with PROC GLIMMIX. Results did not differ from the MIXED procedure and since both variables are continuous and truncated, both tools were fit to the MIXED model.

Cortisol: the model included the main effects of round, trial, day, and hoof injected. A random statement of sow within trial*day and sow within trial*round was used.

Prototype Embedded Microcomputer-based force plate system: the model included the main effects of day, hoof injected, leg (defined as the measurement of weight placed on a hoof), day*leg (comparison of weight distribution on the four hooves on each of the 3 treatment days), trial and round. A random statement of sow within trial*day and sow within trial*round was used.

GAITFour® pressure mat gait analysis walkway system: the model included the main effects of day, round, trial, leg, hoof injected, day*leg and walk (defined as the first, second or third walk across the pressure mat). A random statement of sow within trial*day and sow within trial*round were used. A repeated statement of walk within day was also used.

Pressure algometry: the model included the main effects of landmark (medial claw, lateral claw or cannon bone), replicate (first, second or third completion of landmark order), trial, landmark order, leg, and the interactions of day*hoof status*landmark (hoof status defined as either lame or sound). A random statement of sow within group, sow within trial*day sow within trial*round and landmark order within day was used. A repeated measures statement of replicate within round*day*landmark*hoof status was used.

Thermal sensitivity: the model included the main effects of replicate, round, leg and the interaction of day*hoof status. A random statement of sow within day and sow within round was used. A repeated measures statement of replicate within round*day*hoof status was used.

VIII. Results

Hoof injected

When comparing left or right hoof injected, there were no differences for cortisol, thermal nociception test, mechanical nociception test, embedded force plate, or gait analysis measures of stride length and maximum pressure ($P > 0.34$). There was an increase in the gait analysis for stride- and stance time when the left rear hoof was injected ($P < 0.014$) compared to the right hoof injection although biologically these differences would be challenging to see in a sow (Table 1).

Trial

When comparing first (sows 1-12) and second (sows 13-24) trials, there were no differences for cortisol, mechanical nociception test, or gait analysis measures of stride time, stride length, and stance time ($P > 0.14$). There was however differences between trials for the embedded force plate and the gait analysis measure for a reduction in maximum pressure in trial 2 due to sows being lighter in the second trial (Table 2)

Round

When comparing first and second rounds of hoof injection, there were no differences for cortisol, thermal nociception test, embedded force plate, and gait analysis measures of maximum pressure, stride length and stance time ($P > 0.07$). There were differences between rounds of injection for the mechanical nociception test and the gait analysis measure with a reduction in stride time in trial 2 although biologically these differences would be challenging to see in a sow ($P < 0.042$; Table 3).

Treatment Day

Cortisol

There was no difference between sound and resolved days ($P = 0.45$), but cortisol concentration was greatest on the day when sows were most lame ($P < 0.0001$; Figure 6).

Prototype Embedded Microcomputer-based force plate system

Weight placed on the injected hoof decreased on the most lame day ($P < 0.0001$). For all hooves (except RF when the LH was injected) none of the hooves went back to baseline values by the resolved day (Table 4).

GAITFour ® pressure mat gait analysis walkway system

Stride Time

Stride time increased on most lame day for all hooves ($P < 0.05$). For all hooves, stride time returned to baseline levels by the resolved day (Table 5)

Stride Length

For all hooves, stride length decreased on most lame day compared to baseline levels ($P < 0.05$). All hooves returned to baseline levels by resolved day (Table 6)

Maximum Pressure

Maximum pressure placed on the induced hoof decreased on the most lame day compared to baseline levels ($P < 0.05$). Excluding the hooves that did not change during the treatment days, only 3 of the hooves (RH when LH induced lame, LF and LH when RH induced lame) returned to baseline values on the resolved day (Table 7)

Stance Time

Stance time increased for all sound hooves between sound and most lame day ($P < 0.05$). Excluding the induced hooves, all hooves (except RH when LH induced) returned to baseline on the resolved day. When LH was induced, stance time did not change on the induced hoof during all 3 treatment days ($P > 0.05$; Table 8).

