HAL open science

Key determinants of adaptive strategies of goats to a 2-day nutritional challenge during early lactation

Marcelo Gindri, Nicolas N.C. Friggens, Ophélie Dhumez, Alexandra Eymard, T Larsen, Rachel Rupp, Andrew Ponter, Laurence Puillet

▶ **To cite this version:**

Marcelo Gindri, Nicolas N.C. Friggens, Ophélie Dhumez, Alexandra Eymard, T Larsen, et al.. Key determinants of adaptive strategies of goats to a 2-day nutritional challenge during early lactation. Animal, 2024, 18, 10.1016/j.animal.2024.101153 . hal-04594261

HAL Id: hal-04594261

https://hal.inrae.fr/hal-04594261

Submitted on 30 May 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

Animal 18 (2024) 101153

Contents lists available at ScienceDirect

Animal

The international journal of animal biosciences

Key determinants of adaptive strategies of goats to a 2-day nutritional challenge during early lactation

M. Gindri [a], N.C. Friggens [a,*], O. Dhumez [a], A. Eymard [a], T. Larsen [c], R. Rupp [b], A.A. Ponter [d,e], L. Puillet [a]

[a] Université Paris-Saclay, INRAE, AgroParisTech, UMR Modélisation Systémique Appliquée aux Ruminants, 91120 Palaiseau, France
[b] GenPhySE, Université de Toulouse, INRAE, Castanet Tolosan, France
[c] Dept. of Animal Science, Aarhus University, 8830 Tjele, Denmark
[d] Ecole Nationale Vétérinaire d'Alfort, BREED, 94700 Maisons-Alfort, France
[e] Université Paris-Saclay, UVSQ, INRAE, BREED, 78350 Jouy-en-Josas, France

ARTICLE INFO

Article history:
Received 21 June 2023
Revised 26 March 2024
Accepted 4 April 2024
Available online 16 April 2024

Keywords:
Between individual variance
Energy status
Environment
Genetic and longevity
Resilience

ABSTRACT

Little is known about the key determinants of the physiological adaptations to environmental challenges and how these determinants interact. We evaluated how the response/recovery profiles to a short-term nutritional challenge during early lactation are affected by early-life nutritional strategies in dairy goats divergently selected for functional longevity. We used 72 females, split into two cohorts, daughters of Alpine bucks divergently selected for functional longevity. The females from the two lines were fed with two divergent diets, normal vs low-energy, from weaning until the middle of first gestation, and then fed with the same standard diet. Individual BW, body condition score, morphology, and plasma samples were collected from birth to first kidding. The adaptative physiological strategy to a nutritional challenge was assessed via a 2-day feed restriction challenge, during early lactation, which consisted of a five-day control period on a standard lactation diet followed by a 2-day challenge with straw-only feeding and then a 10-day recovery period on a standard lactation diet. During the challenge, DM intake, BW, milk yield (**MY**), and plasma and milk metabolite composition were recorded daily. Linear mixed-effects models were used to analyze all traits, considering the individual nested in the cohort as a random effect and the 2 × 2 treatments (i.e., line and rearing diet) and litter size as fixed effects. Linear mixed-effects models using a piecewise arrangement were used to analyze the response/recovery profiles to nutritional challenge. Random parameters estimated for each individual, using the mixed-effects models without the fixed effects of rearing diet and genetic line, were used in a stepwise model selection based on R^2 to identify key determinants of an individual's physiological adaptations to environmental challenges. Differences in stature and body reserves created by the two rearing diets diminished during late gestation and the 5-day control period. Genetic line did not affect body reserves during the rearing phase. Rearing diet and genetic line slightly affected the recovery profiles of evaluated traits and had no effects on prechallenge and response to challenge profiles. The prekidding energy status measures and MY before challenge were selected as strong predictors of variability in response-recovery profiles of milk metabolites that have strong links with body energy dynamics (i.e., isoCitrate, ß-hydroxybutyrate, choline, cholesterol, and triacylglycerols; R^2 = 35%). Our results suggested that prekidding energy status and MY are key determinants of adult resilience and that rearing diet and genetic line may affect adult resilience insofar as they affect the animals' energy status.
© 2024 The Author(s). Published by Elsevier B.V. on behalf of The Animal Consortium. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Implications

The shortage of information on key determinants of an individual's adaptive strategies to environmental challenges represents a major hurdle to understanding the components of animal resilience. Identifying the factors that impact nutritional resilience would allow better management of animals in challenging periods. Our findings suggest that body energy dynamics are central to adaptive strategies during a 2-day nutritional challenge in dairy goats. Prekidding energy status measures and milk yield affected adaptive capacity.

Introduction

Drought, heat, and flooding are some of the environmental challenges facing future agricultural production. In this context, live-

* Corresponding author.
E-mail address: nicolas.friggens@inrae.fr (N.C. Friggens).

https://doi.org/10.1016/j.animal.2024.101153
1751-7311/© 2024 The Author(s). Published by Elsevier B.V. on behalf of The Animal Consortium.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

stock production may face feed shortage and/or feed availability at non-affordable prices. Feed shortage brings into play physiological adaptations of farm animals, such as reduction of basal metabolism and digesta flow (both increasing energy efficiency) and the use of body reserves to safeguard the energy source for current and/or next offspring and survival (Chilliard et al., 1998, 2000; Bjerre-Harpøth et al., 2012; Gindri et al., 2021). Studies have also suggested that an animal's ability to cope with environmental challenges depends on the animal's strategies toward energy conservation and may impact its reproductive/productive lifespan (Beerda et al., 2007; Theilgaard et al., 2007). However, little is known about the key determinants of these physiological adaptations to environmental challenges.

Studies have suggested that there is a genetic determinism to physiological adaptations during environmental challenges. Studies comparing breeds within the same species have found significant differences in the sensitivity of adipose tissue to lipolytic regulators and the rate of fat mobilization, demonstrating differences in adaptative capacity (Gilson et al., 1996; Chilliard et al., 2000; Billa et al., 2020). It has also been shown that there is considerable variation between individuals in adaptive capacity (Agrawal, 2001; Ben Abdelkrim et al., 2021, 2023; Friggens et al., 2016). In dairy cows, it has been demonstrated that cows that digest their diet more efficiently partition a greater portion of the incremental energy to body tissues instead of to milk yield (**MY**) (Guinguina et al., 2020). Moreover, cows with high genetic merit for MY are more sensitive to challenges than cows with low genetic merit for MY (Beerda et al., 2007; Poppe et al., 2020). Theilgaard et al. (2007) studying rabbits hyper-selected for reproductive longevity and average prolificacy successfully showed less environmental sensitivity and delayed reproductive senescence. They also suggested these two factors might have been associated with body reserves.

Studies have suggested energy metabolism may be "learned" during early life. Rats, deprived of energy during fetal life, show a pattern of development that favors energy conservation, such as high rates of fat accumulation, and an increased capacity for both gluconeogenesis and basal lipolysis in adulthood (Cameron et al., 2005). In humans, insulin sensitivity and regulation of body fat levels have been related to the phenotypic changes induced by poor early nutrition (Hales and Barker, 2001). This suggests that the ability to cope with nutritional challenges is affected by genotype and early life experience, with energy metabolism being implicated (Tolkamp et al., 2006). However, the effect of maternal feed restriction on goat kids' metabolism during rearing is still controversial (Laporte-Broux et al., 2011). Therefore, the objective of this study was to evaluate how the response and recovery profiles to a short-term nutritional challenge during early lactation are affected by early-life nutritional strategies in dairy goats divergently selected for functional longevity. First, we tested the hypothesis that early-life nutritional strategies in dairy goats divergently selected for functional longevity affect response and recovery profiles to a short-term nutritional challenge during early lactation. Then, we proceed to identify key determinants of an individual's physiological adaptations to environmental challenges.

Material and methods

Experiment, animals, diet, and treatments

All procedures performed on animals were approved by the Ethics Committee on Animal Experimentation and the French Ministry of Higher Education, Research and Innovation (APAFIS#24314-2019120915403741). The experiment used four groups of first lactation Alpine dairy goats in a 2 × 2 design, with two yearly cohorts. In total 72 females, daughters of Alpine bucks divergently selected for longevity were used; longevity plus (**LGV +**) and longevity minus (**LGV-**). The two lines were created in the INRAE experimental facility of GenPhyse in close collaboration with Capgènes, the French AI center for goats. The average estimated lifespan of daughters in the commercial population of the 35 bucks that sired the LGV + and LGV- lines is 909 (±651) and 1 071 (±722) days, respectively (Ithurbide et al., 2022). Moreover, Ithurbide et al. (2022) compared the observed survival of the two lines with a Cox model that estimated life expectancy in a common environment, i.e., LGV- of 787 days and LGV + and 830 days. The average effect of the line over all life stages was significant (P = 0.005), with the LGV + having a decreased risk of culling (hazard ratio 0.63; CI = 0.465; 0.864). The LGV + and LGV- females were then randomly distributed into two nutritional treatments at weaning (56 ± 4 days of life); normal vs low-energy diets (Table S1). These nutritional treatments continued until the middle of the first gestation (298 ± 4 days of life and 91 ± 9 days from kidding), after which all animals were on the same standard total mixed ration (**TMR**). Individual BW (7 ± 2 days interval), body condition score (**BCS**; external and lumbar; 44 ± 14 days interval), and plasma samples (24 ± 12 days interval; every 4 weeks during growth and days −14, −7, +7 and + 14 peripartum) were collected during growth, from birth to first kidding (387 ± 5 days of life).

The adaptative physiological strategy to the nutritional challenge was assessed via a 2-day feed restriction challenge, during early lactation (Friggens et al., 2016). All animals received the same standard lactation TMR (Table S1) *ad libitum* from kidding onwards. The experiment started at 30 ± 4.4 days in milk, after first kidding (the body reserve mobilization phase of lactation). The short-term challenge consisted of a 5-day control period on the standard lactation TMR followed by a 2-day challenge with straw-only feeding and then a 10-day recovery period on the standard lactation TMR. All feeds were offered *ad libitum* twice daily. During the challenge, DM intake, BW, and MY were recorded daily. Each goat had continuous access to its feed trough (ear-tag RFID-operated feed gates) within groups of 8. The feed troughs were on weigh cells that recorded feed weight every 2 s thus allowing identification of quantities ingested throughout the day (described by Cellier et al., 2021). Feed DM was recorded daily for conversion to DM intake, spillage, and refusals DM were monitored weekly. The milking parlor was equipped with a walk-over weigher providing BWs at each milking and averaged to give daily BW (after exclusion of outliers greater than ± 25% of previous BW). Goats were milked twice daily, and MY was recorded at each milking using an automatic device designed for milk recording in small ruminants developed by INRAE (European patent no. 94916284.6). Samples of milk, from morning and afternoon milking, and blood, before morning feeding, were taken daily for detailed milk and blood measures. To investigate the effect of a rearing diet on body fatness, measures of *longissimus dorsi* (height, width, and surface; mm) and kidney knob channel fat thickness were recorded on the day the experiment started, 3 and 12 days after nutritional challenge using real-time ultrasound (Härter et al., 2014).

