Livestock Science 214 (2018) 62–67

Contents lists available at ScienceDirect

Livestock Science

journal homepage: www.elsevier.com/locate/livsci

# Stimulating lipolysis in subcutaneous adipose tissues by chronic dexamethasone administration in goats

Hua Canfeng, Geng Yali, Niu Liqiong, Chen Qu, Cai Liuping, Tao Shiyu, Ni Yingdong*, Zhao Ruqian

*Key Laboratory of Animal Physiology & Biochemistry, Nanjing Agricultural University, Nanjing 210095, PR China*

ARTICLE INFO

*Keyword:*
Adipose tissue
Dexamethasone
Goats
Lipolysis

ABSTRACT

The objective of this study was to investigate the effects of chronic stress induced by a low dosage of dexamethasone (Dex) on the lipolytic response in adipose tissue of goats. Ten male goats were randomly assigned to two groups; one group was injected subcutaneously with 0.2 mg/kg Dex, and the other group was injected subcutaneously with the same volume of saline as a control (Con) for 21 days. The result revealed that plasma triglycerides (TG) ($P < 0.05$) concentrations decreased in response to Dex administration. Plasma glycerol, mainly derived from degradation of TG, increased during the Dex treatment ($P < 0.05$). Expression of genes involved in lipolysis—including G protein β subunit (*Gnb1*) ($P < 0.01$), hormone-sensitive lipase (*Lipe*) ($P < 0.05$), and perilipin-3 (*Plin3*) ($P < 0.05$) — were up-regulated in adipose tissue by Dex. Paralleling the increase in gene expression, the pLIPE/LIPE ratio also increased in response to Dex, which reflected higher LIPE activity, in adipose tissue ($P < 0.05$). However, the expression of genes involved in fatty acids synthesis—such as acetyl CoA carboxylase (*Acc*), fatty acid synthase (*Fas*), and stearoyl-CoA desaturase (*Scd*)—were not changed by Dex, while the abundance of diglyceride acyltransferase 1 and 2 (*Dgat1* and *Dgat2*) mRNA, which catalyze the formation of TGs from diacylglycerol and Acyl-CoA, increased ($P < 0.05$) in adipose tissue of Dex-treated goats compared with Con goats. Moreover, plasma leptin concentration decreased in response to Dex; however, *Leptin* mRNA expression tended to increase in adipose tissue, indicating a negative feedback regulatory mechanism. *Adiponectin* gene expression was also up-regulated in adipose tissue by Dex ($P < 0.05$). Taken together, our findings demonstrate that chronic glucocorticoid administration induces an imbalance in TG metabolism, resulting in a lower level of leptin and a higher level of glycerol in blood by promoting lipolysis and *Gnb1* and *Plin3* expression in adipose tissue, as well as increasing the pLIPE: LIPE ratio.

## 1. Introduction

The hypothalamic-pituitary-adrenal (HPA) axis becomes activated and cortisol is released into circulation when animals are exposed to stressful conditions, such as an unfavorable environment, psychological stress, surgery, or disease (Silanikove, 2000). Plasma cortisol concentration declines to a basal level once an animal has adapted to a chronic stress (Silanikove, 2000). A subcutaneous injection of dexamethasone (Dex) has been experimentally used to simulate the stress response in goats (Shamay et al., 2000).

Subacute ruminal acidosis (SARA) is a common chronic metabolic disease in ruminant animals. Our previous studies showed that SARA induced by feeding a high-concentrate diet to lactating dairy goats, activates the HPA axis and increases plasma cortisol levels (Jia et al., 2014). Furthermore, inducing SARA also disturbs lipid and glucose metabolism by decreasing plasma triglyceride (TG) concentrations and increasing hepatic gluconeogenic enzyme activities (Dong et al., 2017). However, the knowledge of the direct effect of stress hormones on lipid metabolism in goats remains limited.

Adipose tissue plays an essential role in energy metabolism by secreting adipokines that regulate energy storage and dissipation (Stern and Scherer, 2015). In mammals, energy is stored within adipose tissue in the form of TG. During fasting or exercises, TGs are metabolized into non-esterified fatty acids (NEFAs) (Slavin et al., 1994; Xu et al., 2009) and glycerol (Slavin et al., 1994), which are released into circulation to meet the increased energy demands of the organism. Glucocorticoids (GCs) are key regulators of energy flux within adipocytes by activating hormone-sensitive lipase (LIPE) and adipose triglyceride lipase (PNPLA2) (Geer et al., 2014).

GCs are secreted in the body under stress conditions, with broad

* Corresponding author.
*E-mail address:* niyingdong@njau.edu.cn (Y. Ni).

https://doi.org/10.1016/j.livsci.2018.05.020
Received 15 April 2017; Received in revised form 23 May 2018; Accepted 27 May 2018

