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Effect of rumen-protected methionine supplementation to beef cows during the periconception period on performance of cows, calves, and subsequent offspring

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ABSTRACT

Maternal nutrition affects the development of the fetus and postnatal performance of the calf. Methionine may play a critical role in developmental programming and is likely deficient in beef cows fed low-quality forage. The objective of this study was to determine the effect of metabolizable methionine supply to lactating beef cows during the periconception period on performance of cows, calves, and subsequent offspring. This project involved two consecutive production cycles commencing at calving in which dietary treatments were fed to cows during the periconception period along with measurements on cows and initial calves in Production Cycle 1, and measurements on subsequent calves in Production Cycle 2. Brangus-Angus crossbred lactating beef cows ($N = 108$; age = 6.4 (2.8) year) were stratified by previous calving date and assigned to one of three supplements: (1) control, molasses plus urea at 2.72 kg/day as fed, (2) fishmeal, 2.27 kg/day molasses plus urea plus 0.33 kg/day as fed of fishmeal, and (3) methionine, 2.72 kg/day of molasses plus urea plus 9.5 g/day of 2-hydroxy-4-(methylthio)-butanoic acid. Cows were fed supplements and low-quality limpograss (*Hemarthria altissima*) hay while grazing dormant bahiagrass (*Paspalum notatum* Flüggé) pastures during the 115-day periconception period from December 2014 to April 2015 in Production Cycle 1 only. Body weight change and milk yield of cows were measured during the periconception period in Production Cycle 1. Body weight of calves was measured at birth and weaning in both production cycles. Following weaning in Production Cycle 2, eight subsequent steer calves per treatment were individually housed for a 42-day metabolism experiment. Treatment did not affect ($P > 0.10$) BW change of cows, but cows fed methionine tended ($P = 0.09$) to produce more energy-corrected milk than control and fishmeal. Treatment did not affect ($P > 0.10$) 205-day adjusted weaning weight of calves in either production cycle. During the metabolism experiment, subsequent calves from dams fed fishmeal and methionine gained faster ($P < 0.05$) and had greater ($P < 0.05$) gain:feed than control calves. Methionine calves tended ($P = 0.06$) to have greater apparent total tract NDF and ADF digestibility and lesser ($P < 0.05$) blood glucose concentration than control and fishmeal calves. These data indicate that maternal methionine supply during the periconception period plays an important role in programming future performance of the offspring.

Implications

Supplementation of methionine to beef cows during periconception period is beneficial for fetal development when fed poor quality forage that may limit metabolizable methionine supply. More research is required on methionine and fetal programming, specifically furthering our understanding of one-carbon metabolism in ruminants and the supply of methyl donors to the fetus. Additionally, maternal nutrition during the periconception period may be used to improve post-weaning growth and feed conversion through altered nutrient utilization.

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Introduction

In the Southeastern USA, beef cows calve in late fall and rebreed during winter months when the nutritive value of warm-season forages is poor and nutrient requirements of the cow are greatest (National Academies of Science, Engineering, and Medicine [NASEM], 2016). Nutritional management of the pregnant, lactating beef cows impact not only performance of the cow and nursing calf but also the development of the fetus and its subsequent performance (Funston and Summers, 2013).

The periconception period is a critical time during fetal development in which placental development and fetal organogenesis occur (Funston and Summers, 2013; Xu and Sinclair, 2015). Gene expression in 6-day-old embryos was altered in lactating dairy cows deficient in methionine during the periconception period (Peñagaricano et al., 2013). Rodents fed diets adequate in energy and total protein but deficient in methyl donors (methionine, choline, and folate) during early gestation changed the expression of proteins involved in methionine, lipid, and carbohydrate metabolism in liver of the offspring (Maloney et al., 2013). In ruminants, protein supplementation in late gestation has altered intestinal morphology (Meyer et al., 2014) and expression of nutrient transporters (Cruz et al., 2019; Relling et al., 2019) in offspring, and protein supplementation during the periconception period has altered hepatic gene expression of offspring (Copping et al., 2020).

Collectively, these studies indicate that methionine may play an important role in gestating beef cows impacting epigenetics of offspring. Therefore, the hypothesis of this study was that adequate rumen-protected methionine whether in the form of methionine analog or rumen bypass protein to periconceptional, lactating beef cows fed low-quality forage would result in similar improvement in fetal development and nutrient metabolism and performance of subsequent offspring. The objective of this study was to determine the effect of metabolizable protein or metabolizable methionine to lactating beef cows consuming low-quality hay during periconception period on performance of cows, calves, and subsequent offspring.