Blood samples were centrifuged for 10 min at 3 000 × g at 4 °C, and the plasma was analyzed for urea (mM), glucose (mM), ß-hydroxybutyrate (**BHB**; mM), and non-esterified fatty acids (**NEFA**; mEq/L) using a Cobas Mira-Analyzer (Roche, Mannheim, Germany) with Randox commercial kits (Crumlin, United Kingdom) for urea (11489364216), glucose (GL364), NEFA (FA115), and BHB (RB1007). Insulin was measured using an ELISA kit (10-1202-01; Mercodia AB, Uppsala, Sweden). Milk samples were analyzed for standard milk composition measures (fat and protein contents), glucose (mM), glucose-6-phosphate (mM), malate (μM), glutamate (μM), NH_2 free groups glutamate (**NH_2**; micro eqv), urate (μM), L-lactate dehydrogenase (**LDH**; UI), isoCitrate (μM), galactose (mM), choline (mM), urea (mM), cholesterol (μM), triacylglycerols (mM), and BHB (μM) (more details about the methods can be found at Ben Abdelkrim et al., 2023).

Feeds were analyzed using the following standard methods: DM estimated from water content (ISO, 1983), ash (ISO, 1978), and starch (ISO, 2004). Total N was determined by the Dumas technique (Sweeney and Rexroad, 1987). Cell wall content was estimated by the NDF method of Van Soest and Wine (1967). All the cell wall components were expressed on an ash-free basis.

Statistical analysis

BW, morphology, and plasma metabolites during the second half of gestation

The BW, BCS (average between external and lumbar), morphology (i.e., shoulder height and thorax width), and plasma metabolites were tested for fixed effects of diet, line, and litter size at middle gestation (i.e., date in which all individuals switched into normal diet), considering the birth year (i.e., 2020 vs 2021) as a random effect. The trajectories during the second half of gestation (i.e., from middle gestation to kidding) were tested using days from kidding and the interaction with diet and genetic line and litter size as fixed effects, and the effect of individual nested in the birth year in the intercept and slopes as random effects of linear mixed effects models. For the trajectories from middle gestation to kidding, a power variance function structure (*varPower* R function (Pinheiro et al., 2020)) was used to model heteroscedasticity of residuals and a continuous-time autoregressive of order 1 covariance structure to model the lack of independence among observations within each animal. Find a description of model assumptions and outliers in Supplementary Material S1. All models were fitted using the *lme* function of the *nlme* package (Pinheiro et al., 2020) and ANOVA using *anova* function of the *stats R* package (Fox and Weisberg, 2010) of software R (R Core Team, 2020).

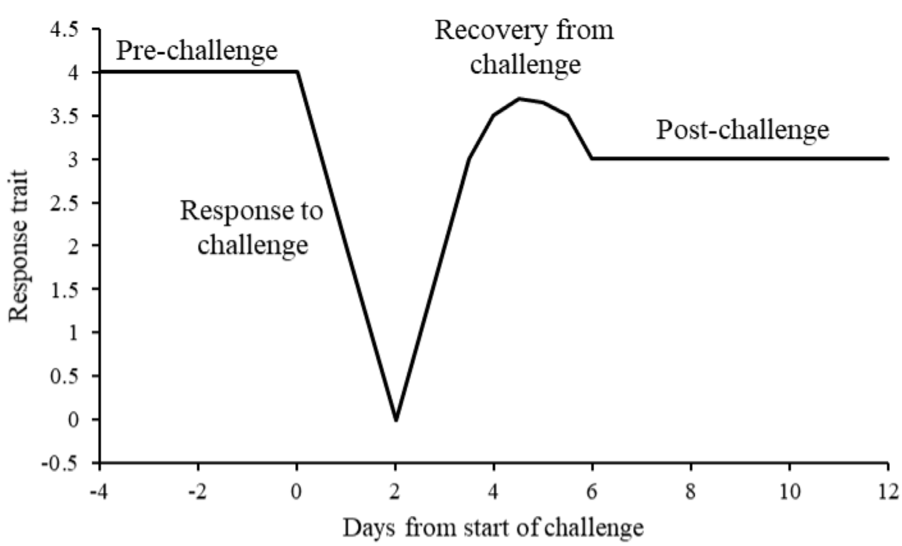
BW, DM intake, milk yield, and metabolites responses to nutritional challenge

The daily records of BW, MY, milk, and plasma composition from the nutritional challenge were analyzed using a piecewise approach (Material S2) in which the response trait is represented by different functions over specific time intervals according to biological responses to challenge, as proposed and validated by Friggens et al. (2016). Briefly, as shown in Fig. 1, we decomposed the response trait into four different phases throughout the challenge experiment. The first phase is the 5-day prechallenge where the response variable is not perturbed and is assumed constant. For this phase, the piecewise model has the parameter V1 which is the overall intercept of the model. The second phase is the 2-day response to the challenge where the challenge is perturbing the animal. For this phase, a linear response is assumed, and the piecewise model has the parameter V2 which gives the response variable change rate per unit of time from the time the challenge starts. The third phase is the 6-day recovery from the challenge where the challenge is no longer perturbating the animal. For this phase, a quadratic recovery is assumed, and the piecewise model has the parameters V3 and V4. The fourth phase is the stabilization period (i.e., postchallenge).

The piecewise approach is based on adding effects. For this, the time variable was expressed as days from the challenge (Fig. 1) and segmented into two-time variables that represent the periods of response and recovery from the challenge and used in the model as regressors for V2, V3, and V4. For this, we fitted the following mixed effects model:

$$Y_{ijkl} = u_{1i*j+g} + T_{v2i*j+g} + T_{v34i*j+g} + T_{v34}2_{i*j+g} + u_{1k} + t_{v2k} + t_{v34k} + t_{v34}2_k + e_{ijkl} \quad (1)$$

where Y_{ijkl} is the dependent variable, u_1 is the model intercept, $_{i^*j}$ is the fixed effect of line i interaction with rearing diet j, $_g$ is the fixed effect of litter size, T_{v2}, and T_{v34} are the time fixed variables that



T_{V2}	0	0	0	0	0	1	2	2	2	2	2	2	2	2	2	2	2
T_{V34}	0	0	0	0	0	0	0	1	2	3	4	4	4	4	4	4	4

Fig. 1. Representation of the piecewise approach with the four phases of the nutritional challenge in dairy goats. The first phase is the 5-day prechallenge where the response variable is not perturbed and is assumed constant (this is the overall intercept of the mixed effects model, i.e., V1, see Material and Methods section). The second phase is the 2-day linear response to the challenge where the challenge is perturbing the animal (this gives the response variable change rate per unit of time from the time the challenge starts, i.e., V2 in the mixed effects model). The third phase is the 6-day quadratic recovery from the challenge where the challenge is no longer perturbating the animal (i.e., V3 and V4 in the mixed effects model). The fourth phase is the stabilization period (i.e., postchallenge, V5, estimated from the orthogonal contrasts using the estimated parameters of the mixed effects model). T_{v2} and T_{v3} are the time-fixed variables that represent the periods during response to challenge and recovery from challenge, respectively, used in the mixed effects model.

Table 1
Average BW, body condition score (BCS), shoulder height, and thorax width at mid-gestation, and rates of change (Δ) in the second part of gestation of first lactation Alpine goats divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-) lifespan) and fed with two different diets from weaning to mid-gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet.

Trait	LGV-		LGV+		SEM	*P*-value			
	Low-energy	Normal diet	Low-energy	Normal diet		Litter size[1]	Longevity	Diet	Longevity*Diet
BW (kg)									
at mid-gestation	47.0	55.4	43.6	48.7	2.23	0.058	0.001	<0.001	0.243
at kidding	63.7	69.8	59.0	61.7	1.82	0.330	<0.001	<0.001	0.220
Δ 2nd half gestation	0.20	0.17	0.18	0.15	0.01	0.030	0.020	<0.001	0.920
BCS									
at mid-gestation	3.12	3.27	3.02	3.2	0.102	0.300	0.060	<0.001	0.779
at kidding	3.21	3.24	3.08	3.13	0.064	0.359	0.105	0.028	0.663
Δ 2nd half gestation	0.00250	−0.00063	0.00098	−0.00029	0.001	0.005	0.526	0.000	0.153
Shoulders height (cm)									
at mid-gestation	72.1	73.6	70.1	72.8	0.65	0.070	0.014	0.001	0.284
at kidding	82.2	83.0	80.3	81.9	0.93	0.140	0.115	0.033	0.905
Δ 2nd half gestation	0.12	0.11	0.10	0.11	0.01	0.590	0.418	0.727	0.438
Thorax width (cm)									
at mid-gestation	75.2	78.8	73.5	76.9	0.90	0.500	0.021	<0.001	0.921
at kidding	84.0	85.4	81.7	83.6	0.89	0.640	0.015	0.001	0.839
Δ 2nd half gestation	0.078	0.051	0.066	0.055	0.01	0.270	0.750	0.018	0.394

[1] Single or Multiple fetuses.

represent the periods during response to challenge and recovery from challenge, respectively, $_{k}$ is the random effect of animal estimated for the intercept (u_1) and all other time variables that represent the different periods (t_{v2} and t_{v34}). The random effects are assumed to be independent and identically normally distributed with mean 0 and variance σ^2_B, and e_{ijkl} is the residual error ($e_{ijkl} \sim N(0, R)$, with R as the heterogenous autoregressive of order 1 error covariance structure (**AR(1)**), used to correct for lack of independence in the residuals and to correct heterogeneity of variance. The *varIdent* R function (Pinheiro et al., 2020) was used to account for the heteroscedastic of the residuals with the AR(1). Contrasts on the fitted models' parameters were used to evaluate the stabilization period (i.e., postchallenge, fourth phase, V5) and to test differences between prechallenge and stabilization periods (V5-V1). The contrasts to calculate the postchallenge period were set according to the following equation:

$$V5 - V1 = V2 \times 2 + V3 \times 4 + V4 \times 4^2 \quad (2)$$

The information on *longissimus dorsi* and kidney knob channel fat thickness was analyzed using an ANOVA model considering the effects of line, diet, litter size, and the interaction between line and diet as fixed effects and birth year as random effect. A full description of model assumptions and outliers is in Supplementary Material S1.

All models were fitted using the *lme* function of the *nlme* package (Pinheiro et al., 2020) and ANOVA using *anova* function of the *stats R* package (Fox and Weisberg, 2010) of software R (R Core Team, 2020). Contrasts were performed using general hypothesis testing, function *glht* of package *multcomp* (Hothorn et al., 2008) of software R (R Core Team, 2020). Statistical significance was set at $P \le 0.05$.

