

Administration of ACTH to Pregnant Sows Alters the Offspring's Physiology in Response to Stress

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Summary and Implications

Modern intensive farming may be stressful to animals because of the high degree of confinement, . . . has the potential to lead to overcrowding and stress. Chronic stress to the pregnant dam may affect her developing fetus, a process that has been termed prenatal stress. Prenatal stress has been shown to cause a number of adverse effects in offspring. These effects are thought to be mediated through maternal glucocorticoids that are released by adrenocorticotropic hormone (ACTH). The object of this study was to determine if administration of ACTH to pregnant sows would alter the physiological response of their offspring during stress later in life. Our data indicate that administration of ACTH to pregnant sows prolongs their offspring's response to a stressor at 2.5 months of age and decreases their ability to heal wounds. Future research needs to identify the specific management practices that are chronically stressful to sows during gestation so that these practices can be altered to form a less stressful environment, and thus produce offspring that are able to perform optimally.

Introduction

In modern-day farming, many management practices are considered to be stressful to livestock species. Specifically, many swine operations subject their animals to intense confinement and this has made intensive hog farming one of the most criticized agricultural systems in the United States. Confinement of swine is considered a potent chronic stressor that may cause a long-term activation of the hypothalamo-pituitary-adrenal (HPA) axis that will increase the concentration of adrenocorticotropic hormone (ACTH) in these sows. Chronic stress to the pregnant dam also may affect her developing fetus, a process that has been termed prenatal stress.

Maternal glucocorticoids are stress hormones that are released by ACTH, and they have been shown to cross the placenta in pigs, and in rats, they have been shown to cross the placenta and bind to the fetal hypothalamus. These maternal hormones have the potential to affect the maturation of the fetal HPA axis, which in turn may alter HPA function later in life.

Stressing pregnant rats causes many effects on the offspring, including alteration of emotional reactivity, decreased inclination for social interaction, alteration of

sexual behavior in males and females, and a prolonged glucocorticoid response in reaction to a restraint stress. However, a limited amount of prenatal stress research has occurred in livestock. It was determined that prenatal stress in swine does not alter the libido and testosterone concentrations of male offspring. However, prenatally stressed calves were reported to have heavier body weights, pituitary glands, and heart weights, as well as a greater increase in plasma cortisol (cortisol is the predominant glucocorticoid in livestock) and slower plasma cortisol clearance rates in response to stressed compared with control calves.

Sows are subjected to a high degree of confinement for most of their lives and this possible potent stress may have diverse effects on the fetus. Because other studies have reported that ACTH administration to pregnant dams replicates the effects of prenatal stress, the objective of this study was to determine differences in the physiology and behavior of pigs whose dams were administered ACTH during gestation compared with pigs from noninjected dams.

Materials and Methods

Nineteen Yorkshire \times Landrace sows were bred to Duroc \times Hampshire boars and were randomly assigned to either the control (C = 8) or the adrenocorticotropic hormone injected (ACTH = 8) treatments. All sows were maintained in gestation stalls and subjected to normal management practices except that ACTH sows were administered ACTH at a dose of 1 IU/kg of body weight at 6, 7, 8, 9, 10, 11, and 12 weeks, whereas the control sows (C) were left undisturbed for the entire gestation period. The ACTH sows were weighed weekly to determine the correct dose and then immobilized by snaring the snout so ACTH could be injected via the jugular vein. To determine the sow's glucocorticoid response to the ACTH injection, four C sows and four ACTH sows had blood collected, via the jugular vein, at 0, 30, 60 and 120 min after administration of treatments (ACTH and saline, respectively) during the 11th and 12th weeks of gestation.

Sows from both treatments farrowed in traditional farrowing stalls (Lage Products Co., Inc., Montezuma, IA) that were 1.5 \times 2.3 m with a width of 61 cm for the sow and creep areas on both sides for piglets (45.72 cm \times 2.3 m). All crates were equipped with plastic-coated expanded metal flooring and a heat lamp, which was placed 20 cm away from the sow's shoulder. Within 12 to 24 h after the completion of farrowing, piglets were weighed and sexed. All other production data (e.g. stillborns, mummies, low viability) also were obtained.

At 75 d of age, one female pig, ranking second in dominance in her pen (n=5 per pen), was used in a stress

test to determine cortisol concentrations and immune function. From these pigs a blood sample was taken and a punch was used to create a biopsy puncture on the pigs right, hind quarter to determine wound healing. These subdominant pigs were then randomly placed into a pen of unfamiliar pigs. Mixing of unfamiliar pigs is recognized as a strong social stress. Blood samples were obtained every other day, at 0800 hours, for a total of 10 days and the wound created by the biopsy was evaluated for inflammation and healing at these times. For inflammation, a score of 1 denoted no inflammation, 2 = slightly red, 3 = red, and 4 = red and pus. Healing ability score was dependent on how much of the puncture created by the punch biopsy was filled in (healed), a score of 1 = the wound is at the level of surrounding tissue, 2 = the wound is above the level of surrounding tissue, 3 = the wound is below the level of surrounding tissue, and 4 = no healing.

Results and Discussion

During the 11th and 12th weeks of gestation, the four ACTH sows that had blood collected, via the jugular vein, at 0, 30, 60, and 120 min after administration of ACTH had greater concentrations of plasma cortisol compared with the four C sows after administration of saline (ACTH = 159.84 ± 16.06 ng/ml, C = 57.54 ± 2.70 ng/ml; P=.0002). Furthermore, a treatment by time interaction indicated that time zero was not different between treatments (P=.30), but at times 30, 60, and 120 ACTH sows had greater concentrations of cortisol than C sows (P=.0001).

