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# Repeatability of metabolic responses to a nutrient deficiency in early and mid lactation and implications for robustness of dairy cows

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## ABSTRACT

Nutrient partitioning toward the mammary gland during insufficient energy and nutrient supply is a strategy to ensure survival of the offspring in mammalian species. This homeorhetic priority of the mammary gland is also present in the modern dairy cow, in particular in early lactation. However, despite similar metabolic loads, the adaptive response to a given metabolic load varies considerably among animals. The aim of this study was to investigate if individual cows respond in a consistent manner to a negative energy balance (NEB) in early and mid lactation. Twenty-five dairy cows experienced the usual NEB after parturition and were subjected to a second 3-wk NEB induced by feed restriction in mid lactation. Animals were retrospectively ranked according to their highest plasma nonesterified fatty acid (NEFA) concentration in wk 1 to 4 postpartum. The animals with the 33% highest and 33% lowest values were selected and classified either as the high response (HR) or low response (LR) group. Before parturition, no differences in the studied parameters, dry matter intake, energy balance, concentrations of glucose, NEFA, β-hydroxybutyrate, cholesterol, triglycerides, growth hormone, and insulin-like growth factor-1, were detected between LR and HR. After parturition, milk yield and energy-corrected milk yield was higher for HR compared with LR in wk 2 to 14 and wk 1 to 6, respectively. During feed restriction in wk 15 to 17 postpartum, no differences in energy-corrected milk between LR and HR were found. Energy balance was more negative in HR during the NEB in early lactation, but not different from LR during feed restriction in mid lactation. Although plasma concentrations of glucose, growth hormone, triglycerides, and cholesterol showed group differences in early lactation, but not during feed restriction, the plasma concentrations of NEFA, β-hydroxybutyrate, and insulin-like growth factor-1 in HR changed repeatedly to a greater extent during the NEB at the 2 stages of lactation compared with LR despite the similar extent of the NEB itself in both groups. The repeatedly greater amplitude of adaptive responses in HR compared with LR at different time points might partly indicate an underlying genetic background to enable a sufficient and rapid supply of mobilization-derived nutrients. The individual characteristics of adaptation to an energy and nutrient shortage might be beneficial when implemented in breeding programs.

**Key words:** adaptation, robustness, metabolic plasticity, negative energy balance, dairy cow

## INTRODUCTION

The inevitable negative energy balance (**NEB**) at the onset of lactation reflects the most challenging period for dairy cows. To meet energy requirements for maintenance and serving the priority of nutrient partitioning to the needs of lactation, a comprehensive homeorhetic adaptation of metabolic and endocrine systems is required (Bauman and Currie, 1980). Metabolic priority of lactation declines with DIM and mammary gland metabolism becomes more sensitive to the homeostatic control of hormones such as insulin (Bauman and Currie, 1980). The different expression patterns of glucose transporters during the gestation-lactation cycle gives evidence for a more insulin-sensitive glucose uptake into the mammary gland in mid- and late lactation (Mattmiller et al., 2011).

Effects of a NEB in early and mid lactation on performance, metabolic, and endocrine parameters have been reported previously (Gross et al., 2011a,b) with markedly lower extent of metabolic stress during the NEB at the later lactational stage. Codrea et al. (2011) noted that the rate of recovery in milk yield due to a temporary nutritional shortage was unaffected by stage of lactation. Similarly, comparable losses in milk yield during short-term feed restrictions in early, mid-, and late lactation indicated that the metabolic responses due to feed restrictions are dependent on milk yield

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(Bjerre-Harpøth et al., 2012). However, the deviations of plasma metabolites from basal values were shown to be dependent on the stage of lactation (Bjerre-Harpøth et al., 2012). In particular, the early lactation period characterizes dairy cows with diverse robustness to cope with the inflicted metabolic load more or less successfully (i.e., occurrence of metabolic disorders and loss in productive performance when failing to adapt).