Between-individual variation in milk metabolites responses to 2-d nutritional challenge

Values that describe the between-individual variability were recovered from the random part of the above-mentioned linear mixed-effects models. However, to explore between-individual variability, rearing diet, and genetic line were not included in the models. Moreover, in the models fitted for milk metabolites only, litter size was also not included. To see what animal factors might account for part of the between-individual variability in response to short-term challenge, values that described the between-individual variability in late gestation trajectories (extracted from the previously described model) and also in early lactation trajectories were used, as follows: The fitted mixed-effects model for MY and BW from kidding to prechallenge was similar to the mixed-effects models used for the body traits during the second half of gestation but the time variable was days from challenge.

With this, we built two datasets. One dataset with body traits and plasma insulin and metabolites recorded during the second half of gestation, litter size, MY and BW from kidding to prechallenge, and *longissimus dorsi* and kidney knob channel fat thickness (i.e. predictor traits) during the prechallenge. These were the traits with the potential to explain the between-individuals variability of milk metabolites responses-recoveries during the 2-d nutritional challenge (i.e., the second dataset, predicted traits).

Using the random parameters estimated for each individual (i.e., assembled dataset of predictor traits and assembled dataset of predicted traits), we first ran, separately for each dataset, principal components analysis (PCA), using orthogonal varimax rotation (i.e. to maximize the sum of the variances of the squared loadings). A correlation matrix was used as input in the PCA. The scores estimated for each individual, from the first two principal components, were used in a hierarchical clustering analysis, using Euclidean distance as a measure of distance among individuals and Ward's Method as the agglomerative approach. Two principal components and three clusters were chosen based on biological interpretation and the amount of variance explained. Traits that presented loadings < |0.40| in one of the first two selected principal components were not interpreted in the PCA and did not continue for the next step. Second, the between-individual variance of each milk metabolite explained by the traits recorded during prekidding and prechallenge (R^2 and R^2 adjusted for the number of predictors) was assessed by fitting multiple linear models that had all possible combinations of candidates' predictor variables.

The PCA was performed using the *corr.test*, *fa.parallel*, and *principal* functions of the *psych* package (Revelle, 2018) of software R (R Core Team, 2020). The hierarchical clustering analysis was performed using the *dist* and *hclust* functions of the *stats* package of software R (R Core Team, 2020). The linear models were fitted using the *lm* function from the *stats* package of R (R Core Team, 2020) using a procedure coded by us that allowed us to fit models with all possible combinations of predictor variables.

Results

BW, morphology, and plasma metabolites during the second half of gestation

Females fed the low-energy rearing diet had low BW, BCS, shoulder height, and thorax width at the end of the diet treatment (i.e., mid-gestation) in comparison to females fed the normal diet ($P \leq 0.001$; Table 1 and Fig. 2). However, after the diet treatments ended, i.e. during the second half of gestation on a common diet, females from the low-energy rearing diet presented higher average daily BW gain and rate of gain in thorax width in comparison to females from the normal rearing diet ($P \leq 0.018$). Moreover, females from the low-energy rearing diet increased BCS during the second half of gestation while females from the normal rearing diet had a reduction in BCS ($P < 0.001$). However, the differences observed between rearing diets on female BW, BCS, shoulder height, and thorax width at the end of the diet treatment were also observed at kidding ($P \leq 0.033$). These differences were smaller at kidding. LGV- females presented higher BW and thorax width than LGV + females at mid-gestation and kidding ($P \leq 0.021$).

Plasma insulin and NEFA concentrations were higher in goats fed a normal energy–rearing diet than in females fed a low-energy–rearing diet at mid-gestation only ($P \leq 0.001$; Table 2). In general, the genetic line did not affect plasma insulin or metabolite levels during the second half of pregnancy ($P \geq 0.281$; Table 2).

BW, DM intake, milk yield, and metabolite responses to nutritional challenge

DM intake, BW, and MY significantly dropped during the 2-day nutritional challenge ($P < 0.001$; Fig. 3). However, BW returned to prechallenge levels during postchallenge ($P = 0.310$) while DM intake presented a tendency to be above ($P = 0.0767$) and MY

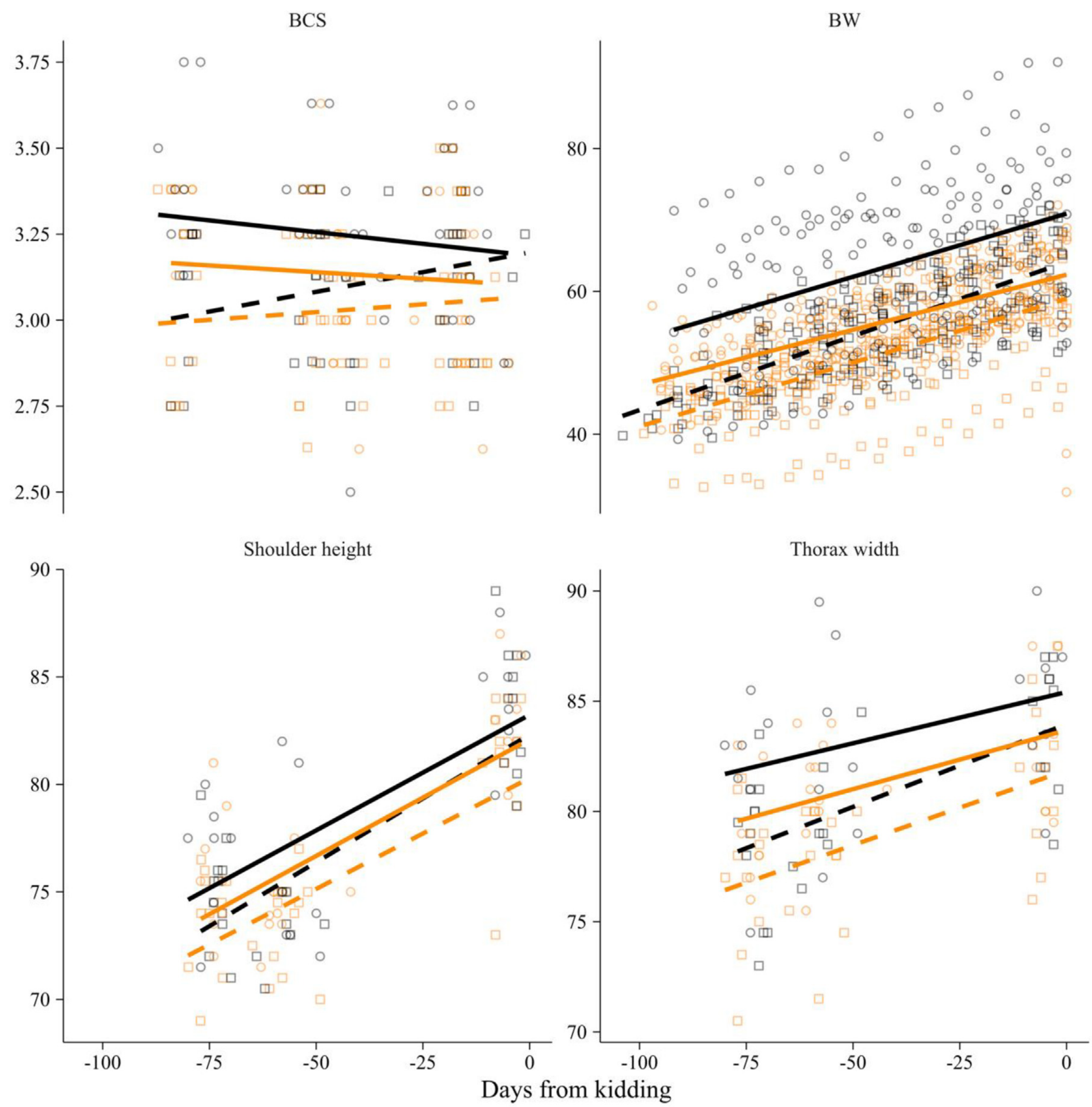


Fig. 2. Time trends in average body condition score (BCS), BW (kg), shoulder height (cm), thorax width (cm), from mid-gestation to kidding of daughters of Alpine breed bucks divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-) lifespan), raised on different diets (low-energy or normal diet) from weaning to mid-gestation; From mid-gestation to kidding all goats were fed with a common diet. The ○ and solid black line represents LGV- fed a normal diet, ○ and the solid dark orange line represents LGV + fed a normal diet, □ and dashed black line represents LGV- fed low-energy diet, □ and dashed dark orange line represents LGV + fed low-energy diet. Symbols and lines show observed and fitted trajectories, respectively.

Table 2
Average plasma insulin and metabolites at mid-gestation, and rates of change (Δ) in the second part of gestation, of first lactation Alpine goats divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-)) and fed with two different diets from weaning to mid-gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet.

Trait	LGV-		LGV+		SEM	*P*-value			
	Low-energy	Normal diet	Low-energy	Normal diet		Litter size[1]	Longevity	Diet	Longevity*Diet
Insulin (µg/L)									
at mid-gestation	0.634	1.104	0.598	1.348	0.1800	0.892	0.560	<0.001	0.368
at kidding	0.498	0.562	0.436	0.442	0.0634	<0.001	0.341	0.944	0.616
Δ 2nd half gestation	−0.0070	−0.0112	−0.0067	−0.0109	0.0023	<0.001	0.622	0.010	0.991
Glucose (mM)									
at mid-gestation	3.92	3.98	3.89	4.02	0.097	0.151	0.952	0.096	0.516
at kidding	3.22	3.34	3.08	3.22	0.1035	<0.001	0.358	0.212	0.992
Δ 2nd half gestation	−0.00860	−0.00516	−0.00975	−0.00580	0.0017	<0.001	0.806	0.104	0.876
Non-esterified fatty acids (µmol/L)									
at mid-gestation	80.5	128.3	94.2	136.1	51.5	0.006	0.360	<0.001	0.808
at kidding	475	524	589	529	99.4	0.007	0.639	0.275	0.582
Δ 2nd half gestation	4.42	5.36	6.36	4.70	1.66	<0.001	0.864	0.667	0.342
ß-hydroxybutyrate (mM)									
at mid-gestation	0.197	0.208	0.200	0.200	0.0144	0.205	0.895	0.687	0.661
at kidding	0.410	0.423	1.090	0.346	0.383	0.732	0.556	0.442	0.823
Δ 2nd half gestation	0.00325	0.00368	0.0136	0.00232	0.0060	0.0263	0.391	0.375	0.219
Plasma urea (mM)									
at mid-gestation	4.97	5.43	5.14	4.81	0.227	0.941	0.281	0.975	0.029
at kidding	3.64	3.59	3.52	3.27	0.174	0.531	0.427	0.126	0.521
Δ 2nd half gestation	−0.0115	−0.0090	−0.0148	−0.0133	0.0034	0.538	0.229	0.665	0.864

[1] Single or Multiple fetuses.