Mechanical Nociception Threshold (MNT) test

Pressure tolerated by the lame hoof decreased for every landmark ($P < 0.05$) when comparing sound and most lame days. The sound hoof tolerated more pressure on most lame and resolved than on baseline sound day ($P < 0.05$). None of the landmarks on the lame hoof returned to baseline levels by the resolved day (Table 9).

Thermal Nociception Threshold (TNT) test

Thermal stimulation tolerated by the sound hoof did not change over the 3 treatment days ($P > 0.05$). However, the sows tolerated less heat stimulation on their lame hoof on most lame day compared to baseline levels ($P < 0.05$). Tolerance of the heat stimulus increased by the resolved day but did not return to baseline levels (Table 10)

Discussion:

Most research has focused on behavioral or physiological changes associated with acute pain (Anil et al., 2002; Ting et al., 2003; Stilwell et al., 2008), but these changes can be complex, with natural variation between animals complicating the differentiation of pain from other factors such as stress (Anderson and Muir, 2005). In addition to variations in physiological responses, variations in disease severity also complicate the study of pain. Induction of lameness allows for controlled evaluation of pain in animals because pre- and post-lameness measurements can be taken from the same animal, thereby reducing the confounding effects of individual differences. This approach has been published by Kotschwar et al., (2009) who examined the efficacy of sodium salicylate for providing analgesia in an amphotericin B-induced bovine synovitis-arthritis model using 10 male Holstein calves, 4 to 6 months old and weighing approximately 250 kg. The authors concluded that the amphotericin B-induced synovitis-arthritis model was a useful tool for studying changes associated with lameness in cattle through the use of pressure mats, heart rate and visual scoring of lameness but that sodium salicylate was not effective in providing analgesia after lameness. Work by Karriker and colleagues (2012) utilized the GaitFour® pressure mat and static force plate to discriminate between painful and non-painful states when analyzing use of Amphotericin B as a synovitis model. This approach concluded that injection of amphotericin B induced predictable acute transient lameness in sows.

Several tools have been described to assess pain associated with bovine lameness (Coetzee 1998a,b; Kotschwar et al., 2009). Sprecher et al., (1997) has used lameness scoring systems based on visual gait analysis, based on behavior and posture in dairy cattle. This system is most useful in categorizing general lameness for serial monitoring, in setting intervention points for herd level decisions, and in identifying individuals for immediate treatment. Although visual scoring systems do allow for noninvasive categorization of lameness that can be correlated with the other diagnostic tools, they are limited by inter- and intra-observer variability (Kotschwar et al., 2009). Wells et al. (1993) found 91.3% inter-observer agreement between 2 investigators when using a standardized visual lameness scoring system. Kinematics, for example pressure mat technology provides objective data through determination of BW distribution and temporality. Both kinematics and behavior allows for non-invasive analysis of lameness that can be correlated with the other diagnostic tools. The determination of serum cortisol concentration is a physiological measurement to allow for minimally invasive measurement of stress in animals (Coetzee et al., 2007). However, objective assessment tools to detect pain caused by lameness in swine that in turn can support drug approvals are needed and must be validated.