Up to now, studies with nutritional challenges in dairy cows at different stages of lactation only focused on the extent of responses in performance and metabolism, but did not consider if cows responding more intensely in early lactation might again react more intensely in mid lactation at an individual level. This unique approach enables the characterization of adaptive responses in dairy cows. Therefore, the objective of this study was to investigate the plasticity in metabolic, endocrine, and performance traits in dairy cows during a NEB at 2 different stages of lactation. The hypothesis tested was that cows responding more intensely to an energy and nutrient shortage in early lactation also react more intensely to a feed-restriction-induced NEB in later lactation.

## MATERIALS AND METHODS

### Animal Trial

Twenty-five multiparous Holstein dairy cows (3.0 ± 1.1 parities; mean ± SD) were studied during a period from parturition up to wk 17 postpartum (**p.p.**). Cows experienced a NEB during the first week of lactation, and after getting into a positive energy balance (**EB**), all cows were exposed to a 3-wk feed restriction period (wk 15–17 p.p.) providing 50% of energy and nutrient requirements starting at 98 ± 7 DIM. Feed allowance was adjusted weekly during feed restriction to maintain the degree of NEB. Details on housing and feeding conditions were described earlier (Gross et al., 2011a).

### Data Collection

Data on DMI and milk yield were collected daily, whereas BW, BCS, and backfat thickness (**BFT**) were determined weekly. Milk samples for determination of fat and protein content by FTIR were taken twice weekly. Energy balance and energy expenditure for maintenance and lactational requirements were calculated according to the guidelines of the German Society of Nutrition Physiology (GfE, 2001). Blood samples for analysis of plasma concentrations of glucose, NEFA, BHBA, triglycerides, cholesterol, IGF-1, and growth hormone (**GH**) were obtained weekly. Details on feed, milk, and blood analysis as well as calculation of the RQUICKI index for estimation of insulin sensitivity were reported earlier (Gross et al., 2011a,b).

### Statistical Analysis

For analysis of individual responses to an energy deficiency in early and mid lactation, data of the respective parameters of individuals were normalized relative to the mean value and SD of all animals. This method of normalization avoids the bias by different absolute values depending on the lactational stage and reflects the ranking of the individual animal. A regression analysis considering the repeated exposure to a NEB (in wk 3 and 15 p.p.) was performed with cow as the repeated subject. These particular weeks were selected as milk production steeply increased during a period of a NEB (in early lactation), metabolic load was highest (in wk 3 p.p. and wk 15 p.p. after the initiation of feed restriction) and metabolic adaptation still ongoing. In an additional retrospective analysis, cows were ranked according to their highest plasma NEFA concentration in early lactation (observations from wk 1–4 p.p.). The cows with the 33% highest and 33% lowest NEFA concentrations (8 animals each) were selected and classified as either high response (**HR**) or low response (**LR**) groups, respectively. Data were checked for normal distribution by the UNIVARIATE procedure in SAS (version 9.4, SAS Institute Inc., Cary, NC). In cases of not being normally distributed, data were log-transformed. One animal showed a very high plasma BHBA concentration, which was repeatedly confirmed by laboratory analysis. Interestingly, the same animal, after a distinct time-span, again showed elevated plasma BHBA concentration during the nutritional challenge at a later lactational stage. Therefore, this individual animal contributes very much to the finding of a repeated pattern of individual adaptation responses, even in animals that show an extreme reaction. During data evaluation, we had a special focus on this animal, and even repeated our laboratory analyses to exclude any type of mistake in the measurements. We decided to keep this extreme individual in the data set. After log-transformation, all data were normally distributed and the one individual was not identified as an outlier anymore. Weekly data on performance, metabolic, and endocrine parameters of the 2 groups (HR and LR) were compared using the MIXED model in SAS (version 9.4, SAS Institute Inc.) including week, group (HR or LR), parity, and the week × group interaction as fixed effects and the individual cow as repeated subject. Differences between HR and LR over time were detected by the Bonferroni *t*-test. Significant effects were assumed at a level of $P < 0.05$.