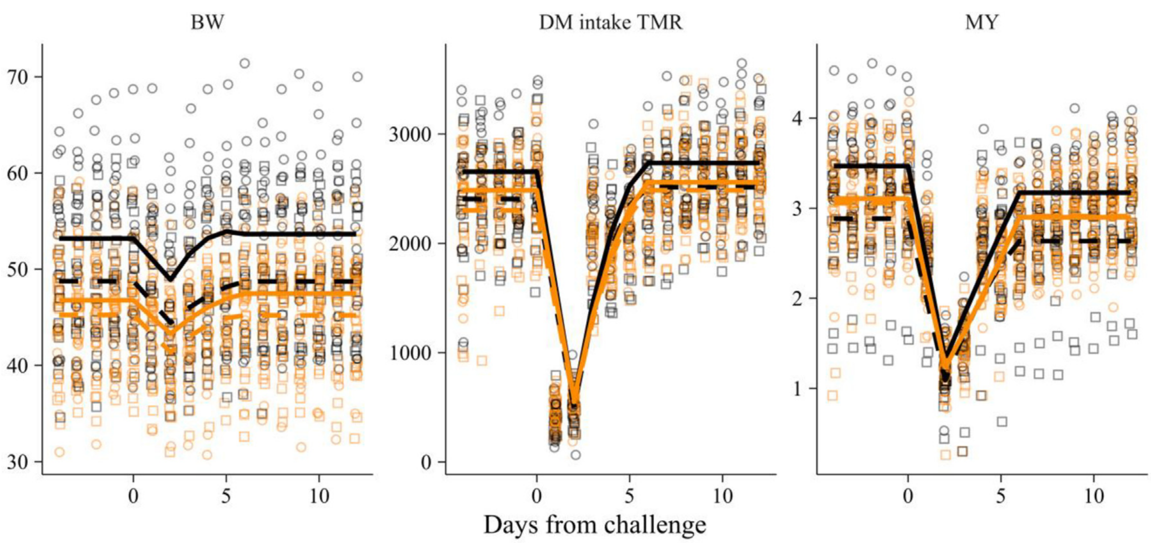


Fig. 3. Time trends of BW (kg), DM intake of total mixed ratio (TMR; g), and milk yield (MY, kg) pre-, during, and postnutritional challenge in first lactation Alpine goats from two divergent lines; longevity line plus (LGV +) and longevity line minus (LGV-), and reared on different diets from weaning to mid-gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet. The ○ and solid black line represents LGV- fed a normal diet, ○ and the solid dark orange line represents LGV + fed a normal diet, □ and dashed black line represents LGV- fed low-energy diet, □ and dashed dark orange line represents LGV + fed low-energy diet. Symbols and lines represent observed and fitted trajectories, respectively.

was significantly below the prechallenge level ($P \leq 0.001$). DM intake demonstrated a tendency to be affected by the rearing diet during the challenge ($P = 0.061$; Table 3). The DM intake of LGV- females showed a tendency for a quicker and sharper recovery from the challenge than LGV + females ($P = 0.0646$ for rate of recovery; $P = 0.107$ for rate of deceleration in recovery; Table 3). As observed at kidding, females fed the low-energy rearing diet and LGV + females had the lowest BW during the prechallenge ($P = 0.035$ and $P = 0.051$; Table 3). Females fed the normal rearing diet had the highest MY during the prechallenge and consequently the fastest drop during the challenge ($P = 0.0032$ and $P = 0.031$; Table 3). LGV- females' MY presented a quicker and sharper recovery from the challenge than LGV + females' MY ($P = 0.042$ and $P = 0.012$). No significant effects of rearing diet and longevity line were found on *Longissimus dorsi* and kidney knob channel fat thickness.

During the nutritional challenge, plasma levels of insulin and glucose dropped while NEFA, BHB, and urea increased (Table 4). However, plasma insulin and glucose returned to prechallenge levels during postchallenge ($P \geq 0.167$) while plasma BHB, NEFA, and urea presented postchallenge levels below the prechallenge level ($P \leq 0.001$). We did not observe any significant effect of a rearing diet on the evaluated plasma metabolites (Table 4). LGV- females presented a tendency for a quicker and sharper plasma

Table 3
Average time trends of DM intake of total mixed ratio, BW, milk yield during the different phases of the nutritional challenge in first lactation Alpine goats divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-)), raised on different diets from weaning to mid-gestation (low-energy or normal diet). Average *longissimus dorsi* and kidney knob channel fat thickness measurements across the whole challenge are also shown; From mid-gestation to kidding, all goats were fed with a common diet.

Item	LGV-		LGV+		SEM	*P*-value			
	Low-energy	Normal diet	Low-energy	Normal diet		Litter size[1]	Longevity	Diet	Longevity*Diet
DM intake									
Prechallenge level (g)	2 400	2 640	2 310	2 470	96.06	0.482	0.425	0.061	0.661
Rate of response (g/d)	−953	−1040	−877	−952	45.42	0.809	0.204	0.167	0.899
Rate of recovery (g/d)	943	991	823	857	143.2	0.810	0.107	0.532	0.891
Rate of deceleration in recovery (g/d^2)	−110	−114	−84.6	−91.8	36.99	0.433	0.065	0.781	0.868
BW									
Prechallenge level (kg)	49.3	54.2	45.3	47.3	1.598	0.107	0.0513	0.035	0.344
Rate of response (kg/d)	−2.21	−2.13	−1.9	−1.67	0.2831	0.144	0.381	0.845	0.775
Rate of recovery (kg/d)	1.44	2.8	1.72	1.39	0.4075	0.024	0.585	0.019	0.028
Rate of deceleration in recovery (kg/d^2)	−0.0966	−0.407	−0.195	−0.101	0.08542	0.044	0.362	0.010	0.012
Milk yield									
Prechallenge level (kg)	2.88	3.47	3.06	3.11	0.1415	0.927	0.307	0.003	0.04
Rate of response (kg/d)	−0.891	−1.07	−0.903	−0.944	0.07796	0.976	0.877	0.031	0.21
Rate of recovery (kg/d)	0.516	0.496	0.346	0.43	0.3505	0.774	0.042	0.831	0.4
Rate of deceleration in recovery (kg/d^2)	−0.0333	−0.008	0.0173	−0.00204	0.0804	0.725	0.012	0.258	0.132
Longissimus dorsi									
height (mm)	17.3	18.2	16.8	17.5	1.43	0.000	0.215	0.242	0.819
width (mm)	40.7	39.3	38.7	39.4	1.01	0.245	0.076	0.284	0.214
surface area (mm^2)	556	570	513	541	51.5	0.002	0.079	0.615	0.695
Kidney knob channel fat thickness (cm)	0.219	0.213	0.217	0.225	0.00977	0.703	0.877	0.635	0.411

[1] Single or Multiple fetuses.

Table 4
Average plasma metabolites and insulin values during the different phases of the nutritional challenge in first lactation Alpine goats divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-)), and raised on different diets from weaning to mid-gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet.

Item	LGV-		LGV+		SEM	*P*-value			
	Low-energy	Normal diet	Low-energy	Normal diet		Litter size[1]	Longevity	Diet	Longevity*Diet
Insulin									
Prechallenge level (µg/L)	0.152	0.159	0.136	0.211	0.01979	0.019	0.547	0.790	0.072
Rate of response (µg/L/d)	−0.0564	−0.0578	−0.0477	−0.0766	0.007103	0.078	0.329	0.889	0.038
Rate of recovery (µg/L/d)	0.115	0.11	0.0825	0.124	0.01374	0.149	0.067	0.800	0.072
Rate of deceleration in recovery (µg/L/d^2)	−0.0214	−0.0199	−0.0142	−0.0224	0.003351	0.196	0.086	0.738	0.116
Glucose									
Prechallenge level (mM)	3.5	3.52	3.64	3.63	0.06529	0.502	0.084	0.786	0.777
Rate of response (mM/d)	−0.433	−0.369	−0.411	−0.483	0.04855	0.039	0.727	0.351	0.136
Rate of recovery (mM/d)	0.892	0.767	0.673	0.871	0.09551	0.453	0.051	0.315	0.051
Rate of deceleration in recovery (mM/d^2)	−0.168	−0.147	−0.123	−0.163	0.01989	0.921	0.053	0.427	0.078
Non-esterified fatty acids									
Prechallenge level (µmol/L)	574	693	576	505	108.9	0.003	0.972	0.093	0.045
Rate of response (µmol /L/d)	648	640	612	667	54.25	0.717	0.609	0.923	0.542
Rate of recovery (µmol /L/d)	−1100	−1120	−1070	−1110	82.52	0.742	0.841	0.808	0.956
Rate of deceleration in recovery (µmol/L/d^2)	173	178	173	179	14.35	0.809	0.983	0.809	0.955
ß-hydroxybutyrate									
Prechallenge level (mM)	0.538	0.585	0.526	0.484	0.04146	0.066	0.808	0.373	0.211
Rate of response (mM/d)	0.0724	0.0701	0.0737	0.126	0.03317	0.940	0.974	0.957	0.341
Rate of recovery (mM/d)	−0.26	−0.276	−0.283	−0.289	0.04473	0.303	0.657	0.781	0.899
Rate of deceleration in recovery (mM/d^2)	0.0498	0.053	0.0573	0.054	0.007838	0.407	0.407	0.746	0.625
Urea									
Prechallenge level (mM)	3.54	3.19	3.63	3.39	0.5079	0.172	0.725	0.209	0.764
Rate of response (mM/d)	0.605	0.674	0.927	0.708	0.3055	0.602	0.174	0.792	0.409
Rate of recovery (mM/d)	−2.43	−2.4	−2.81	−2.45	0.4271	0.733	0.329	0.948	0.564
Rate of deceleration in recovery (mM/d^2)	0.554	0.546	0.609	0.558	0.07509	0.741	0.479	0.922	0.703

[1] Single or Multiple fetuses.

insulin ($P = 0.067$ and $P = 0.080$, respectively) and a quicker and sharper plasma glucose ($P = 0.051$ and $P = 0.0534$, respectively) recovery from the challenge than LGV + females (Table 4).

During the 2-day nutritional challenge, milk triacylglycerols, urea, urate, LDH, isoCitrate, galactose, choline, and cholesterol had increased concentrations while lactose, glucose, glucose-6-phosphate, malate, glutamate, and NH_2 had decreased concentrations (Table 5; Table S2; Fig. 4 shows the profiles of BHB, cholesterol, choline, isoCitrate, LDH, and triacylglycerols). Milk glucose-6-phosphate, glucose, malate, glutamate isoCitrate, NH_2, BHB, choline, and lactose presented postchallenge levels below prechallenge levels while the opposite was observed for cholesterol and

Table 5
Average time trends of milk metabolite concentrations during the different phases of the nutritional challenge in first lactation Alpine goats divergently selected for functional longevity (longevity line plus (LGV +) and longevity line minus (LGV-)), and fed with two nutritional strategies from weaning to the middle of gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet.