There was no difference in litter size (11.25 ± .81), number of piglets born alive (10.31 ± .73), stillbirths (.94 ± .38), or crushing (.38 ± .15) between C and ACTH sows (P>.5). In addition, gestation length did not differ between C and ACTH sows (115.38 ± .34 days; P=.23). Piglet birth interval also was not different for C and ACTH sows (22.33 ± 3.76 min; P=.69).

Control pigs had lesser concentrations of plasma cortisol than ACTH pigs during the mixing stress (C = 59.61 ± 3.83 ng/ml, ACTH = 70.58 ± 3.79 ng/ml; P=.03). Although there was no treatment by day interaction, it appears as if ACTH pigs plasma cortisol concentration remained higher then C pigs until day 5 of the mixing stress (Figure 1).

Observation of punch wounds indicated C pigs healed more slowly than ACTH pigs (C = 2.47 ± .06, ACTH = 2.77 ± .09; P=.006). Specifically, day 3, 5 and 7 did not differ between treatment groups (P>.56), but C pigs had lesser

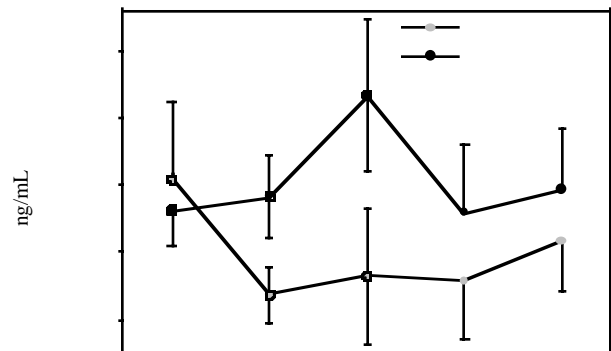


Figure 1. Plasma cortisol concentrations in response to the mixing stress test for C and ACTH pigs (P = .03).

evaluation scores than ACTH pigs during days 9 (C = 1.70 ± .10, ACTH = 2.78 ± .10, P=.0001) and 11 (C = 1.83 ± .15, ACTH = 2.94 ± .15; P=.0001; Figure 2). This suggests that the C pigs= punch wounds healed at a faster rate than the ACTH pigs= wounds.

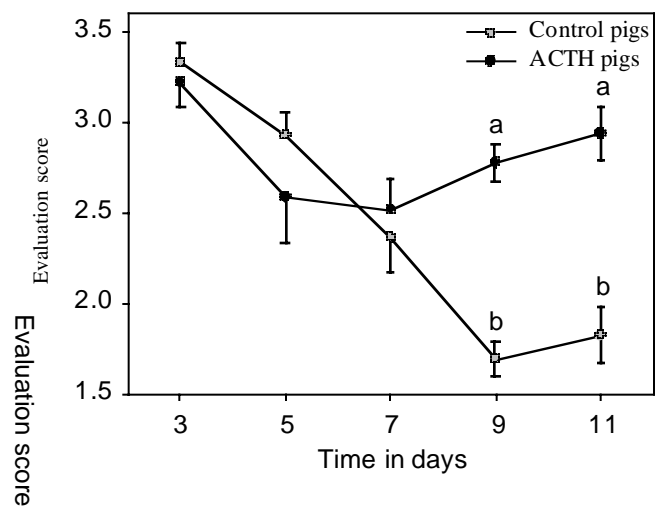


Figure 2. Indirect evaluation score of biopsy puncture for inflammation and healing during mixing stress test for C and ACTH pigs. Biopsy puncture was produced on day 1 and evaluated initially on day 3. ^{a,b}Means ±SEM with different superscripts differ (P<.0001).

The results of this study indicate that administration of exogenous ACTH during gestation alters the HPA axis of the sow's subsequent offspring. Similar to previous research, this study indicates that administration of ACTH to pregnant dams replicates the effects of various prenatal stressors, including restraint and heat, unpredictable noise, and transportation stress. The findings that ACTH administration is similar to prenatal stress suggest that although stressors cause the synthesis and release of many hormones in the pregnant female, the predominant causal agent of prenatal stress may be activation of the HPA axis.

In this study, ACTH administration to sows caused a 3-fold increase in plasma cortisol concentrations at the 30-, 60-, and 120-min time periods. Plasma cortisol concentrations were still maximal at the last sampling period, which indicates that administration of 1 IU/kg bodyweight ACTH will effectively raise plasma cortisol concentrations for a minimum of 2 h and probably longer.

During the mixing stress, C pigs had lesser concentrations of plasma cortisol than ACTH pigs. This agrees with previous evidence that prenatally stressed animals are physiologically predisposed to overreact to stressful stimuli. This has been proven in a number of

studies, wherein prenatally stressed animals have exhibited an increased concentration of ACTH and/or glucocorticoids in response to stressful situations compared with control animals. Because mixing of unfamiliar individuals is considered stressful in swine, mixing of litters served as a potent stressor in this study.

There is also evidence that stress can alter multiple aspects of immune function, including inhibiting the production of proinflammatory cytokines that are important for wound repair. Stress also can cause a decrease in neutrophil function, which increases the risk of infection after wounding. To investigate the effects of the mixing stress on immune function, a small puncture was created in pigs with the use of a punch biopsy. Observation of punch wounds showed it took the ACTH pigs longer to heal the wound than it did for the C pigs.

In conclusion, prenatal stress, in the form of weekly injections of ACTH to pregnant sows, results in pigs that react to stressful stimuli with a robust cortisol response and that have a decreased immune function. It is possible that during stressful situations later in life this state may compromise growth, health, reproduction, and welfare.