Lameness and pain

Lameness in swine, poultry, horses, and cattle have a large negative economic impact to livestock producers (Wells, 1984). The abnormal locomotion of pigs has been described as having a shorten stride length, stiff movements, and lowered ability to accelerate and change direction (Corr, 2003). Lameness has been defined as "*having a body part and especially a limb so disabled as to impair freedom of movement*" or as "*impaired movement or deviation from normal gait*" (Corr, 2003). Locomotor disorders can be associated with neurological disorders, lesions of the hoof or limb, or a mechanical-structural problem, trauma, or metabolic and infectious disease (Main et al., 2000; Smith, 1988; Wells, 1984). Pain is defined by the International Association for the Study of Pain (IASP) *as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."* The IASP adds, "*The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment.*" This is an important point, especially when discussing pain in animals, and even more so in food-producing animals, such as pigs. Animals can visibly communicate their pain to us only through physical signs. Pain is a complex phenomenon. It involves many nerve cells, many types of nerve chemicals, and many different nerve cell receptors to which the nerve chemicals bind in order to continue a pain signal's trip to the spinal cord and brain (Coetzee, 2008a,b). Not only is pain complex from the standpoint of transmission, processing, and control, it is also complex in that there are different types of pain that have been identified based on cause or pathophysiology, the most important of which are acute pain and chronic pain. Because the causes, transmission, and methods of processing of pain are complex issues, it is understandable that pain management and pain control are complicated and difficult. Acute pain is a protective mechanism that can be defined as the everyday experience of discomfort that occurs in response to a simple insult or injury (Besson, 1997). Acute pain makes us notice an injury, move away from the danger that caused the injury, and then take care of the injury; thus, it is generally short-lived pain. Pain associated with more severe trauma, like surgery, begins as acute pain but can become chronic with prolonged inflammation (Lascelles et al., 2002). Chronic pain is a persistent kind of pain that may or may not be associated with injury, but is generally associated with inflammation, changes to nerve cells, and hyperexcitability of the nerve cells in the spinal cord and brain (Gudin, 2004). This hyperexcitability phenomenon, or “wind up,” is a physiologic increase in sensitization of excitable nerve cells. Because the brain and spinal cord are now wound up to detect pain, they are hypersensitive to future painful stimuli, thus, something normally mildly painful becomes very painful after repeated physical insults. In addition, the wind-up phenomenon changes in the spinal cord and brain make pain resistant to treatment with analgesic (Coetzee, 2008a). Prolonged inflammation caused by damaged tissue helps perpetuate the wind-up phenomenon and plays a large role in chronic pain. Preventing the wind-up phenomenon is an important human pre-surgery consideration; studies have shown that if analgesic or anti-inflammatory drugs are given to a patient prior to surgery, less analgesic or anti-inflammatory drugs are needed to control pain after surgery.

Physiology

Research to evaluate animal welfare is mostly predicated on assessment of the sympatho-adrenal (SA) and hypothalamic-pituitary-adrenal (HPA) hormones, such as cortisol (Mellor et al., 2000; Molony and Kent, 1997; Toscano et al., 2003). Cortisol has been widely used as a measurement of distress since its response magnitude, as indicated by peak height, response duration and/or integrated response usually accords with the predicted noxiousness of different procedures (Benson et al., 1986; Chase et al., 1995; Prunier et al., 2005). However, much of the cortisol work in pigs has been linked to castration, tail docking and teeth crippling rather than pain associated with lameness. Limitations in measuring cortisol to directly quantify nociceptive response have been acknowledged in the literature. While peak cortisol response has been shown to correlate with the noxiousness of a procedure, interpretation at the lower and upper extent of the response range are reported to be less predictive (Coetzee et al., 2007). At the lower end, for example, studies have shown that tail docking with a ring and tail docking with a docking iron cause cortisol responses similar to control handling in older lambs. At the upper end of the range, there are several studies, including two published by Coetzee and others (2008a) that show cortisol responses do not increase proportionally with the severity of different treatments as might be expected. These observations may suggest a “ceiling effect” on plasma cortisol responses. Other studies have shown that plasma cortisol concentrations following surgical castrations vary greatly between animals (Earley and Crowe, 2002; Fisher et al., 2001). Based on these data, it has been hypothesized that low responses may be due to individuals having high pain thresholds. This theory supports the supposition that psychological factors influence interpretation and response to stimuli, reinforcing the need for validation using multiple methods. Variations may also come about due to differences in the way in which a particular castration method is performed by different operators. These data indicate that plasma cortisol concentrations may not always reflect the extent of pain response in animals. Since interpretation of elevated cortisol responses is complex and may be confounded, a more precise indicator of pain that can be measured independently or in conjunction with cortisol is urgently needed. ***Findings from our study indicate that lameness induced with amphotericin B was associated with elevated plasma cortisol levels relative to baseline and resolution days and could be considered a useful tool.***