Item	LGV-		LGV+		SEM	*P*-value			
	Low-energy	Normal diet	Low-energy	Normal diet		Litter size[1]	Longevity	Diet	Longevity*Diet
L-lactate dehydrogenase									
Prechallenge level (UI)	12	12.6	10.6	12	1.217	0.018	0.248	0.667	0.669
Rate of response (UI/d)	29.4	31.1	25.6	24.7	2.68	0.009	0.257	0.640	0.595
Rate of recovery (UI/d)	−37	−40	−32.3	−31.7	3.509	0.010	0.253	0.511	0.551
Rate of deceleration in recovery (UI/d^2)	5.48	5.95	4.75	4.69	0.6211	0.021	0.250	0.497	0.561
isoCitrate									
Prechallenge level (µM)	177	197	186	189	8.521	<.0001	0.372	0.086	0.270
Rate of response (µM/d)	41.4	42.8	40	50.7	7.062	0.051	0.858	0.871	0.422
Rate of recovery (µM/d)	−101	−119	−109	−121	10.23	0.861	0.481	0.181	0.722
Rate of deceleration in recovery (µM/d^2)	18	21.7	19.4	21.7	1.858	0.473	0.555	0.157	0.689
ß-hydroxybutyrate									
Prechallenge level (µM)	39.1	34.3	31.5	29.2	4.197	0.144	0.146	0.407	0.741
Rate of response (µM/d)	1.96	2.57	−0.187	7.4	2.181	0.728	0.414	0.835	0.073
Rate of recovery (µM/d)	−5.34	−7.2	−3.83	−11.9	3.027	0.502	0.694	0.662	0.275
Rate of deceleration in recovery (µM/d^2)	0.526	1.07	0.748	1.97	0.5308	0.778	0.740	0.467	0.494
Choline									
Prechallenge level (mM)	1.21	1.26	1.09	1.1	0.05043	0.337	0.071	0.464	0.644
Rate of response (mM/d)	1.07	1.18	0.993	0.961	0.07319	0.009	0.433	0.267	0.285
Rate of recovery (mM/d)	−1.6	−1.81	−1.49	−1.46	0.1137	0.048	0.430	0.179	0.249
Rate of deceleration in recovery (mM/d^2)	0.261	0.295	0.237	0.231	0.0217	0.123	0.390	0.261	0.323
Cholesterol									
Prechallenge level (µM)	220	204	216	207	15.14	0.294	0.819	0.400	0.801
Rate of response (µM/d)	250	250	243	242	19.31	0.465	0.697	0.997	0.953
Rate of recovery (µM/d)	−275	−278	−258	−273	23.22	0.235	0.548	0.899	0.779
Rate of deceleration in recovery (µM/d^2)	40.2	41.5	35.9	37.1	5.708	0.296	0.441	0.838	0.671
Triglycerides									
Prechallenge level (mM)	52.6	54.5	50.7	50.6	4.153	0.575	0.456	0.482	0.562
Rate of response (mM/d)	23.5	26.4	24.4	22.4	10.95	0.026	0.775	0.386	0.273
Rate of recovery (mM/d)	−36.3	−42.2	−37.6	−35.3	13.86	0.351	0.798	0.293	0.274
Rate of deceleration in recovery (mM/d^2)	6.7	7.65	6.59	6.4	2.149	0.669	0.908	0.379	0.428

[1] Single or Multiple fetuses.

triacylglycerols ($P \leq 0.0467$). Milk urate, galactose, urea, and protein presented postchallenge levels similar to prechallenge levels ($P \geq 0.145$) while LDH presented a tendency to be different ($P = 0.0655$). Milk protein response to challenge slightly decreased for LGV- females and slightly increased for LGV + females ($P \leq 0.01$; Table S2). There were few treatment effects on a small number of milk metabolite response-recovery profiles. Milk fat, urea, glucose, LDH, glutamate, BHB, and cholesterol prechallenge level, response, and recovery from challenge were similar between genetic lines and rearing diets ($P \geq 0.124$; Table 5; Table S2). Milk isoCitrate, galactose, and choline response and recovery from challenge were similar between genetic lines and rearing diets ($P \geq 0.125$; Table 5; Table S2). Milk urate and NH_2 during the prechallenge, and response-recovery from challenge were not affected by genetic line ($P \geq 0.213$). Females fed a low-energy rearing diet had a quicker and sharper milk glucose-6-phosphate and urate recovery from the challenge ($P \leq 0.050$). Milk protein response to challenge was similar between genetic lines and rearing diets ($P = 0.137$); however, LGV- females presented a quicker and sharper recovery from challenge ($P = 0.002$).

Between-individual variation in milk metabolite responses to 2-d nutritional challenge

To further explore variation between individuals in milk metabolite response-recovery profiles from the nutritional challenge, a PCA of the individual values of the piecewise model parameters (V1, V2, V3, and V4) of all milk metabolites was carried out (Table S3; Fig. 5). The first two principal components of this PCA explained 28% of the total between-individual variance. The first principal component, which retained 15% of the total variance, described the response-recovery profiles of milk metabolites that have strong links with body energy dynamics (i.e., V2, V3, and V4 of isoCitrate, BHB, choline, cholesterol, and triacylglycerols). The major loadings on the second principal component, which retained less variance (13%), were chiefly related to milk metabolites expected to reflect protein dynamics as well as the prechallenge levels of the milk metabolites related to energy dynamics (in the first principal component). These results identified the milk metabolite dynamics that are the main contributors to the between-individual variation in response-recovery profiles. They suggest that energy dynamics are the most responsive to nutritional challenges in dairy goats during early lactation.

Accordingly, indicators of body reserves just before kidding and during the prechallenge (27 in all) were explored as predictor traits with the potential to explain between-individual variation in milk metabolites responses to the 2-d nutritional challenges in early-lactation. In the first step, a PCA was done on these prekidding and prechallenge measures (Table S4; Fig. 6). The principal components analysis using the 27 candidate predictor traits demonstrated that 38% of the between-individuals' variance can be summarized in two principal components. It identified which of the prekidding and prechallenge measures were the main contributors to between-individual variation. The first principal component, accounting for 19% of the variance, opposed plasma glucose against plasma NEFA, plasma BHB, and litter size. The second prin-

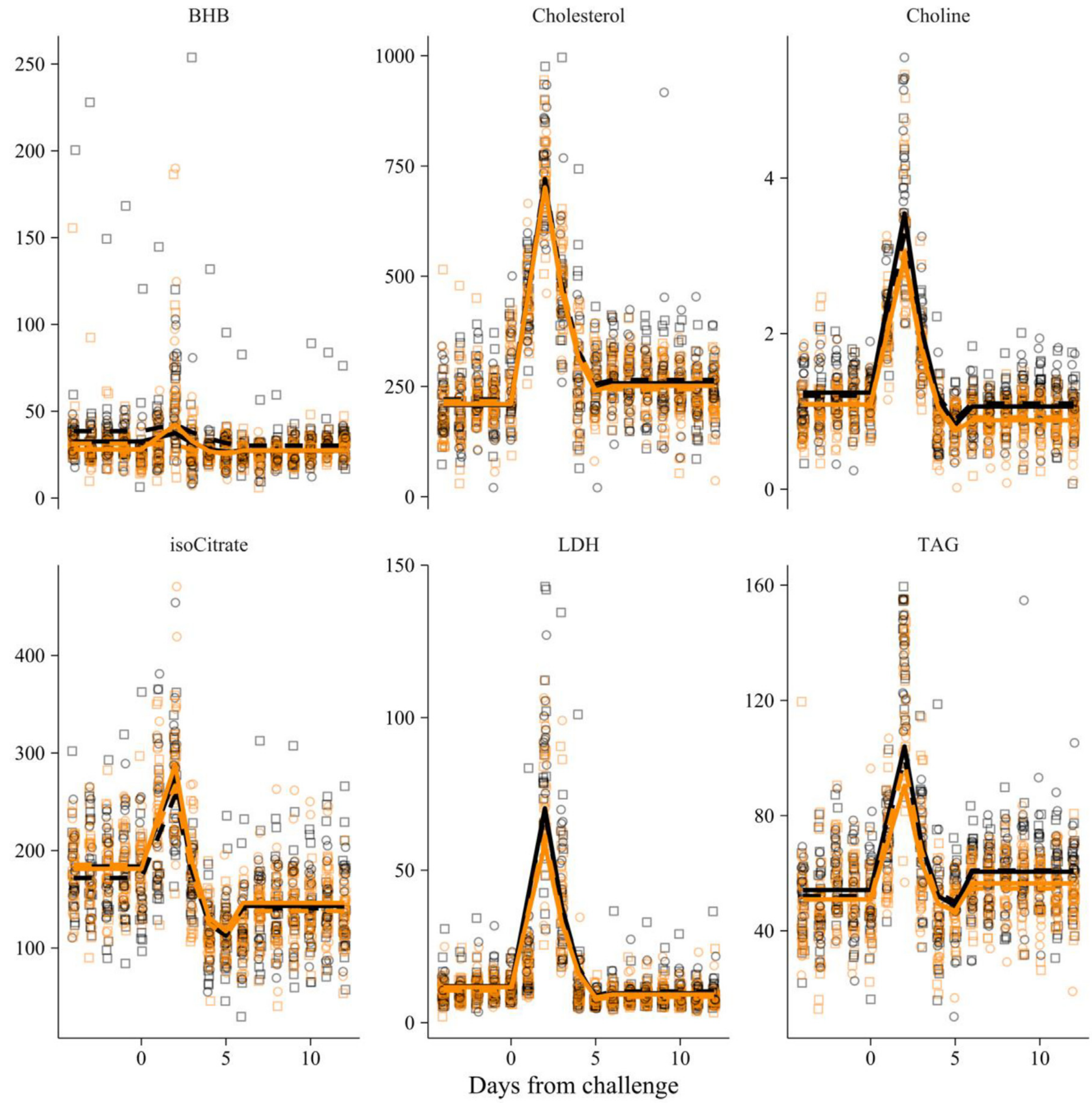


Fig. 4. Time trends of milk metabolites pre-, during, and postnutritional challenge in first lactation Alpine goats from two divergent lines selected for productive lifespan; longevity line plus (LGV +) and longevity line minus (LGV-), and reared on different diets from weaning to mid-gestation (low-energy or normal diet); From mid-gestation to kidding, all goats were fed with a common diet. The milk metabolite concentrations are ß-hydroxybutyrate (BHB; μM), cholesterol (μM), choline (mM), isoCitrate (μM), L-lactate dehydrogenase (LDH; UI), and triacylglycerols (mM). The ○ and solid black line represents LGV- fed a normal diet, ○ and the solid dark orange line represents LGV + fed a normal diet, □ and dashed black line represents LGV- fed low-energy diet, □ and dashed dark orange line represents LGV + fed low-energy diet. Symbols and lines show observed and fitted trajectories (from a mixed-effects model), respectively.

cipal component, which retained 19% of the total variance, was strongly related to the between-individual variance of BW, morphology (i.e., shoulder height and thorax width), and BCS at kidding, and prechallenge BW, and *longissimus dorsi* measurements and weakly related to prechallenge MY. To explore the extent to which these prekidding and prechallenge energy status measures could account for variation in response-recovery profiles in early lactation of the most prominent energy-related milk metabolites (identified above; Figure S1), clustering analyses in both datasets followed by stepwise linear regression were carried out.

