J. Dairy Sci. 99:1549–1559
http://dx.doi.org/10.3168/jds.2015-10131

Longitudinal changes in adipose tissue of dairy cows from late pregnancy to lactation. Part 1: The adipokines apelin and resistin and their relationship to receptors linked with lipolysis

M. Weber,* L. Locher,† K. Huber,‡[1] Á. Kenéz,‡[1] J. Rehage,† R. Tienken,§ U. Meyer,§ S. Dänicke,§ H. Sauerwein,* and M. Mielenz*[2,3]

*Institute of Animal Science, Physiology and Hygiene Unit, University of Bonn, 53115 Bonn, Germany
†Clinic for Cattle, University of Veterinary Medicine Hannover, 30173 Hannover, Germany
‡Department of Physiology, University of Veterinary Medicine Hannover, 30173 Hannover, Germany
§Institute of Animal Nutrition, Friedrich-Loeffler-Institute (FLI), Federal Research Institute for Animal Health, 38116 Braunschweig, Germany

ABSTRACT

The transition from pregnancy to lactation is characterized by major changes in glucose and adipose tissue metabolism. Anti- and prolipolytic pathways mediated via the hydroxycarboxylic acid receptors 1 (HCAR1) and 2 (HCAR2) and tumor necrosis factor-α receptor 1 (TNFR1), as well as the adipokines apelin and resistin, are likely involved in regulating these processes. This study aimed to determine the mRNA abundance of the aforementioned receptors in both subcutaneous and visceral adipose tissue, to characterize the adipokine concentrations in serum, and to test the effects of feeding diets with either high or low portions of concentrate and a concomitant niacin supplementation from late gestation to early lactation. Twenty pluriparous German Holstein cows were all kept on the same silage-based diet until d 42 antepartum, when they were allocated to 2 feeding groups: until d 1 antepartum, 10 animals each were assigned to either a high-concentrate (60:40 concentrate-to-roughage ratio) or a low-concentrate diet (30:70). Both groups were further subdivided into a control and a niacin group, the latter receiving 24 g/d of nicotinic acid from d −42 until 24. From d 1 to 24 postpartum, the concentrate portion was increased from 30 to 50% for all cows. Biopsies of subcutaneous (SCAT) and retroperitoneal adipose tissue (RPAT) were taken at d −42, 1, 21, and 100 relative to parturition. Blood samples were drawn along with the biopsies and on d −14, 3, 7, 14, and 42. The concentrations of the adipokines apelin and resistin in serum were measured via ELISA. The mRNA of the 3 receptors in AT was quantified as well as the protein abundance of HCAR2 by Western blot. The feeding regimen did not affect the variables examined. The concentrations of apelin remained fairly constant during the observation period, whereas the resistin concentrations increased toward parturition and decreased to precalving levels within 1 wk after calving. The mRNA abundance of *HCAR1*, *HCAR2*, and *TNFR1* changed in SCAT and RPAT during the considered time period. For the HCAR2 protein, time-dependent changes were restricted to SCAT. The mRNA abundance of all receptors was greater in RPAT than in SCAT. The tissue-specific correlations observed between the receptors point to a link between these factors and may indicate different regulatory roles in the respective tissues. This study provides insight into the complex metabolic adaptations during the transition period and supports a differential regulation of lipolysis among SCAT and RPAT in dairy cows.
Key words: dairy cow, transition period, hydroxycarboxylic acid receptor, apelin, resistin

INTRODUCTION

In dairy cows, the transition from late gestation to lactation is characterized by major metabolic changes. The requirements for nutrients increases rapidly after calving and not all animals can increase nutrient intake fast enough to meet those requirements (Grummer, 1995). Homeorhetic adaptations are necessary to facilitate the nutrient partitioning toward the mammary gland and to cover the energy demands for milk production (Bauman and Currie, 1980). These adaptations are accompanied by decreased peripheral insulin sensitivity (Bell and Bauman, 1997) and increased lipolysis (McNamara and Hillers, 1986).

Received July 18, 2015.
Accepted October 16, 2015.
[1]Present address: Institute of Animal Science, University of Hohenheim, 70599 Stuttgart-Hohenheim, Germany
[2]Present address: Institute of Nutrition Physiology "Oskar Kellner," Leibniz Institute for Farm Animal Biology (FBN), 18196 Dummerstorf, Germany
[3]Corresponding author: mielenz@fbn-dummerstorf.de

As discussed by Duncan et al. (2007), the hydrolysis of triacylglycerols displays the initial step of lipolysis. In adipose tissue of dairy cows this process is mediated via phosphorylation of hormone-sensitive lipase (**HSL**) under stimulation of catecholamines (McNamara and Hillers, 1986; Sumner and McNamara, 2007; Locher et al., 2011). The increased lipolysis is at least partly mediated via an increased expression of the β-adrenergic receptors, with the β-2 receptors being suggested as the most important subtype (Sumner and McNamara, 2007; Sumner-Thomson et al., 2011). The adipocyte-derived factors (adipokines) apelin and resistin, as well as the hydroxycarboxylic acid receptors 1 (**HCAR1**) and 2 (**HCAR2**) and tumor necrosis factor-α receptor 1 (**TNFR1**) are likely relevant as regulatory elements in these processes.