Embedded Force plate and GAITFour®

Many techniques have been employed in other species to qualify and quantify lameness. Numerical rating scoring and visual analog scoring systems are common, but highly subjective with varying degrees of inter- and intra- observer correlation. Kinetic and kinematic gait analysis parameters have been collected and compared between limbs of the same animal. A study by Karriker et al., (2012) analyzed the use of GaitFour® walkway sensor system and static force plate to validate use of amphotericin B as a transient lameness model in sows. After induction of lameness the sows exhibited a decrease in maximum pressure, stance time and number of sensors activated. Their use of the static force plate also demonstrated a decrease in weight (kgs) being placed on the induced hoof when all feet were injected. Through the use of videography (kinematics), a pig’s gait can be recorded and the stride and joint angle parameters measure (Morrow et al., 1991; Thorup et al., 2007). Compensatory stride length and diagonality can be affected based on the traction conditions of the walking surfaces under the pigs’ feet (von Wachenfelt et al., 2008). Thorup and others (2008) showed differences in the maximum ground reaction forces between the front and hind limbs under varying flooring traction situations. This helps illustrate that the pig is able to redistribute its weight to assure a stable stance and locomotory capabilities.

Findings from our study indicate that the embedded force plate exhibited differences between sound and most lame indicating the force plate is an objective tool for detecting differences in weight distribution when sows are sound and lame. Furthermore, less weight was placed on the induced hoof between sound and resolved days, indicating that the transient lameness had not resolved. The GaitFour® walkway system

variables of maximum pressure, stride length, and stride time all demonstrated differences between sound and most lame days, suggesting that all are objective tools for differentiating between sound and lame states in sows. Stance time and maximum pressure showed differences between sound and resolved days, indicating that the transient lameness did not resolve for these tools. The stance time measure did not change over the 3 treatment days for the induced hooves, indicating that more research needs to be conducted with this measure to validate if it is an objective tool for lameness detection.

Pressure Algometry (PA) and Thermal Sensitivity (TS)

Mechanical nociceptive threshold (MNT) is defined as the amount of applied pressure necessary to produce pain (Fischer, 1987). Lower MNTs correlate with increased pain. Several published studies have researched the reliability and repeatability over consecutive days, and found that the pain threshold does not change in healthy human subjects over consecutive testing days (Nussbaum and Downes, 1998; Persson et al., 2004; Ylinen et al., 2007). Inter-examiner variability has also been tested using pressure algometry and results found good inter-rater reliability (Antonaci et al., 1998; Chesterton et al., 2007) concluded that inter-rater reliability has greater observer mean values than their first rating, and suggests that means rather than single measurements should be used in multiple-observer studies of MNT. Dyer and colleagues (2007) demonstrated that magnitude of claw pain in dairy cattle, as measured by MNT, correlated to the number and severity of lesions and locomotor disturbances. Stubsjøen and colleagues (2009) used an electric algometer to compare pain induced when a tourniquet was inflated on lambs' forelimbs. Varco-Cocks and colleagues (2006) quantified the intensity muscle pain in racehorses suspected to have sacroiliac dysfunction (SID) and found a significant correlation between the MNT and suspected manual palpation response, confirming that MNT was a repeatable test that can objectively measure muscle pain in horses.