Material and methods

This study was conducted at the University of Florida Range Cattle Research and Education Center (81°53'W, 27°23'N) in Ona, FL following approval by the University of Florida Institutional Animal Care and Use Committee (protocol #201408583). The study involved two consecutive production cycles from October 2014 to September 2016 (Fig. 1). During Production Cycle 1 from October 2014 to October 2015, cows were fed dietary treatments during the 115-day periconception period from December 2014 to April 2015, and performance of cows and initial calves was measured. During Production Cycle 2 from October 2015 to September 2016, cows were managed similarly, and performance of subsequent calves conceived during the periconception period in Production Cycle 1 was measured pre- and post-weaning.

Production Cycle 1

Cow management

Prior to the start of calving in October 2014, 108 pregnant, Brangus-Angus crossbred beef cows [age = 6.4 (SD = 2.8) year; initial BW = 448.6 (SD = 54.0) kg; initial body condition score (**BCS**) = 4.35 (SD = 0.49)] were stratified by 2013 calving date and assigned to 1 of 6 herds (2 herds per treatment; 1 herd per pasture; 18 cows per herd) to have similar calving distribution among herds. At calving (October through December 2014), birth date and birth weight of calves were recorded and male calves were castrated. No growth-promoting implants were used. Supplement treatments were randomly assigned to herd and began on December 8, 2014 at 18 (SD = 24) days postpartum along with free choice long-stem low-quality limpograss (*Hemarthria altissima*) hay while grazing dormant bahiagrass (*Paspalum notatum* Flüggé) pasture during the 115-day periconception period from December 2014 to April 2015. Supplement treatments consisted of: (1) control, supplemented with molasses plus urea (16% CP as fed basis) at 2.72 kg as fed/day, (2) fishmeal, 2.27 kg as fed/day of molasses plus urea plus 0.33 kg as fed/day of fishmeal (methionine concentration 2.85% of RUP; NASEM, 2016) to meet metabolizable protein requirement providing an estimated 3.5 g/day of bypass methionine, and (3) methionine, 2.72 kg as fed/day of molasses plus urea plus 9.5 g/day of 2-hydroxy-4-(methylthio)-butanoic acid (10 g/day of Metasmart© Liquid, Adisseo, Alpharetta, GA, USA) to provide 3.7 g/day of bypass methionine. A vitamin and mineral supplement was provided free choice throughout Production Cycle 1 and 2. The control diet was formulated to provide 24.5 Mcal metabolizable energy (**ME**)/day (+0.68 Mcal/day; 103%) and 637 g/day of metabolizable protein (−96 g/day; 87%) with predicted rumen nitrogen balance of 55 g/day (139%) for lactating beef cows having 7 kg/day peak milk yield using Level One of the Large Ruminant Nutrition System (LRNS ver. 1.1). The fishmeal and methionine treatments were designed to provide similar ME as the control diet with fishmeal meeting or exceeding metabolizable protein requirement and methionine providing similar bypass methionine as fishmeal. The periconception period corresponded to days 18–133 postpartum (average calving date of November 20, 2014), and days −64 to 51 post-conception based on a 283-day gestation length. Brangus bulls were placed in each pasture (one bull per herd) on January 18, 2015 and removed on April 2, 2015 for a 74-day breeding season.

On day 35 (January 12, 2015) and 115 (April 2, 2015) of the periconception period, cows were weighed following overnight withdrawal from feed, and BCS of cows assessed by two trained personnel.

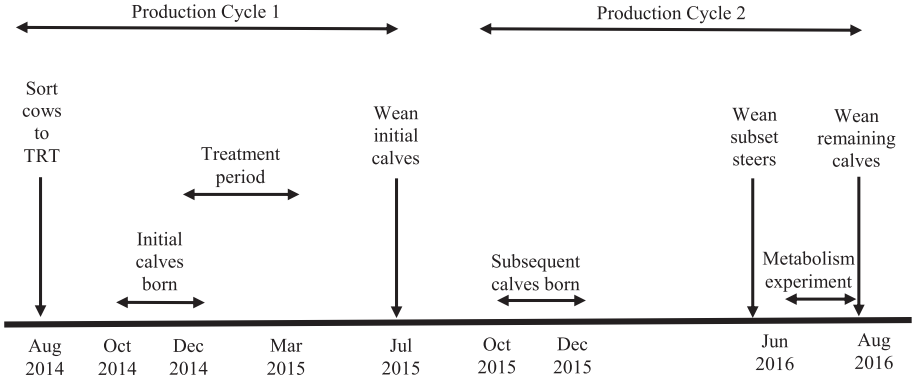

Fig. 1. Timeline illustrating key time points of data collection of beef cows and calves during Production Cycles 1 and 2 of the study. Vertical lines indicate a specific time point and horizontal lines indicate a period of time. TRT = treatment.

Cows were not weighed at the beginning of dietary treatments on December 8, 2014 as some calves were very young and gathering pairs from the pastures to working facilities was deemed too risky to the health of these calves. On day 115, hay feeding and supplementation ceased, and cows grazed 20 4-ha bahiagrass pastures in rotation from April to December 2015. In June 2015, pregnancy status of cows was determined by rectal palpation. Calves were weaned and weighed on July 22, 2015 at an average age of 245 (SD = 24) days. Weaning weight was adjusted to standard 205 days of age.