**Table 1**
Primers and sequences used in this study.

| Genes | Sequences 5′ – 3′ | Source | Accession number | Product size (bp) |
|---|---|---|---|---|
| **Lipolysis** | | | | |
| *ANGPTL4* | F:GGGCTGTCATTCGTCTTTCCTC<br>R:CGCATCCTTCCTGGTGGTTCA | | HQ008534 | 89 |
| *PNPLA2* | F:GGAGCTTATCCAGGCCAATG<br>R:TGCGGGCAGATGTCACTCT | (Shi et al., 2013) | | 226 |
| *GNB1* | F:GCCACAGTGACTGGAAGAC<br>R: TGAAGTTCTGAAGGGTGC | | XM_018060496 | 132 |
| *LIPE* | F:CTTTCGCACCAGCCACAAC<br>R:CTCGTCGCCCTCAAAGAAGA | (Xu et al., 2015) | | 136 |
| *PLIN3* | F:GGTGGAGGGTCAGGAGAAA<br>R:TCACGGAACATGGCGAGT | (Shi et al., 2013) | | 170 |
| **Triglyceride synthesis** | | | | |
| *DGAT1* | F:CCACTGGGACCTGAGGTGTC<br>R:GCATCACCACACACCAATTCA | (Shi et al., 2013) | | 101 |
| *DGAT2* | F:TCCTGTCTTTCCTCGTGC<br>R:TGACCTCCTGCCACCTT | | NM_001314305 | 183 |
| *PDE3B* | F:CAACAATGGCAAACGG<br>R:TTCGGGACTGTCAGTAGAT | | XM_018059586 | 79 |
| **Lipogenesis** | | | | |
| *ACC* | F:AGCCTGCGGAATAGCATCTC<br>R:CCACGTAGGAGTTTGGGGAC | (Yang et al., 2016) | | 157 |
| *FAS* | F:GCTTCCTTCTTCGGTGTCCA<br>R:CATGCTGTAGCCTACGAGGG | (Yang et al., 2016) | | 213 |
| *SCD* | F:CCATCGCCTGTGGAGTCAC<br>R:GTCGGATAAATCTAGCGTAGCA | (Shi et al., 2013) | | 257 |
| **Nuclear transcription factors** | | | | |
| *GR* | F:GGAATAGATGCCAAGGGTC<br>R:CAGAGTTTGGGAGGTGGTC | | NM_001114186 | 169 |
| *PPARα* | F:TAAAGCCAACCAAGATAACCC<br>R:TCACCAAACAGCCGAAGA | | HM600810.1 | 243 |
| *PPARγ* | F:GACCACTCCCATGCCTTTGA<br>R:AACCATCGGGTCAGCTCTTG | (Yang et al., 2016) | | 108 |
| **Adenylate cyclase** | | | | |
| *ADCY3* | F:ATGGACTGCCTGAAAGGAGA<br>R:TTGGAAGCGATGATGAGGTA | (Zhao et al., 2016) | | 107 |
| *ADCY6* | F:GCAGCAAGTACAGCCATCC<br>R:GCCGCTAAACCACGACAT | | XM_018047857 | 158 |
| *ADCY8* | F:CCTTGTATGCTAATGCCTTGCG<br>R:GGAATAGAGGGTCTCCTTTACGC | | XM_018058572 | 201 |
| **Cytokines** | | | | |
| *LEPTIN* | F:GACATCTCACACACGCAGTC<br>R:TGGCGAGGATCTGTTGGTAG | (Yang et al., 2016) | | 133 |
| *ADIPONECTIN* | F:GGCTCTGATTCCACACCTGA<br>R:GAATGCCTGCCATCCAACCT | (Yang et al., 2016) | | 145 |
| **Housekeeping** | | | | |
| *18S RRNA* | F:GTGATGGGGATCGGGGATTG<br>R:GTAGCGACGGGCGGTGTGTA | (Bai et al., 2014) | | 125 |

ANGPTL4: angiopoietin-like 4; Pnpla2: adipose triglyceride lipase; GNB1: G protein β subunit; LIPE: hormone-sensitive lipase; PLIN3: perilipin-3; DGAT1: diglyceride acyltransferase 1; DGAT2: diglyceride acyltransferase 2; PDE3B: phosphodiesterase 3B; ACC: acetyl CoA carboxylase; FAS: fatty acid synthase; SCD: stearoyl-CoA desaturase; GR: glucocorticoid receptor; PPARα: peroxisome proliferator-activated receptor α; PPARγ: peroxisome proliferator-activated receptor γ; ADCY3: adenylate cyclase isoforms 3; ADCY6: adenylate cyclase isoforms 6; ADCY8: adenylate cyclase isoforms 8.

effects on anti-inflammation and carbohydrate, lipid, and protein metabolism; GCs are also widely used as drugs. Studies on rats demonstrate that administering Dex increases the amount of glycerol (Slavin et al., 1994) and NEFA (Slavin et al., 1994; Xu et al., 2009) released from adipocytes. Dex down-regulates mRNA and protein levels of phosphodiesterase 3B (*Pde3b*), thereby elevating cellular cAMP production and activating protein kinase A (PKA) (Xu et al., 2009). Activation of LIPE (Sztalryd et al., 2003) and PNPLA2 (Watt and Steinberg, 2008) induced by GCs cooperatively regulates the lipolytic reaction in adipocytes. However, the mechanism of lipolysis induced by chronic Dex treatment in ruminants is unclear. The objective of this study was to investigate the effects of chronic stress, induced by low dosage of Dex, on the lipolytic response in adipose tissue of goats.

## 2. Materials and methods

### 2.1. Ethics

The Institutional Animal Care and Use Committee (IACUC) of Nanjing Agricultural University approved all animal procedures. The "Guidelines on Ethical Treatment of Experimental Animals" (2006) No. 398 set by the Ministry of Science and Technology, China, and "Regulation regarding the Management and Treatment of Experimental Animals" (2008) No. 45 set by the Jiangsu Provincial People's Government, were strictly followed during the slaughter and sampling procedures.

### 2.2. Animals and experimental procedures

Ten 6-month-old Chinese Boer goats (body weight 25 ± 1.0 kg) were raised in individual pens with free access to water and fed twice daily (08:00 h and 18:00 h). The diet containing 43% corn, 5% wheat