Thermal nociception effects have been evaluated on humans classified as healthy and in pain (Granot et al., 2003; Djouhri et al., 2006; Agostinho et al., 2009). The TNT assessment using a laser technique has been used successfully to measure nociceptive thresholds in humans (Arendt-Nielsen and Bjerring, 1988), laboratory rodents (Fan et al., 1995) and farm animals (Veissier et al., 2000; Herskin et al, 2003, 2009). Veissier and colleagues (2000) first measured response latencies to a CO_2 laser in cattle and found that response latencies were lower at higher power settings and also and at least three tests were required to obtain reliable measures. Herskin and colleagues (2009) measured cutaneous thermal nociception on the hind limbs of group-housed swine using a CO_2 laser. Negative correlations were found between the output of the laser and latency to respond as well as positive correlations between output and forcefulness of the withdrawal response by the sow. ***Findings from our study indicates that both thermal- and mechanical tests (including all landmarks) were able to exhibit less tolerated thresholds when sows were acutely lame. However, both tools show a difference***

between sound and resolved days indicating that transient lameness did not resolve. Therefore, in conclusion, the physiology, kinematics and pain sensitivity tests within this study detected changes when sows were sound and in acute lameness and show promise in application on farm.

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Table 1. LSMeans for right and left hoof injected (±SE) for cortisol, embedded force plate, gait analysis, mechanical nociception and thermal nociception.

	Hoof injected[1]		
Test	**Right**	**Left**	**P-Value**
Cortisol (ng/ml)	20.96 ± 2.92	22.77 ± 2.85	0.66
Embedded Force Plate (kg)[2]	54.93 ± 1.06	54.79 ± 1.06	0.93
Gait Analysis			
Stride Time (sec)	0.494 ± 0.01	0.512 ± 0.01	0.01
Stride Length (cm)	88.34 ± 1.88	88.08 ± 1.88	0.71
Maximum Pressure (kg)	47.38 ± 1.06	47.25± 1.06	0.73
Stance Time (sec)	0.33 ± 0.01	0.34 ± 0.01	0.01
Mechanical Nociception (kgf/sec)	5.15 ± 0.21	5.37 ± 0.2	0.34
Thermal Nociception (sec)	9.95 ± 0.83	9.48 ± 0.83	0.68

[1]Hoof injected is either the right or left hoof made lame during induction

[2]Values represent the average weight placed on a hoof when right or left hoof is injected

Table 2. LSMeans for first and second trial of sows (±SE) for cortisol, embedded force plate, gait analysis, mechanical nociception and thermal nociception.

Test	Trial[1]		P-Value
	1	2	
Cortisol (ng/ml)	21.36 ± 3.02	22.36 ± 2.76	0.81
Embedded Force Plate (kg)[2]	57.08 ± 1.06	52.46 ± 1.06	0.005
Gait Analysis			
Stride Time (sec)	0.52 ± 0.02	0.49 ± 0.02	0.35
Stride Length (cm)	89.79 ± 2.61	86.62 ± 2.61	0.40
Maximum Pressure (kg)	51.52 ± 1.48	43.12 ± 1.48	0.0006
Stance Time (sec)	0.33 ± 0.01	0.34 ± 0.01	0.14
Mechanical Nociception (kgf/sec)	5.04 ± 0.23	5.48 ± 0.23	0.16
Thermal Nociception (sec)[3]	NA	NA	NA

[1]Trial defined as first (1) or second (2) group of sows. Trial 1= sows 1-12; Trial 2 = sows 13-24.

[2] Values represent the average weight placed on a hoof for trial 1 or 2.

[3]Thermal nociception test was only completed for trial 2 sows.

Table 3. LSMeans for first or second round of lameness induction (±SE) for cortisol, embedded force plate, gait analysis, mechanical nociception and thermal nociception.

	Round[1]		
Test	**1**	**2**	**P-Value**
Cortisol (ng/ml)	22.80 ± 2.95	20.92 ± 2.83	0.65
Embedded Force Plate (kg)[2]	54.29 ± 1.04	55.25 ± 1.04	0.52
Gait Analysis			
Stride Time (sec)	0.51 ± 0.01	0.50 ± 0.01	0.04
Stride Length (cm)	88.89 ± 1.88	87.53 ± 1.88	0.07
Maximum Pressure (kg)	47.54 ± 1.06	47.09 ± 1.06	0.22
Stance Time (sec)	0.34 ± 0.01	0.33 ± 0.01	0.09
Mechanical Nociception (kgf/sec)	5.52 ± 0.2	5.00 ± 0.21	0.04
Thermal Nociception (sec)	8.90 ± 0.82	10.53 ± 0.83	0.18

[1]Round defined as first (1) or second (2) induction of lameness

[2]Values represent average weight placed on a hoof during either first or second round of induction

Table 4. LSMeans for weight distribution on hooves (±SE) when sows were sound (D-1) most lame (D+1) and resolved (D+6) for the Prototype Embedded Microcomputer-based force plate system[1].