Milk production

On day 35, 70, and 115 of the periconception period, milk yield was recorded on all cows using the weigh-suckle-weigh technique. Three herds (1 herd per treatment; 54 pairs) were measured at a time. The other three herds were measured on the following 2 days. Cows and calves were gathered to the working pens at 0900 h. Calves were separated from dams at 1200 h, allowed to suckle for 30 min at 1600 h, and again separated from dams overnight. Cows and calves had access to water but not feed. At 0800 h, calves were weighed, placed with their dams for 30 min to suckle, and weighed again. Milk yield for full 24 h was calculated from calf removal and suckling times and beginning and ending calf weights. A sample of milk from each cow was collected prior to suckling at 1600 h from at least one front and rear quarter of the udder, and samples composited by volume into a single sample per cow for analysis of milk components. Energy-corrected milk (**ECM**) yield was computed using Eq. (1).

$$\text{ECM} = 0.327 \times \text{milk yield} + (\text{milk fat} \times 12.95) + (\text{milk protein} \times 7.65) \quad (1)$$

where milk yield is 24-h milk yield, milk fat is 24-h milk fat yield, and milk protein is 24-h milk protein yield.

Feed samples

Samples of limpograss hay, bahiagrass pasture, molasses, and fishmeal were collected weekly during the periconception period from December 2014 to April 2015. Samples of limpograss hay were collected by hand after cows had partially consumed the bale. Samples of bahiagrass pasture were collected every 10 paces along 3 transects in each pasture by observing the type and height of grass grazed by cows. Hay and grass samples were dried at 55 °C in a forced air oven until constant weight, ground through a 1-mm sieve using a Wiley mill (Thomas Scientific, Swedesboro, NJ, USA), then composited by weight within pasture and month. Samples of molasses and fishmeal were composited by weight into a single sample of each for chemical analysis. All samples (hay, grass, molasses, and fishmeal) were sent to Dairy One Forage Laboratory (Ithaca, NY, USA) for chemical analysis.

Production Cycle 2

Cow management

Of the 108 cows fed dietary treatments during Production Cycle 1, 88 cows (31 control; 30 fishmeal; 27 methionine) birthed subsequent calves in fall 2015. At calving (October through December 2015), data collection and management of calves was the same as described for Production Cycle 1. All cows were fed the control diet from December 2015 to April 2016 then grazed bahiagrass pastures as previously described for Production Cycle 1. A subset of 24 steers (4 per herd; 8 per treatment) was selected based on birth date to be similar to the overall average (318 vs. 323 calendar day) such that the stage of fetal development relative to feeding of dietary treatments during the periconception period in Production Cycle 1 was similar. Based on a 283-day gestation length, average conception date of selected steers was February 4, 2015 corresponding to 58 days after initiation of dietary treatments. The subset of steers was weaned on June 1, 2016 for a post-weaning metabolism experiment. The remaining calves were weaned on August 10, 2016. Weight of calves was recorded at weaning and adjusted to standard 205 days of age.

Post-weaning metabolism experiment

A subset of 24 subsequent steer calves (4 per herd; 8 per treatment) was weaned on June 1, 2016 at 199 (SD = 8) days of age, placed in individual pens, and fed concentrate at 1% of BW/day with ad libitum hay for 14 days, then fed a grain and hay diet (70:30) at 2.2% of BW/day for 10 days before the final diet of grain and hay (80:20) at 2.2% of BW/day was introduced 2 days before initial BW was recorded. Steers were fed concentrate plus mineral salt and hay separately at 0800 h daily. Steers were weighed on days 0 and 42 after overnight withdrawal of feed and water. Body weight was measured on days 14 and 28 without overnight withdrawal to adjust feed offered to 2.2% of BW. There were no feed refusals during the whole metabolism experiment.

Nutrient digestibility

Apparent total tract digestibility of DM, organic matter (**OM**), starch, CP, NDF and ADF was determined during the post-weaning metabolism experiment using indigestible NDF (iNDF) as an internal marker as described by Krizsan and Huhtanen (2013). At 0800 and 1700 h, both diet and fecal samples from the rectum were collected beginning on days 36 and 37, respectively, of the metabolism experiment for 4 consecutive days. There were no feed refusals. After collection, samples were frozen at −20 °C until further processing, then dried at 55 °C for 48 h in a forced-air oven, ground in a Willey mill to pass a 2-mm sieve and pooled within steer, on an equal weight basis per sample, for determination of nutrient and marker concentration.