Using the hierarchical clustering analysis, we clustered the individuals into three different groups (Figure S2). Combining the cluster and PCA results, we identified that 53% (9 out of 17 individuals) of the individuals that were in the cluster powered by milk metabolites linked to body energy dynamics were also in the cluster powered by the body traits and MY (Fig. 5). This link between the prekidding and prechallenge energy status measures and the metabolites linked to body energy dynamics was subsequently confirmed by the stepwise linear regressions.

Using stepwise multiple linear regressions, it was found that prekidding and prechallenge measures were significant predictors of between-individual variation in response-recovery profiles from challenge for the milk metabolites; BHB, choline, cholesterol, triacylglycerols, LDH, and isoCitrate (7% < R^2 < 37%; Table 6). MY at prechallenge, when alone in the model, was the trait that explained most of the between-individual variation of the above-cited traits ($R^2 \approx 20\%$). In addition to these traits, between-individual variation of BW at prechallenge, morphology (i.e., shoulder height and thorax width), BCS at kidding and litter size also contributed to explaining the between-individual variation of the above-mentioned traits ($R^2 \approx 15\%$;). The addition of plasma insulin and plasma metabolites prekidding did not significantly increase

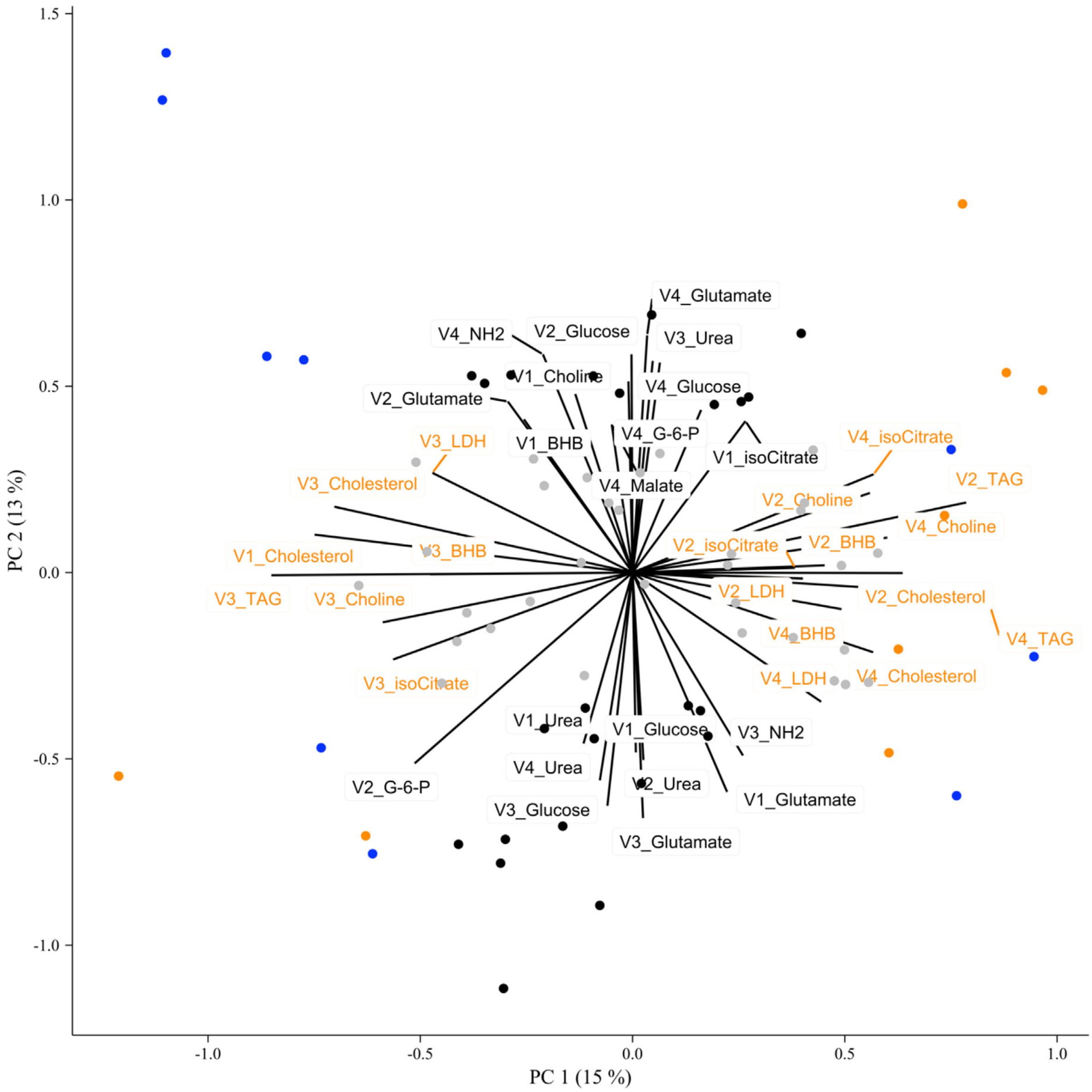


Fig. 5. Principal components (for loadings ≥ |0.4|) of milk metabolite (glucose (mM), glucose-6-phosphate (mM), malate (μM), glutamate (μM), NH_2 free groups glutamate (NH_2; micro eqv), urate (μM), L-lactate dehydrogenase (LDH; UI), isoCitrate (μM), choline (mM), urea (mM), cholesterol (μM), triacylglycerols (mM), and ß-hydroxybutyrate (BHB; μM)) response-recovery profiles descriptors in first lactation dairy goats subjected to 2-days feed restriction during early lactation. The descriptors V1, V2, V3, and V4 correspond to pre-, rate of response-, rate of recovery-, rate of deceleration in recovery- nutritional challenge. The dots are the individuals and the colors represent the clusters. The ● and ● are individuals in the cluster powered by body energy dynamic-related metabolites. ● also represents the individuals that were in the cluster powered by body and milk traits in Fig. 6. The ● and ● are individuals in the cluster not powered by body energy dynamic metabolites.

the variance already explained by the other traits (R^2 < 5%). The addition of *Longissimus dorsi* surface area did not significantly increase the variance already explained by the other traits (R^2 < 2.5%). The R^2 of all fitted models is available in the repository indicated in the 'Data and Model Availability Statement' section.

Discussion

The first hypothesis tested was related to the effect of two rearing diets designed to create differences in body fat content during growth. As expected, the differences in stature and body reserves created by these diets during the rearing phase diminished during late gestation on a common feed, indicating that the goats compensated for their prior nutritional treatments (Tolkamp et al., 2006; Bjerre-Harpøth et al., 2012). Indeed, the average BW, kidney knob channel fat thickness, and *longissimus dorsi* surface area, are considered indexes of body lean and non-carcass fat content (Teixeira et al., 2008; Härter et al., 2014; Morales-Martinez et al., 2020), were no longer affected by rearing diet or even genetic line at the start of the early lactation challenge. Nevertheless, variation in energy status measures during prekidding was able to account for some of the variations in the early lactation challenge response-recovery profiles of those milk metabolites most associated with energy metabolism. In terms of treatment means, the rearing diet had no significant effect on response-recovery profiles of plasma metabolites and only a few effects on MY and milk metabolites. Females raised on the normal rearing diet had the highest MY during the prechallenge and consequently the fastest drop during the challenge. Females raised on the low-energy rearing diet presented a quicker and sharper milk glucose-6-phosphate and urate recovery from challenge.

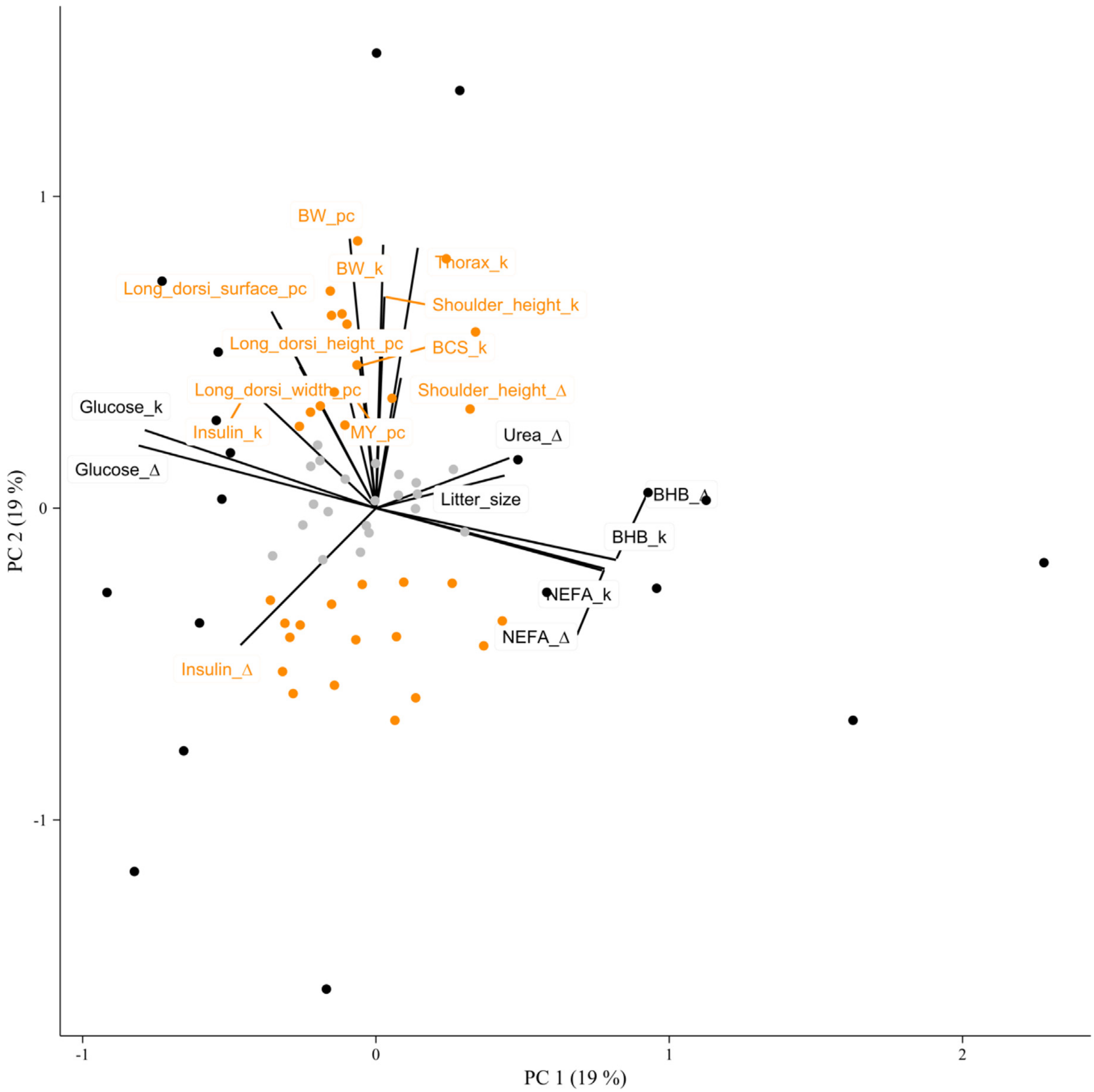


Fig. 6. Principal components (for loadings ≥ |0.4|) of goat prekidding (_k measures) BW (kg), body condition score (BCS), body morphology (shoulder height and thorax width; cm), plasma metabolites (glucose (mM), ß-hydroxybutyrate (BHB; µM), non-esterified fatty acids (NEFAs; mEq/L), and insulin (µg/L)), and early lactation prechallenge (_pc measures) milk yield (MY; kg), BW (kg) and *longissimus dorsi* (Long_dorsi; height, width, and surface; mm). The average values and the rates of change (Δ) of prekidding measures are included. The ● are individuals in the cluster powered by body traits during prekidding and BW and milk traits during the prechallenge. The ● and ● are individuals in the cluster not powered by body energy dynamic metabolites.