		Treatment day[4]		
Hoof induced[2]	**Hoof[3]**	**D-1**	**D+1**	**D+6**
LH	LF	61.56 ± 1.14[a]	66.25 ± 1.15[b]	65.41 ± 1.14[b]
	RF	66.18 ± 1.14[a]	66.19 ± 1.15[a]	66.38 ± 1.14[a]
	LH	**46.37 ± 1.14[a]**	**30.63 ± 1.15[b]**	**34.89 ± 1.14[c]**
	RH	46.47 ± 1.14[a]	52.55 ± 1.15[b]	54.42 ± 1.14[c]
RH	LF	61.58 ± 1.10[a]	65.38 ± 1.10[b]	64.94 ± 1.10[b]
	RF	66.19 ± 1.10[a]	66.81 ± 1.10[a]	68.53 ± 1.10[b]
	LH	44.54 ± 1.10[a]	54.57 ± 1.10[b]	53.46 ± 1.10[c]
	RH	**48.16 ± 1.10[a]**	**29.18 ± 1.10[b]**	**35.22 ± 1.10[c]**

[1]The Embedded Microcomputer Force Plate System (static force plate) was developed at Iowa State University to objectively identify sows that possess varying lameness severities (Sun et al., 2011).

[2]Left or Right hind hoof induction.

[3]LF = Left front hoof, RF = Right front hoof, LH = Left hind hoof, RH = Right hind hoof.

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 5. LSMeans for weight (±SE) when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the GaitFour® pressure mat gait analysis walkway system stride time[1]

		Treatment day[4]		
Hoof Induced[2]	**Hoof[3]**	**D-1**	**D+1**	**D+6**
LH	LF	0.459 ± 0.023[a]	0.574 ± 0.023[b]	0.496 ± 0.023[a]
	RF	0.457 ± 0.023[a]	0.569 ± 0.023[b]	0.493 ± 0.023[a]
	LH	**0.459 ± 0.023[a]**	**0.585 ± 0.023[b]**	**0.497 ± 0.023[a]**
	RH	0.460 ± 0.023[a]	0.592 ± 0.023[b]	0.505 ± 0.023[a]
RH	LF	0.470 ± 0.017[a]	0.546 ± 0.018[b]	0.474 ± 0.018[a]
	RF	0.468 ± 0.017[a]	0.544 ± 0.018[b]	0.472 ± 0.018[a]
	LH	0.468 ± 0.017[a]	0.551 ± 0.018[b]	0.475 ± 0.018[a]
	RH	**0.466 ± 0.017[a]**	**0.550 ± 0.018[b]**	**0.470 ± 0.018[a]**

[1]Stride time defined as the time in seconds between 2 successive footfalls by the same hoof

[2]Left or Right hind hoof induction.

[3]LF = Left front hoof, RF = Right front hoof, LH = Left hind hoof, RH = Right hind hoof.