For determination of DM and OM, 0.5 g of sample was weighed in duplicate, dried in a forced-air oven at 100 °C for 24 h, and ashed at 550 °C for 6 h. For determination of the fibrous components, 0.5 g of dry feed and fecal samples was weighed in duplicate into F57 bags (Ankom Technology Corp., Macedon, NY, USA) and analyzed for NDF, using heat-stable α-amylase and sodium sulfite, and subsequently for ADF in an Ankom 200 Fiber Analyzer (Ankom Technology Corp). Concentration of CP in the samples was determined by rapid combustion using a micro elemental N analyzer (Vario Max CN; Elementar Americas Inc., Mt. Laurel, NJ, USA) according to the official method 992.15 (AOAC, 1995). Starch concentration in feed and feces was measured by an enzymatic-colorimetric method as described by Hall (2015).

For the determination of iNDF, 0.5 g of feed and fecal samples was weighed in duplicate into F57 bags (Ankom Technology Corp.), incubated in the rumen of a cannulated steer fed a high forage diet for 288 h, and the residue analyzed for NDF as previously described. Apparent total tract digestibility of DM, OM, CP, NDF, ADF, and starch was calculated using the following formula:

$$100 - 100 \times \left[\left(\frac{\text{markerconcentrationinfeed}}{\text{markerconcentrationinfeces}}\right) \times \left(\frac{\text{nutrientconcentrationinfeces}}{\text{nutrientconcentrationinfeed}}\right)\right]$$

Blood collection. On day 28 of the post-weaning metabolism experiment, blood was collected before feeding at 0800 h and 4 h after feeding via jugular venipuncture into sodium-heparin (158 USP) containing tubes (Vacutainer, Becton Dickinson, Franklin Lakes, NJ, USA). Blood samples were immediately placed on ice following collection, centrifuged at 1 200 × *g* for 25 min at 4 °C to separate plasma, then stored at −20 °C until analysis. Commercial colorimetric kits were used to determine concentrations of plasma urea nitrogen (**PUN**; B7551; Pointe Scientific Inc., Canton, MI, USA) and glucose (G7521; Pointe Scientific, Inc.) and had inter- and intra-assay CV of 2.9 and 3.5%, and 3.7 and 5.8%, respectively.

Statistical analysis of results

Data were analyzed as a completely randomized design. Herd (two herds per treatment) was the experimental unit for cow and calf performance data in both production cycles. Individual animal (four steers per treatment) was the experimental unit for data collected during the post-weaning metabolism experiment in Production Cycle 2. Continuous variables were analyzed using PROC MIXED of SAS (version 9.4; SAS Inst. Inc., Cary, NC, USA) with treatment and calf sex as fixed effects where appropriate. The interaction between treatment and calf sex was not significant ($P > 0.10$) and removed from the model for all dependent variables. For cow and calf performance data during Production Cycles 1 and 2, cow age was not a significant ($P > 0.10$) covariate for cow BW and body condition measurements, calf birth and weaning weight, and cow milk yield and removed from the model for all dependent variables. For cow performance data during Production Cycle 1, cow initial BW and BCS were significant ($P \leq 0.05$) covariates for cow final BW and cow ADG, and final BCS and change in cow BCS, respectively, but not milk yield data. Days in milk, calf sex, and average calf BW during weigh-suckle-weigh measurements were significant ($P \leq 0.05$) covariates for milk yield. For calf performance data during Production Cycles 1 and 2, calf birth weight was a significant ($P \leq 0.05$) covariate for 205-day adjusted weaning weight. For steer performance data during the metabolism experiment, initial BW was a significant ($P \leq 0.05$) covariate for final BW and ADG. Binary data of pregnancy status and calf sex were analyzed using PROC GLMMIX of SAS with treatment as a fixed effect and the ILINK option used to compute SEs in the LSMEANS statement. Blood metabolite data during the metabolism trial were analyzed as repeated measures using PROC MIXED of SAS with fixed effects of treatment, time of sampling, and treatment × time interaction using variance component option for the repeated measures covariance structure with steer as the subject based on Bayesian information criterion. Treatment comparisons were performed using Tukey-Kramer method of adjusting for multiple pairwise comparisons. Least square means were considered significant at $P \leq 0.05$ and tendencies at $0.05 < P \leq 0.10$.

Results

Production Cycle 1

There was no difference ($P > 0.10$) between treatments in nutrient composition of dormant bahiagrass pasture or limpograss hay during the supplementation period (statistical analysis not shown). The mean and SD for each nutrient analyzed in bahiagrass pasture and limpograss hay are presented in Table 1, as well as the nutrient composition of molasses and fishmeal supplements. Crude protein concentration of bahiagrass pasture and limpograss hay for control, fishmeal, and methionine were 7.1, 7.7, and 7.8%, and 3.6, 4.5 and 4.6%, respectively. The molasses-urea supplement was 19.5% CP and the fishmeal was 71.2% CP.

Table 1
Nutrient composition of bahiagrass pasture, limpograss hay, molasses, and fishmeal fed to beef cows during the periconception period (115 days) in Production Cycle 1.