The second hypothesis tested was that goats sired with bucks divergently selected for longevity would have differences in response-recovery profiles during an early lactation nutritional challenge. The BCS and plasma-related metabolites during growth and kidney knob channel fat thickness and *longissimus dorsi* surface area at the prechallenge were not affected by the genetic line. Regarding recovery profile, we identified that DM intake, plasma insulin and glucose, MY, and milk protein presented a slightly quicker and sharper recovery profile from challenge for LGV− females relative to LGV + females. As MY has been demonstrated to be a key driver of feed intake in dairy cows (Allen et al., 2019; de Souza et al., 2019), and insulin and glucose are key molecules related to MY (Knowlton et al., 1998), the combined effects of longevity line on DM intake, MY, insulin and glucose appear consistent and the slight differences observed in the recovery phase of the challenge period suggest that LGV- have a metabolism more focussed towards restoring MY when compared to LGV + females.

Body reserve dynamics have been suggested to be the mediator of the link between the two factors tested in this study (i.e., early life nutritional strategies and functional longevity) and adaptive capacity to environmental challenges (Hales and Barker, 2001; Cameron et al., 2005; Theilgaard et al., 2007). However, no treatment differences were found in the response-recovery profiles (i.e., V2, V3, and V4) of milk metabolites that have strong links with body energy dynamics, and that presented high between-individual variability in the PCA (i.e., isoCitrate, BHB, choline, cholesterol, and triacylglycerols). Two interpretations for these findings are possible. The first is that inherent differences in longevity and also in early life growth trajectory do not impact the resilience mechanisms related to body reserves by which animals respond to short-term nutritional challenges. The second explanation is that these factors do affect resilience, i.e. response-recovery profiles, but that the between-individual variation in resilience mechanisms is substantially greater than the between-treatment

Table 6
Summary of multiple linear regression equations with the highest $R^2_{adjusted}$ for predicting the different aspects of the response-recovery profiles in milk metabolites using prekidding and prechallenge energy status measures in first lactation Alpine goats. Equations are shown for those regressions in which prekidding and prechallenge measures explain more than 25% of the between-individual variability (Data and model availability statement section). Equations that included plasma traits were not considered. The coefficient for each predictor is given unless it was not included in that particular equation (symbol –).

Traits	Predictors											
	Intercept	BW at kidding	BCS at kidding	Shoulders height at kidding	Shoulders height Δ 2nd half gestation	Thorax at kidding	Litter size	MY prechallenge	BW prechallenge	R^2adj	R^2	RSE
L-lactate dehydrogenase												
Rate of response (UI/d)	5.83	−0.514	10.5	–	–	0.679	−3.41	–	0.407	9.03	15.4	9.249
Rate of recovery (UI/d)	−2.35E-14	1.35	−17.8	–	−136	–	–	−6.47	−1.23	26	31.2	11.79
Rate of deceleration in recovery (UI/d^2)	3.25E-15	−0.27	2.28	–	–	–	–	1.39	0.262	32.6	36.4	2.085
isoCitrate												
Prechallenge level (μM)	56.5	1.84	–	–	–	–	−33	–	−1.35	28.8	31.8	31.84
Rate of response (μM/d)	1.1E-13	0.778	–	–	–	–	–	9.32	−0.803	4.72	8.75	21.94
Rate of recovery (μM/d)	−25.9	−1.81	–	–	–	–	15.2	−22.7	1.92	18.4	23	34.24
Rate of deceleration in recovery (μM/d^2)	5.75	0.354	5.01	–	–	–	−3.37	3.95	−0.419	22.6	28.1	6.262
ß-hydroxybutyrate												
Prechallenge level (μM)	8.4	1.55	–	–	–	–	−4.92	−9.49	−1.68	25.6	29.8	15.37
Rate of response (μM/d)	−5.31E-14	–	16	–	–	1.33	–	7.23	−0.537	22.8	27.1	10.76
Rate of recovery (μM/d)	1.06E-13	0.634	−23.2	–	–	−1.98	–	−11.4	–	23.7	28	15.94
Rate of deceleration in recovery (μM/d^2)	−2.44E-14	−0.14	3.91	–	–	0.383	–	2.51	–	26.3	30.4	3
Choline												
Prechallenge level (mM)	0.0779	0.0102	–	–	–	−0.0126	−0.0456	−0.0291	–	15.7	20.4	0.1322
Rate of response (mM/d)	0.186	0.0139	–	−0.0194	8	–	−0.109	0.154	−0.00844	27	33.2	0.2317
Rate of recovery (mM/d)	−0.259	−0.011	–	0.0367	−12.6	–	0.152	−0.276	–	26.6	31.8	0.3631
Rate of deceleration in recovery (mM/d2)	0.0416	0.00169	–	−0.00681	2.21	–	−0.0244	0.0525	–	26.3	31.4	0.06409
Cholesterol												
Prechallenge level (μM)	4.09E-13	1.26	−32	–	–	–	–	−36.9	–	27.2	30.3	33.71
Rate of response (μM/d)	−2.37E-13	1.63	–	−2.57	–	–	–	29.8	−3.35	21	25.5	36.46
Rate of recovery (μM/d)	2.36E-14	2.42	−50.1	–	633	–	–	−27	−1.32	19.9	25.5	39.82
Rate of deceleration in recovery (μM/d^2)	2E-14	−0.744	12.9	–	−128	–	–	4.07	0.66	22.3	27.8	8.308
Triglycerides												
Prechallenge level (mM)	1.9	0.146	–	–	–	–	−1.11	−1.61	–	3.36	7.44	5.062
Rate of response (mM/d)	3.32	0.208	7.71	–	–	–	−1.94	4.34	−0.413	18.1	23.9	6.28
Rate of recovery (mM/d)	−3.9E-15	0.279	−9.79	1.09	–	−0.751	–	−7.78	–	21.6	27.2	9.164
Rate of deceleration in recovery (mM/d2)	−2.59E-15	−0.0398	2.42	−0.142	–	–	–	1.55	–	24	28.3	1.672

Abbreviations: RSE = Square root of the estimated variance of the random error; BCS = Body condition score; Δ = rates of change in the second part of gestation; MY = Milk yield; R^2adj = R^2 adjusted for the number of predictors.

differences. Concerning the longevity lines, Ithurbide et al. (2022) have shown that the survival curves of the lines are affected by some body reserve-related measures (weight change in first lactation, milk fat:protein ratio). They also have recently shown differences in longevity between groups of animals clustered according to their multivariate metabolic responses (Ithurbide et al., 2023). These results support the second interpretation presented above. Similarly, the links between the individual's prekidding energy status measures and milk response-recovery profiles found in the present study (35% of the between-individual variability in response-recovery profiles to challenge at peak lactation can be described by the energy status measures at kidding together with prechallenge MY) suggest that rearing conditions will affect adult resilience, insofar as they affect the animals' energy status.

In addition to the prekidding energy status measures, MY before the challenge was a strong predictor of variability in response-recovery profiles of milk metabolites that have strong links with body energy dynamics. Collectively, these results fit with the literature relating body reserves and MY to the ability to cope with environmental challenges in dairy animals (Calus and Veerkamp, 2003; König and May, 2019). These studies have suggested that a more balanced and robust individual may be associated with decreased productivity because a cow allocates more resources to cope with environmental challenges. Studies have also shown that cows more efficiently digesting diets partitioned a greater proportion of the incremental energy to body tissues instead of to MY (Guinguina et al., 2020), and cows with high genetic merit for MY are more sensitive to challenges than cows with low genetic merit for MY (Beerda et al., 2007). Therefore, our findings support previous research suggesting a significant link between energy status measures, productivity, and metabolic responses to address environmental challenges.

A major goal of future dairy farming is to identify and select dairy animals with superior ability to cope with environmental challenges using on-farm sensors. In this study, we demonstrated that around 35% of the between-individual variability in response-recovery profiles to challenge at peak lactation can be described by the energy status measures at kidding together with prechallenge MY. However, careful consideration of the wider context is needed for further use of these promising results. When it comes to identifying outstanding individuals using on-farm sensors, there is also a high variety of responses between farms and within the same individual (Friggens et al., 2016; Adriaens et al., 2020; Ben Abdelkrim et al., 2021). It has also been suggested that there is a homeorhetic influence on the different coping strategies that cows use in different lactation stages in response to a dietary nutrient restriction (Bjerre-Harpøth et al., 2012). Accordingly, the robustness of the relation between prior energy status measures and response-recovery profiles to nutritional challenges should be explored across different lactation stages.

Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.animal.2024.101153.

Ethics approval

The experiment was carried out following French legislation on animal experimentation and Directive 2010/63/EU European Union [Protection of animals used for scientific purposes] regulation S.I. 543/2012 and was approved by the Ethics Committee on Animal Experimentation and the French Ministry of Higher Education, Research and Innovation (APAFIS#8613-2017012013585646V4).

Data and model availability statement

None of the raw original data was deposited in an official repository. The raw original data that support the study findings are available from the authors upon request. However, the fit statistics (R^2, R^2 adjusted, and root mean squared errors (RMSEs)) for all models fitted during the iterative procedure aimed at identifying the key determinants of adaptive strategies are available at https://doi.org/10.57745/HQLGLF as the data input for the tutorial presented at Supplementary Material S1.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) did not use any AI and AI-assisted technologies.

Author ORCIDs

Gindri, M.: https://orcid.org/0000-0003-3569-8827.
Friggens, N.C.: https://orcid.org/0009-0008-0410-7223.
Larsen, T.: https://orcid.org/0000-0002-7378-5967.
Rupp, R.: https://orcid.org/0000-0003-3375-5816.
Puillet, L.: https://orcid.org/0000-0003-2358-7302.
Ponter, A.A.: https://orcid.org/0000-0002-7650-3494.

CRediT authorship contribution statement

M. Gindri: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **N.C. Friggens:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **O. Dhumez:** Writing – review & editing, Methodology, Investigation, Data curation. **A. Eymard:** Writing – review & editing, Methodology, Investigation. **T. Larsen:** Writing – review & editing, Methodology. **R. Rupp:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **A.A. Ponter:** Methodology, Writing – review & editing. **L. Puillet:** Writing – review & editing, Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization.