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 6. LSMeans for weight (±SE) when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the GaitFour® pressure mat gait analysis walkway system stride length[1]

		Treatment day[4]		
Hoof Induced[2]	**Hoof[3]**	**D-1**	**D+1**	**D+6**
LH	LF	92.60 ± 2.27[a]	81.65 ± 2.28[b]	89.90 ± 2.27[a]
	RF	92.41 ± 2.27[a]	81.82 ± 2.28[b]	89.60 ± 2.27[a]
	LH	**92.72 ± 2.27[a]**	**81.70 ± 2.28[b]**	**90.09 ± 2.27[a]**
	RH	92.77 ± 2.27[a]	81.24 ± 2.28[b]	90.50 ± 2.27[a]
RH	LF	93.09 ± 2.14[a]	81.68 ± 2.16[b]	90.10 ± 2.16[a]
	RF	92.74 ± 2.14[a]	81.38 ± 2.16[b]	89.46 ± 2.16[c]
	LH	93.11 ± 2.14[a]	81.29 ± 2.16[b]	90.76 ± 2.16[a]
	RH	**92.88 ± 2.14[a]**	**81.36 ± 2.16[b]**	**89.90 ± 2.16[a]**

[1]Stride length defined as the distance in cm between 2 sequential footfalls from the same hoof

[2]Left or Right hind hoof induction.

[3]LF = Left front hoof, RF = Right front hoof, LH = Left hind hoof, RH = Right hind hoof.

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 7. LSMeans for weight (±SE) when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the GaitFour® pressure mat gait analysis walkway system maximum pressure[1]

		Treatment day[4]		
Hoof Induced[2]	**Hoof[3]**	**D-1**	**D+1**	**D+6**
LH	LF	57.73 ± 1.32[a]	55.83 ± 1.33[a]	57.82 ± 1.32[a]
	RF	56.90 ± 1.32[a]	57.59 ± 1.33[a]	57.48 ± 1.32[a]
	LH	**38.21 ± 1.32[a]**	**30.46 ± 1.33[b]**	**34.85 ± 1.32[c]**
	RH	36.19 ± 1.32[a]	42.46 ± 1.33[b]	41.47 ± 1.32[b]
RH	LF	57.16 ± 1.32[a]	60.23 ± 1.34[b]	58.21 ± 1.34[ab]
	RF	56.73 ± 1.32[a]	54.52 ± 1.34[a]	56.23 ± 1.34[a]
	LH	38.71 ± 1.32[a]	43.50 ± 1.34[b]	41.79 ± 1.34[b]
	RH	**37.27 ± 1.32[a]**	**28.72 ± 1.34[b]**	**35.42 ± 1.34[a]**

[1]Maximum pressure defined as the greatest amount of weight placed on a single hoof

[2]Left or Right hind hoof induction.

[3]LF = Left front hoof, RF = Right front hoof, LH = Left hind hoof, RH = Right hind hoof.

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 8. LSMeans for weight (±SE) when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the GaitFour® pressure mat gait analysis walkway system stance time[1]

		Treatment day[4]		
Hoof Induced[2]	**Hoof[3]**	**D-1**	**D+1**	**D+6**
LH	LF	0.306 ± 0.017[a]	0.394 ± 0.017[b]	0.330 ± 0.017[a]
	RF	0.302 ± 0.017[a]	0.423 ± 0.017[b]	0.341 ± 0.017[a]
	LH	**0.297 ± 0.017[a]**	**0.337 ± 0.017[a]**	**0.306 ± 0.017[a]**
	RH	0.294 ± 0.017[a]	0.440 ± 0.017[b]	0.344 ± 0.017[c]
RH	LF	0.313 ± 0.014[a]	0.402 ± 0.014[b]	0.325 ± 0.014[a]
	RF	0.309 ± 0.014[a]	0.365 ± 0.014[b]	0.305 ± 0.014[a]
	LH	0.301 ± 0.014[a]	0.417 ± 0.014[b]	0.318 ± 0.014[a]
	RH	**0.304 ± 0.014[ab]**	**0.322 ± 0.014[a]**	**0.286 ± 0.014[b]**

[1]Stance time defined as the duration of time (seconds) the sensors were activated by a hoof in a single stride

[2]Left or Right hind hoof induction.

[3]LF = Left front hoof, RF = Right front hoof, LH = Left hind hoof, RH = Right hind hoof.

