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Stress-related gene expression in brain and adrenal gland of porcine fetuses and neonates

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Abstract

This study was conducted to examine stress-induced effects on gene expression of specific markers for HPA axis and neuronal activity in fetuses and neonatal pigs. Brain, pituitary gland, and adrenal gland were obtained to determine the mRNA levels for corticotropin-releasing hormone (CRH), CRH receptor 1 (CRHR1), pro-opiomelanocortin (POMC), ACTH receptor (MC2R), c-jun and c-fos. The suitability of these molecular markers was determined in neonatal pigs which were maternally deprived for two hours. It was found that maternal deprivation caused significantly higher transcript levels of c-fos and CRH in brain accompanied by a down-regulation of CRHR1 mRNA and an up-regulation of c-jun in the pituitary gland. To determine the effect of elevated maternal cortisol levels on gene expression of these molecular markers in fetuses, pregnant sows were treated with 100 IU ACTH (Synacthen® Depot) s.c. every two days between Day 49 and Day 75 of gestation (normal gestation length 114 days). Animals were killed 48 hours after the last ACTH administration and fetuses of each sow were isolated. The ACTH treatment of sows significantly increased mRNA expression of c-fos but not of CRH in the fetal brain, and significantly decreased MC2R mRNA expression in the adrenal gland. However, HPA axis seems not to be fully developed in Day 77-fetuses

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because fetal pituitary CRHR1 and POMC mRNA expression was low in most of the fetuses. Although the expression of endocrine regulatory factors was partially incomplete in fetuses at the beginning of the third-trimester, ACTH dependent activation of c-fos mRNA in brain indicates a stress-related increase of neuronal activity. Based on these results it is assumed that prenatal stress in pigs may also have effects on the activity of the HPA axis in the offspring.

Keywords: Stress response; HPA axis; Prenatal stress; Fetus; Pig

1. Introduction

The activation of the hypothalamo–pituitary–adrenal (HPA) response to stress is under central regulation. Stress-related stimuli facilitate the hypothalamic secretion of CRH which stimulates pituitary ACTH secretion through type 1 CRH receptors [1]. POMC synthesized in the brain and pituitary gland is the pro-hormone for ACTH [2], and in the adrenal gland the ACTH receptor is involved in biosynthesis and release of glucocorticoids.

Maternal stress during gestation was found to cause short-term and persistent effects on the behaviour, physiology and performance in the offspring of many species e.g., [3–6]. The HPA axis has been proposed as a possible neurobiological substrate for these physiological and behavioural consequences of prenatal stressful events [4,7]. Although several stress-induced factors, e.g., neurotransmitters, opioids and neurosteroids were assumed to be involved in long-term changes of the HPA axis, it was shown that maternal glucocorticoids play a major role in mediating the effects of maternal stress to the fetuses [8,9]. They are able to cross the placental barrier in various species, e.g., rats [10], sheep [11], pigs [12,13], and numerous studies have shown that excess levels of these maternal hormones can cause a dysregulation of the HPA axis response in the offspring [4,5,7].

In livestock farming, many management practices are considered to be stressful to farm animals [14,15]. Housing conditions, handling by humans and disruption of social contacts during gestation may influence the performance, behaviour and stress susceptibility of the offspring. Therefore, prenatal stress in farm animals may affect economic aspects of production as well as animal health and welfare. Furthermore, livestock species such as pigs may serve as an appropriate model for studying effects of prenatal stress in humans due to many similarities in physiology and development.

In pigs, prenatal restraint stress during late gestation resulted in a dysregulation of the HPA axis shortly after birth, an impaired immune response and a higher morbidity and mortality during the suckling period [16–18]. In addition, it was shown that ACTH injections in combination with restraint during mid-gestation of sows caused long-term effects with higher adrenal cortex-to-medulla area ratios, increased plasma cortisol concentrations after regrouping of animals and delayed wound healing in the offspring [19]. Based on these results it is assumed that prenatal stress in pigs may have a profound influence on the HPA axis activity in the offspring.

Because no information is available about the expression of stress-related genes during fetal development of pigs, this study was conducted to examine the mRNA abundance of