Declaration of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors wish to acknowledge the whole team of the experimental farm of MoSAR for their assistance and Faten Bouaicha and Marine Denis by recording the ultrasound measurements.

Financial support statement

The funding of this work by APIS-GENE project ResiLait and project ADAPTHERD, part of the PRIMA program supported by the European Union, is gratefully acknowledged.

References

Adriaens, I., Friggens, N.C., Ouweltjes, W., Scott, H., Aernouts, B., Statham, J., 2020. Productive life span and resilience rank can be predicted from on-farm first-parity sensor time series but not using a common equation across farms.

Journal of Dairy Science 103, 7155–7171. https://doi.org/10.3168/jds.2019-17826.
Agrawal, A.A., 2001. Phenotypic plasticity in the interactions and evolution of species. Science 294, 321–326. https://doi.org/10.1126/SCIENCE.1060701.
Allen, M.S., Sousa, D.O., VandeHaar, M.J., 2019. Equation to predict feed intake response by lactating cows to factors related to the filling effect of rations. Journal of Dairy Science 102, 7961–7969. https://doi.org/10.3168/JDS.2018-16166.
Beerda, B., Ouweltjes, W., Šebek, L.B.J., Windig, J.J., Veerkamp, R.F., 2007. Effects of genotype by environment interactions on milk yield, energy balance, and protein balance. Journal of Dairy Science 90, 219–228. https://doi.org/10.3168/jds.S0022-0302(07)72623-1.
Ben Abdelkrim, A., Ithurbide, M., Larsen, T., Schmidely, P., Friggens, N.C., 2023. Milk metabolites can characterise individual differences in animal resilience to a nutritional challenge in lactating dairy goats. Animal 17, 100727. https://doi.org/10.1016/j.animal.2023.100727.
Ben Abdelkrim, A., Tribout, T., Martin, O., Boichard, D., Ducrocq, V., Friggens, N.C., 2021. Exploring simultaneous perturbation profiles in milk yield and body weight reveals a diversity of animal responses and new opportunities to identify resilience proxies. Journal of Dairy Science 104, 459–470. https://doi.org/10.3168/jds.2020-18537.
Billa, P.A., Faulconnier, Y., Larsen, T., Leroux, C., Pires, J.A.A., 2020. Milk metabolites as noninvasive indicators of nutritional status of mid-lactation Holstein and Montbéliarde cows. Journal of Dairy Science 103, 3133–3146. https://doi.org/10.3168/jds.2019-17466.
Bjerre-Harpøth, V., Friggens, N.C., Thorup, V.M., Larsen, T., Damgaard, B.M., Ingvartsen, K.L., Moyes, K.M., 2012. Metabolic and production profiles of dairy cows in response to decreased nutrient density to increase physiological imbalance at different stages of lactation. Journal of Dairy Science 95, 2362–2380. https://doi.org/10.3168/jds.2011-4419.
Calus, M.P.L., Veerkamp, R.F., 2003. Estimation of environmental sensitivity of genetic merit for milk production traits using a random regression model. Journal of Dairy Science 86, 3756–3764. https://doi.org/10.3168/jds.S0022-0302(03)73982-4.
Cameron, N.M., Champagne, F.A., Parent, C., Fish, E.W., Ozaki-Kuroda, K., Meaney, M. J., 2005. The programming of individual differences in defensive responses and reproductive strategies in the rat through variations in maternal care. Neuroscience Biobehavioral Reviews 29, 843–865. https://doi.org/10.1016/j.neubiorev.2005.03.022.
Cellier, M., Duvaux-Ponter, C., Nielsen, B.L., 2021. Inter- and intra-individual variability of feeding behaviour in group housed dairy goats. Applied Animal Behaviour Science 234, 105167. https://doi.org/10.1016/j.applanim.2020.105167.
Chilliard, Y., Bocquier, F., Doreau, M., 1998. Digestive and metabolic adaptations of ruminants to undernutrition, and consequences on reproduction. Reproduction Nutrition Development 38, 131–152. https://doi.org/10.1051/rnd:19980201.
Chilliard, Y., Ferlay, A., Faulconnier, Y., Bonnet, M., Rouel, J., Bocquier, F., 2000. Adipose tissue metabolism and its role in adaptations to undernutrition in ruminants. Proceedings of the Nutrition Society 59, 127–134. https://doi.org/10.1017/S002966510000015X.
de Souza, R.A., Tempelman, R.J., Allen, M.S., VandeHaar, M.J., 2019. Updating predictions of dry matter intake of lactating dairy cows. Journal of Dairy Science 102, 7948–7960. https://doi.org/10.3168/jds.2018-16176.
Fox, J., Weisberg, S., 2010. An R companion to applied regression. Sage Publications, Thousand Oaks, CA, USA.
Friggens, N.C., Duvaux-Ponter, C., Etienne, M.P., Mary-Huard, T., Schmidely, P., 2016. Characterizing individual differences in animal responses to a nutritional challenge: toward improved robustness measures. Journal of Dairy Science 99, 2704–2718. https://doi.org/10.3168/jds.2015-10162.
Gilson, T.L., Kennedy, A.D., Rampersand, T., 1996. Effects of breed and adipose depot location on responsiveness and sensitivity to adrenergic stimulation in ovine adipose tissue. Comparative Biochemistry and Physiology Part c: Pharmacology, Toxicology and Endocrinology 115, 19–26. https://doi.org/10.1016/S0742-8413(96)00070-9.
Gindri, M., Moraes, L.E., Teixeira, I.A.M.A., 2021. Disentangling digesta passage rate in the gastrointestinal tract of male and female growing goats fed varying feeding levels using multivariate and metanalytical approaches: Inferring growth, sex, and intake effects on goats' digesta passage rate. Livestock Science 251, 104645. https://doi.org/10.1016/j.livsci.2021.104645.
Guinguina, A., Yan, T., Lund, P., Bayat, A.R., Hellwing, A.L.F., Huhtanen, P., 2020. Between-cow variation in the components of feed efficiency. Journal of Dairy Science 103, 7968–7982. https://doi.org/10.3168/jds.2020-18257.
Hales, C.N., Barker, D.J.P., 2001. The thrifty phenotype hypothesis type 2 diabetes. British Medical Bulletin 60, 5–20. https://doi.org/10.1093/BMB/60.1.5.
Härter, C.J., Silva, H.G.O., Lima, L.D., Castagnino, D.S., Rivera, A.R., Neto, O.B., Gomes, R.A., Canola, J.C., Resende, K.T., Teixeira, I.A.M.A., 2014. Ultrasonographic measurements of kidney fat thickness and Longissimus muscle area in predicting body composition of pregnant goats. Animal Production Science 54, 1481. https://doi.org/10.1071/AN14282.
Hothorn, T., Bretz, F., Westfall, P., 2008. Simultaneous inference in general parametric models. Biometrical Journal 50, 346–363. https://doi.org/10.1002/bimj.200810425.
Ithurbide, M., Huau, C., Palhière, I., Fassier, T., Friggens, N.C., Rupp, R., 2022. Selection on functional longevity in a commercial population of dairy goats translates into significant differences in longevity in a common farm environment. Journal of Dairy Science 105, 4289–4300. https://doi.org/10.3168/jds.2021-21222.
Ithurbide, M., Wang, H., Fassier, T., Li, Z., Pires, J., Larsen, T., Cao, J., Rupp, R., Friggens, N.C., 2023. Multivariate analysis of milk metabolite measures shows potential for deriving new resilience phenotypes. Journal of Dairy Science 106, 8072–8086. https://doi.org/10.3168/jds.2023-23332.
Knowlton, K.F., Dawson, T.E., Glenn, B.P., Huntington, G.B., Erdman, R.A., 1998. Glucose metabolism and milk yield of cows infused abomasally or ruminally with starch. Journal of Dairy Science 81, 3248–3258. https://doi.org/10.3168/jds.S0022-0302(98)75889-8.
König, S., May, K., 2019. Invited review: Phenotyping strategies and quantitative-genetic background of resistance, tolerance and resilience associated traits in dairy cattle. Animal 13, 897–908. https://doi.org/10.1017/S1751731118003208.
Laporte-Broux, B., Roussel, S., Ponter, A.A., Perault, J., Chavatte-Palmer, P., Duvaux-Ponter, C., 2011. Short-term effects of maternal feed restriction during pregnancy on goat kid morphology, metabolism, and behavior. Journal of Animal Science 89, 2154–2163. https://doi.org/10.2527/JAS.2010-3374.
Morales-Martinez, M.A., Arce-Recinos, C., Mendoza-Taco, M.M., Luna-Palomera, C., Ramirez-Bautista, M.A., Piñeiro-Vazquez, Á.T., Vicente-Perez, R., Tedeschi, L.O., Chay-Canul, A.J., 2020. Developing equations for predicting internal body fat in Pelibuey sheep using ultrasound measurements. Small Ruminant Research 183, 106031. https://doi.org/10.1016/j.smallrumres.2019.106031.
Pinheiro J, Bates D, DebRoy S, Sarkar D, R Core Team (2020). nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1-150. Retrieved on 25 March 2024 from: https://CRAN.R-project.org/package=nlme.
Poppe, M., Veerkamp, R.F., van Pelt, M.L., Mulder, H.A., 2020. Exploration of variance, autocorrelation, and skewness of deviations from lactation curves as resilience indicators for breeding. Journal of Dairy Science 103, 1667–1684. https://doi.org/10.3168/jds.2019-17290.
R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Retrieved on 25 March 2024 from: https://www.R-project.org/.
Revelle, W. 2018. psych: Procedures for personality and psychological research. R package version 1.8.10. 1–453. Retrieved on 25 March 2024 from: https://CRAN.R-project.org/package=psych.
Sweeney, R.A., Rexroad, P.R., 1987. Comparison of LECO FP-228 "nitrogen determinator" with AOAC copper catalyst Kjeldahl method for crude protein. Journal of the Association of the Official Analytical Chemists 70, 1028–1030. https://doi.org/10.1093/jaoac/70.6.1028.
Teixeira, A., Joy, M., Delfa, R., 2008. In vivo estimation of goat carcass composition and body fat partition by real-time ultrasonography. Journal of Dairy Science 86, 2369–2376. https://doi.org/10.2527/jas.2007-0367.
Theilgaard, P., Sánchez, J.P., Pascual, J.J., Berg, P., Friggens, N.C., Baselga, M., 2007. Late reproductive senescence in a rabbit line hyper selected for reproductive longevity, and its association with body reserves. Genetics Selection Evolution 39, 1–17. https://doi.org/10.1186/1297-9686-39-2-207.
Tolkamp, B.J., Emmans, G.C., Kyriazakis, I., 2006. Body fatness affects feed intake of sheep at a given body weight. Journal of Animal Science 84, 1778–1789. https://doi.org/10.2527/jas.2005-514.
Van Soest, P.J., Wine, R.H., 1967. use of detergents in the analysis of fibrous feeds. IV. determination of plant cell-wall constituents. Journal of the Association of Official Analytical Chemists 50, 50–55. https://doi.org/10.1093/jaoac/50.1.50.