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 9. LSMeans (±SE) on the sound and lame hoof for each landmark when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the mechanical nociception test (kgf)[1]

		Treatment day[4]		
Hoof status[2]	**Landmark[3]**	**D-1**	**D+1**	**D+6**
Sound	Cannon	6.58 ± 0.30^{a}	6.91 ± 0.30^{ab}	7.57 ± 0.30^{b}
	Medial claw	6.10 ± 0.30^{a}	6.96 ± 0.30^{b}	7.47 ± 0.30^{b}
	Lateral claw	5.51 ± 0.30^{a}	6.35 ± 0.30^{b}	6.68 ± 0.30^{b}
Lame	Cannon bone	7.03 ± 0.30^{a}	3.77 ± 0.31^{b}	4.33 ± 0.30^{b}
	Medial claw	7.34 ± 0.30^{a}	0.95 ± 0.31^{b}	2.08 ± 0.30^{c}
	Lateral claw	6.60 ± 0.30^{a}	0.92 ± 0.31^{b}	1.66 ± 0.30^{b}

[1]Mechanical nociception test used to quantify mechanical nociceptive thresholds (MNTs) in kilograms of force tolerated by the sow on the lame and sound limb (kgf)

[2]Status of hoof being measured; either sound or lame

[3]Cannon landmark defined as middle of cannon on the hind limb, Medial claw defined as1 cm above the coronary band on the medial hind claw, Lateral claw defined as 1 cm above the coronary band on the lateral hind claw

[4]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Table 10. LSMeans (±SE) on the sound and lame hoof when sows were sound (D-1) most lame (D+1) and resolved (D+1) for the thermal nociception threshold (TNT) test (seconds)[1]

Hoof status[2]	**Treatment day[3]**		
	D-1	**D+1**	**D+6**
Sound	10.25 ± 0.86[a]	9.87 ± 0.89[a]	11.60 ± 0.87[a]
Lame	11.99 ± 0.86[a]	5.02 ± 0.89[b]	9.55 ± 0.87[c]

[1]Thermal nociception threshold (TNT) test used to quantify the latency for a sow to withdraw her hind hoof in response to radiant heat stimulation

[2]Status of hoof being measured; either sound or lame

[3]D-1 defined as sound day (pre-induction), D+1 defined as most lame day (1 day post-induction), D+6 defined as resolved day (6 days post-induction).

[ab]Within a row, means without a common superscript differ ($P < 0.05$).

Figure 1. Aerial view of the Prototype Embedded Microcomputer-based force plate system

Figure 2. Data being collected on a sow embedded microcomputer-based force plate system

Figure 3a. The GAITFour® pressure mat

Figure 3b. Data being collected on the GaitFour® pressure mat

Figure 4a. Mechanical Nociception Threshold (MNT) test on Cannon landmark

Figure 4b. Mechanical Nociception Threshold (MNT) test landmarks. 1. 1 cm above the coronary band on the lateral hind claw (Outer), 2. 1 cm above the coronary band on the medial hind claw (Inner) and 3. Middle of cannon on the hind limb (Cannon)

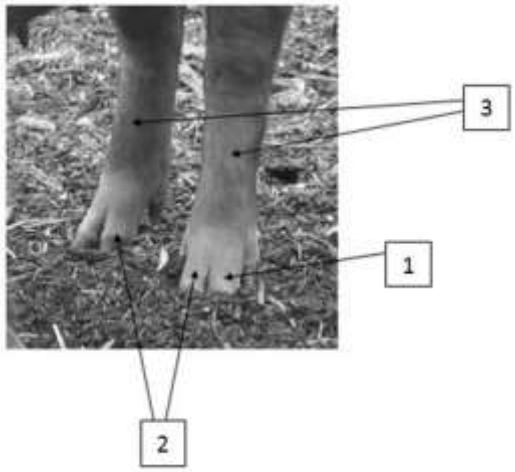

Figure 5. Thermal Nociception Threshold (TNT) test

Figure 6. Cortisol concentrations (ng/ml) when sows were sound (D-1) most lame (D+1) and resolved (D+6). Differences *P* < 0.0001.