Nutrient[1]	Bahiagrass		Limpograss		Molasses	Fishmeal
	Mean	SD	Mean	SD		
DM, %	50.53	1.50	86.52	1.08	77.50	91.90
CP, % DM	7.53	0.52	4.20	0.57	19.50	71.2
ADICP, % DM	1.87	0.10	0.77	0.10	–	–
NDICP, % DM	3.40	0.34	1.70	0.30	–	–
NDF, % DM	74.20	1.19	80.28	1.09	–	–
ADF, % DM	46.67	1.00	42.32	1.39	–	–
Lignin, % NDF	5.35	0.80	6.58	0.47	–	–
EE, % DM	1.32	0.12	0.98	0.40	2.00	11.20
Ash, % DM	5.61	0.22	2.96	0.75	16.37	21.40
TDN, % DM	54.00	1.67	53.50	1.38	75.00	83.00

[1] ADICP = acid detergent insoluble CP; NDICP = neutral detergent insoluble CP; EE = ether extract; TDN = total digestible nutrients.

Table 2
Effect of dietary treatment on performance of beef cows during the periconception period (115 days) in Production Cycle 1.

Item[1]	Control	Fishmeal	Methionine	SEM	*P*-value
Cow age, year	6.6	6.1	6.7	0.5	0.69
IBW, kg	429.0	446.3	448.4	8.9	0.37
FBW,[2] kg	435.8	443.5	435.2	6.3	0.64
ADG,[2] kg/day	−0.07	0.03	−0.08	0.08	0.64
Initial BCS	4.15	4.55	4.21	0.11	0.15
Final BCS[3]	3.96	4.03	4.07	0.06	0.46
BCS change[3]	−0.32	−0.25	−0.21	0.06	0.46
MY,[4] kg/day	4.97	4.81	6.52	0.51	0.17
ECM,[5] kg/day	3.93^{x}	4.00^{xy}	5.54^{y}	0.37	0.09
Milk composition					
Fat, %	1.83	2.22	2.30	0.31	0.56
Protein, %	2.84^{x}	3.07^{y}	2.98^{y}	0.04	0.08
Lactose, %	4.99	4.97	4.96	0.04	0.87
MUN, mg/dl	10.82	13.35	11.73	0.91	0.28
SCC, 1000/ml	69.63	129.73	117.21	29.30	0.43
Pregnancy rate, %	93.9	89.3	82.4	5.61	0.45

[xy] Means within a row without a common superscript differ ($0.05 < P \leq 0.10$).
[1] IBW = initial BW; FBW = final BW; ADG = average daily gain; BCS = body condition score; MY = milk yield; ECM = energy-corrected milk yield; MUN = milk urea nitrogen; SCC = somatic cell count.
[2] Cow initial BW was a significant covariate ($P \leq 0.05$).
[3] Cow initial BCS was a significant covariate ($P \leq 0.05$).
[4] Significant effect of calf sex ($P \leq 0.05$), and days in milk and calf BW were significant covariates ($P \leq 0.05$).
[5] Days in milk and calf BW were significant covariates ($P \leq 0.05$).

Treatment had no effect ($P > 0.11$) on final BW, ADG, or final BCS of cows during the periconception period or ensuing pregnancy rate (Table 2). Covariate-adjusted means for final BW are not sensible with ADG values; unadjusted means are 426.6, 448.6, and 441.8 ± 8.3 kg for control, fishmeal, and methionine, respectively. There was no difference in milk yield, but there was a trend ($P = 0.09$) for methionine dams to have greater ECM than control dams with fishmeal dams being intermediate. Average days in milk during weigh-suckle-weigh measurements were 90 days, and there was no difference ($P = 0.86$) among treatments. Control dams tended ($P = 0.08$) to have lesser milk protein concentration than fishmeal and methionine dams, but there was no difference in milk fat, urea N, lactose, or somatic cell count.

There was no interaction ($P > 0.10$) between treatment and sex for traits measured on initial calves; thus, LSMeans of main effects are presented in Table 3. Calendar day of birth, proportion of heifer calves, birth weight, and 205-day adjusted weaning weight did not differ ($P > 0.15$) among treatments for initial calves. There was no difference ($P > 0.10$) in calendar day of birth or 205-day adjusted weaning weight between sexes, but birth weight tended ($P = 0.09$) to be greater for male than female calves.

Production Cycle 2

There was no interaction ($P > 0.10$) between treatment and sex for traits measured on subsequent calves; thus, LSMeans of main effects are presented in Table 3. There was no difference ($P > 0.10$) in calendar day of birth, the proportion of female calves born, birth weight, or 205-day adjusted weaning weight among treatments for subsequent calves. There was no difference ($P > 0.10$) in calendar day of birth or birth weight between male and female calves, but 205-day adjusted weaning weight tended ($P = 0.07$) to be greater for steers than heifers.