Apelin is an adipokine, which is upregulated by insulin (Boucher et al., 2005) and was shown to increase glucose uptake by adipose tissue (**AT**) and skeletal muscle in mice (Dray et al., 2008). It is supposed to play a physiological role in glucose metabolism (Dray et al., 2008). In addition, apelin decreases lipolysis in mice by inhibiting the phosphorylation of HSL (Yue et al., 2011). In dairy cows, apelin was demonstrated in serum and milk (Aydin, 2013), but the time-course of the serum apelin concentrations during lactation was unknown.

The prolipolytic tumor necrosis factor-α (**TNF-α**), whose main effects are mediated by its receptor TNFR1 (Sethi et al., 2000), was shown to upregulate apelin expression (Daviaud et al., 2006); thus, a negative feedback loop has been suggested between these 2 factors (Yue et al., 2011). The abundance of *TNF-α* mRNA in bovine subcutaneous AT (**SCAT**) was reported to increase from wk 8 antepartum (**a.p.**) to the day of parturition without further change until 5 wk thereafter (Sadri et al., 2010), to remain unchanged when considering pluriparous cows from d 21 a.p. to 252 DIM, or to increase in primiparous cows from d 1 to d 42 postpartum (**p.p.**) (Saremi et al., 2014). To our knowledge, the mRNA expression pattern of *TNFR1* in bovine AT is still unknown.

The adipokine resistin is associated with blood glucose concentrations and insulin sensitivity (Steppan et al., 2001). Recently, the plasma resistin concentrations in dairy cows were demonstrated to increase 1 wk after calving; moreover, recombinant resistin stimulated lipolysis in vitro (Reverchon et al., 2014).

The receptors HCAR1 and HCAR2 belong to the family of G-protein-coupled receptors and are activated by hydroxylated carboxylic acids (Offermanns et al., 2011). The receptor HCAR1, which is mainly expressed on adipocytes (Wise et al., 2003), mediates insulin-induced antilipolytic effects via binding lactate (Cai et al., 2008), a quantitatively important substrate for gluconeogenesis next to propionate (Aschenbach et al., 2010). After parturition, the hepatic uptake of lactate increases without affecting the circulating concentrations (Larsen and Kristensen, 2009). Significant amounts of lactate are produced by the ruminal microbes when cows are fed a diet rich in starch (Aschenbach et al., 2010).

The receptor HCAR2 is activated by its endogenous ligand BHB (Gille et al., 2008), as well as by pharmacological doses of nicotinic acid, and exerts antilipolytic effects after binding of its ligands (Tunaru et al., 2003). In humans and mice, HCAR2 is mainly expressed on adipocytes and immune cells (Tunaru et al., 2003; Wise et al., 2003). In cattle, HCAR2 was also found in different brain regions, including the hypothalamus; this might enable the central nervous system to sense the circulating BHB concentrations (Titgemeyer et al., 2011). Recently, the mRNA abundance of *HCAR2* was shown to decrease from d 21 a.p. to d 105 p.p. in bovine SCAT (Friedrichs et al., 2014). Both, HCAR1 and HCAR2 are regulated via peroxisome proliferator-activated receptor γ (Jeninga et al., 2009). During the transition period, AT is important for providing energy in the form of fatty acids (Drackley, 1999).

Studies in humans and rodents have shown that AT from different sites (i.e., visceral AT and SCAT) differ in their metabolic activity (Smith and Zachwieja, 1999). Comparable to SCAT, retroperitoneal AT (**RPAT**) is not draining into the portal circulation (Rebuffé-Scrive et al., 1989; Björntorp, 1990). Further, RPAT contains more transcripts of genes related to lipogenesis and lipolysis, whereas the mRNA of genes related to fatty acid β-oxidation are more abundant in the portal draining mesenteric AT (Rebuffé-Scrive et al., 1989; Palou et al., 2009). To our knowledge, less data are available on RPAT dynamic during the transition period of dairy cows. In primiparous German Holstein cows with rather low BW and milk production, the mass of SCAT was shown to change only marginally during the first 105 d of lactation, whereas the RPAT depot decreased significantly during this time (von Soosten et al., 2011). Furthermore, the postpartum feeding regimen influences the phosphorylation pattern of HSL, especially in RPAT (Locher et al., 2011); this suggests that RPAT might be more sensitive to periparturient challenges than SCAT (Locher et al., 2011). Therefore, the aim of the current study was to test whether feeding different amounts of concentrate in the prepartum period and a concomitant niacin supplementation, both aiming at inducing differences in energy balance, may affect the serum concentrations of apelin and resistin as