There was no difference ($P = 0.52$) in initial BW of subsequent steers between treatments at the beginning of the post-weaning metabolism experiment (Table 4), which coincides with the lack of difference in weaning weight of calves. Dry matter intake did not differ ($P = 0.59$)

Table 3
Pre-weaning performance of initial calves (Production Cycle 1) and subsequent calves (Production Cycle 2) conceived in cows when treatments were fed to cows during the periconception period (115 days) in Production Cycle 1.

Item[1]	Dietary treatment			SEM	*P*-value	Calf sex		SEM	*P*-value
	Control	Fishmeal	Methionine			Steers	Heifers		
Initial calf									
DOB	320.4	322.0	323.6	4.1	0.86	325.7	318.3	3.4	0.19
Heifers,[2] %	54.56	53.92	44.09	9.88	0.73	–	–	–	–
Birth weight, kg	34.3	34.2	34.1	1.1	0.99	35.5	32.9	0.9	0.09
205-day Adj. WW,[3] kg	205.5	221.4	214.3	5.2	0.25	217.9	209.6	4.0	0.19
Subsequent calf									
DOB	324.2	325.0	321.0	3.7	0.74	324.2	322.6	3.0	0.73
Heifers,[2] %	37.38	55.14	47.89	13.27	0.68	–	–	–	–
Birth weight, kg	32.6	32.6	32.1	1.2	0.96	32.9	32.0	1.0	0.55
205-day adj. WW,[3] kg	201.3	213.8	213.5	8.4	0.54	215.2	203.9	5.5	0.07

[1] DOB = calendar day of birth; WW = weaning weight.
[2] Percentage of heifer calves born.
[3] Calf birth weight was a significant covariate ($P \leq 0.05$).

Table 4
Post-weaning performance in Production Cycle 2 of subsequent steer calves conceived in cows when treatments were fed to cows during the periconception period (115 days) in Production Cycle 1.

Item[1]	Control	Fishmeal	Methionine	SEM	*P*-value
IBW, kg	222.6	210.9	206.0	10.7	0.52
FBW,[2] kg	248.1[a]	255.3[b]	255.7[b]	2.2	0.04
ADG,[2] kg/day	0.83[a]	1.00[b]	1.01[b]	0.01	0.04
DMI, kg/day	5.47	5.27	5.10	0.26	0.60
DMI, % BW	2.27	2.28	2.25	0.02	0.60
Gain:feed, kg/kg	0.16[a]	0.19[b]	0.19[b]	0.01	0.02

[ab] Means within a row without a common superscript differ ($P \leq 0.05$).
[1] IBW = initial BW; FBW = final BW; ADG = average daily gain; DMI = DM intake.
[2] Initial BW was a significant covariate ($P \leq 0.05$).

among treatments; this was expected as feed offered was limited to 2.2% of BW and there were no feed refusals. However, final BW, ADG, and feed efficiency were greater ($P < 0.05$) in subsequent steers from fishmeal or methionine dams compared with control steers.

Treatment did not affect ($P > 0.10$) intake of any nutrient analyzed, which was expected since feed was offered at constant 2.2% of BW (Table 5). Treatment did not affect ($P > 0.10$) DM, OM, CP, or starch digestibility. There was a trend ($P = 0.06$) for steers born to methionine dams having greater apparent NDF and ADF digestibility than steers born to fishmeal dams, with steers born to control dams being intermediate.

Table 5
Nutrient intake during the fecal collection period and apparent total tract digestibility during the post-weaning metabolism experiment in Production Cycle 2 of subsequent steer calves conceived in cows when treatments were fed to cows during the periconception period (115 days) in Production Cycle 1.

Item[1]	Control	Fishmeal	Methionine	SEM	*P*-value
Intake, kg/day					
DM	5.99	5.27	5.88	0.29	0.20
OM	5.58	4.94	5.42	0.26	0.23
NDF	2.30	2.02	2.36	0.12	0.14
ADF	1.42	1.29	1.45	0.07	0.29
CP	1.10	0.95	1.00	0.07	0.36
Starch	0.49	0.45	0.45	0.05	0.80
Digestibility, %					
DM	76.47	75.99	78.35	1.53	0.52
OM	78.08	77.82	79.94	1.40	0.52
NDF	68.17[xy]	65.24[x]	71.85[y]	1.81	0.06
ADF	69.95[xy]	67.80[x]	73.75[y]	1.64	0.06
CP	79.66	80.15	79.16	1.77	0.93
Starch	92.38	90.71	92.60	2.29	0.82

[xy] Means within a row without a common superscript differ ($0.05 < P \leq 0.10$).
[1] OM = organic matter.

There was no treatment × time interaction ($P > 0.10$) for concentrations of PUN and glucose of subsequent steers before and after feeding during the post-weaning metabolism experiment (Table 6). Steers born to methionine and control dams had greater ($P < 0.05$) PUN concentration than steers born to fishmeal dams, and steers born to methionine dams had lesser ($P < 0.05$) plasma glucose concentration than steers born to control and fishmeal dams. Plasma urea nitrogen concentrations were greater ($P < 0.05$) and plasma glucose concentrations tended ($P = 0.10$) to be lower post-meal compared with pre-meal.

Discussion

Production Cycle 1

Supplementation of rumen bypass protein to cows during the periconception period had minimal impact on performance of cows and initial calves with the exception of protein composition of milk. Similarly, addition of rumen bypass protein to diets adequate in rumen degradable protein has not improved BW or body condition change and has not increased milk yield in lactating beef cows (Lents et al., 2000; Encinias et al., 2005). The lack of an effect may be due to low metabolizable protein requirements of beef cows, but rumen undegradable protein has not consistently increased milk yield in dairy cows either (Santos et al., 1998).

Contrasting results have been reported for BW change in beef cows supplemented with rumen-protected methionine – Clements et al. (2017) reported no effect on BW change, whereas Waterman et al. (2007) reported an increase in nitrogen retention. In the current study, methionine supplementation did not affect BW or BCS change.

Varner et al. (1975) reported increased milk yield and butterfat concentration and weaning weight of calves in beef cows supplemented with methionine hydroxy analog, but other studies have not (Clements et al., 2017; Redifer et al., 2018). The different responses to rumen-protected methionine in beef cows may be related to CP of consumed forage. Cows consuming forages with high CP concentration (>10% CP; Clements et al., 2017; Redifer et al., 2018) reported no response to supplemental methionine, whereas the control diet in the current study was deficient in metabolizable protein (8.2% CP, MP balance = −96 g/d); Varner et al. (1975) did not report nutrient composition of the basal diet.

The mechanism by which methionine influences milk yield and composition may be two-fold. First, supplemental methionine may provide the limiting amino acid for protein synthesis, which agrees with greater milk protein concentration of both fishmeal and methionine cows than control cows. In dairy cows, fishmeal, which has a more

Table 6
Plasma metabolite concentrations during the post-weaning metabolism experiment in Production Cycle 2 of subsequent steer calves conceived in cows when treatments were fed to cows during the periconception period (115 days) in Production Cycle 1.

Item[1]	Treatment			Time[2]		SEM	*P*-value[3]		
	Control	Fishmeal	Methionine	Pre-meal	Post-meal		Trt	Time	Trt × Time
PUN, mg/dl	13.59[b]	11.75[a]	13.31[b]	12.20	13.57	0.33	0.01	0.01	0.51
Glucose, mg/dl	82.00[b]	86.57[b]	72.43[a]	82.82	77.85	2.34	0.01	0.10	0.70

[ab] Means within a row and treatment main effect without a common superscript differ ($P \leq 0.05$).
[1] PUN = plasma urea nitrogen.
[2] Pre-meal = blood collected prior to the morning feeding; post-meal = blood collected 4 h following the morning feeding.
[3] Trt = treatment.

favorable methionine and lysine profile for milk protein synthesis, increased milk protein concentration (Santos et al., 1998), and rumen-protected methionine increased milk protein concentration (Patton, 2010) especially when rumen undegradable protein sources low in methionine have been used (Noftsger and St-Pierre, 2003).

Second, methionine influences lipid and glucose metabolism through one carbon metabolism (Niculescu and Zeisel, 2002; McFadden et al., 2020). Methionine deficient diets can increase choline utilization as a methyl donor (Niculescu and Zeisel, 2002) thus decreasing very low density lipoprotein (**VLDL**) secretion from the liver (McFadden et al., 2020). Rumen-protected choline increased milk yield and serum LDL in dairy cows fed a methionine deficient (lysine adequate) diet, but rumen-protected methionine did not indicating that choline is functioning in the cytidine diphosphate (**CDP**) -choline pathway rather than as a methyl donor (Davidson et al., 2008). When choline and methionine are deficient, conversion of homocysteine to methionine via methionine synthase becomes the dominant pathway resulting in greater requirement for folic acid, vitamin B12, and serine, which is synthesized from glucose (Niculescu and Zeisel, 2002). Graulet et al. (2007) reported increased plasma glucose concentration in dairy cows administered folate and vitamin B12 likely due to a serine sparing effect, which was evident in the increased plasma serine concentration. Reducing the need for serine could result in greater glucose availability and milk lactose synthesis as with the combination of rumen-protected methionine and folic acid supplementation (Girard et al., 2005). Additionally, increased choline requirement in methionine deficient diets would require additional glucose for choline synthesis. In the current study, methionine supplementation most likely reduced the need for endogenous choline and/or serine synthesis allowing greater glucose availability for lactose synthesis resulting in greater milk yield.

Production Cycle 2

Maternal nutrition affects epigenetic mechanisms of DNA and histone methylation (Mentch and Locasale, 2016) which influences fetal development and offspring physiology (Xu and Sinclair, 2015). S-adenosylmethionine (**SAM**) functions as the primary methyl donor for transmethylation of DNA and histones and is influenced by folate and methionine cycles involving vitamins B2 (riboflavin), B6 (pyridoxine), B9 (folate) and B12 (cobalamin), and choline, betaine, and methionine. As discussed previously, choline, betaine, or folate can provide methyl units for remethylation of homocysteine to methionine followed by synthesis of SAM (McFadden et al., 2020). Methionine concentration is rate limiting for SAM synthesis (Mentch and Locasale, 2016).

In ruminants, B-vitamins are synthesized by rumen microorganisms (NASEM, 2016) and have generally been of little dietary concern other than in high-producing dairy cows (Girard et al., 2005; Graulet et al., 2007; McFadden et al., 2020). Likewise, it is believed that beef cows can synthesize adequate amounts of choline to meet requirements (NASEM, 2016). Leaving methionine, which is typically the first limiting amino acid from microbial protein (NASEM, 2016), as the primary dietary essential nutrient involved in nutritionally induced epigenetic changes in the fetus of beef cows. In isolated hepatocytes of Holstein cows, the transmethylation pathway was more responsive to methionine supply, whereas the CDP-choline pathway was more responsive to choline supply (Zhou et al., 2018). In support of this, Jaeger et al. (2009) reported no effect of rumen-protected choline supplementation in periparturient beef cows (−50 to 120 days relative to calving) on pre- or post-weaning growth or carcass characteristics of calves.

In the current study, control cows were expected to be deficient in metabolizable protein by 96 g/day. The increase in milk protein concentration in fishmeal and methionine cows indicates the cows were deficient in methionine. As discussed above, the increased milk yield of methionine cows likely indicates altered one-carbon metabolism. Methionine supplementation likely changed one-carbon metabolism in granulosa cells (Sinclair et al., 2007), which is critical for gametogenesis and embryogenesis (Xu and Sinclair, 2015), resulting in a change in DNA and/or histone methylation of the embryo during the periconception period.

Subsequent calves from fishmeal and methionine cows did not have altered pre-weaning growth performance, but had increased growth and feed efficiency post-weaning likely due to the slightly increased nutrient digestibility and altered carbohydrate and protein metabolism. Maternal nutrition can affect intestinal development in ruminants (Meyer et al., 2014; Gionbelli et al., 2017; Cruz et al., 2019; Relling et al., 2019) that could have influenced nutrient digestion. But, protein supplementation of beef cows in mid through late gestation did not affect nutrient digestibility in offspring (Cruz et al., 2019). In contrast, late gestation supplementation of rumen-protected methionine to ewes increased protein expression of intestinal amino acid transporters and global methylation (Relling et al., 2019). In the current study, methionine increased NDF and ADF digestion compared with fishmeal indicating differential effects of methionine versus total metabolizable protein supplementation on fetal development.

Given that fiber digestibility was the nutrient most affected in the current study, the rumen microbiome may be impacted. Yanez-Ruiz et al. (2015) indicated that host immune function could be one mechanism by which DNA/histone methylation may influence the rumen microbiome. Additionally, genetic markers have been associated with the rumen microbiome (Golder et al., 2018). However, no specific studies have evaluated the effect of maternal nutrition on the rumen microbiome of the offspring.

With regard to post-absorptive metabolism, restriction of methyl donors (methionine and vitamin B12 deficiency) during the periconception period of ewes increased plasma insulin but not glucose in offspring indicating lesser insulin sensitivity (Sinclair et al., 2007), and protein supplementation of cows during the periconception period increased gene expression of several hepatic signaling factors in 98-day-old fetuses (Copping et al., 2020). In contrast to these and the current study focused on the periconception period, rumen-protected methionine supplementation of cows in late gestation did not affect plasma glucose, urea nitrogen, cortisol, or IGF-1 in offspring (Redifer et al., 2018; Moriel et al., 2020). The difference between results of these studies further indicates the divergent impact of maternal nutrition on fetal development depending upon the stage of gestation.

Conclusion

Dietary supplementation with rumen-protected methionine in the form of rumen bypass protein or methionine analog for 115 days during the periconception period of lactating beef cows tended to produce more ECM in dams, as well as improved apparent total tract fiber digestibility and feed efficiency of fetal-programmed beef calves. These data indicate that maternal methionine balance plays an important role in fetal-programming of the bovine; however, the mechanisms by which fetal programming improves performance need to be elucidated.

Ethics approval

All animal handling and techniques were approved prior to data collection by the University of Florida Institutional Animal Care and Use Committee (protocol #201408583).

Data and model availability statement

None of the data were deposited in an official repository. Data are available upon request.

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Declaration of interest

The authors have no conflict of interest.

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