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Metritis and clinical mastitis events in lactating dairy cows were associated with altered patterns of rumination, physical activity, and lying behavior monitored by an ear-attached sensor

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ABSTRACT

Understanding changes in parameters recorded by automated health monitoring systems based on ear-attached sensors on the days immediately before and after diagnosis of metritis and clinical mastitis can help develop dairy cow health monitoring strategies. The objective of this observational cohort study was to characterize rumination time, physical activity, and lying time monitored by an ear-attached sensor before, during, and after clinical diagnosis (CD) of metritis and clinical mastitis. Lactating Holsteins monitored daily for 21 d in milk for detection of health disorders were retrospectively included in the no clinical health disorder group (NCHD; n = 616) if no disorders were diagnosed. Cows were included in the metritis (MET; n = 69) or clinical mastitis (MAST; n = 36) group if diagnosed only with nonsevere metritis (watery, reddish, and fetid uterine discharge with or without pyrexia) or nonsevere clinical mastitis (visibly abnormal milk secretion with or without signs of udder inflammation, with no pyrexia and no systemic signs of disease), respectively. Cows diagnosed with severe metritis (signs of metritis plus systemic signs of disease) or severe clinical mastitis (signs of mastitis plus pyrexia and systemic signs of disease), and cows diagnosed with nonsevere metritis or clinical mastitis plus another disorder within −7 to +7 d of CD of metritis or clinical mastitis diagnosis, were included in the metritis plus (MET+; n = 25) or the clinical mastitis plus (MAST+; n = 15) group, respectively. Cows were fitted with an ear-attached accelerometer to measure rumination time, physical activity, and lying time. Mean daily values, mean value absolute change, and relative change for the mean daily value from 3 or 5 d before CD to the nadir for cows with metritis and clinical mastitis, respectively, were analyzed with linear mixed models with or without repeated measures. Rumination time and physical activity were lesser, and lying time was greater for the MET and MET+ groups than for the NCHD group for most days from −4 to +7 d of CD of metritis. Generally, daily rumination time, physical activity, and lying time differences were greater and more prolonged between the MET+ and NCHD than between the MET and NCHD groups. Similarly, cows in the MAST and MAST+ groups had lesser rumination time and physical activity than cows in the NCHD group for several days before diagnosis. Lying time was greater for the MAST+ than the NCHD group on d −1 and 0 relative to CD. Absolute values and relative changes from 3 d before CD to the day of the nadir for rumination time and physical activity, or peak for lying time, were different for cows in the MET and MET+ groups than for the NCHD group. Similar results were observed for the MAST and MAST+ groups compared with the NCHD group. For cows with metritis, either an increase in rumination time and physical activity or a decrease in lying time was observed from the day of CD to resolution of clinical signs, but no changes were observed for the NCHD. Cows with clinical mastitis and the NCHD group had different rumination times, physical activity, and lying times on the day of CD and resolution of clinical signs, but cows with clinical mastitis had no significant changes from the day of CD to resolution of clinical signs. We conclude that cows affected by metritis and clinical mastitis presented substantial alterations of the patterns of rumination time, physical activity, and lying time captured by an ear-attached sensor. Thus, automated health monitoring systems based on ear-attached sensors might be used as an aid for identifying cows with metritis and clinical mastitis. Moreover, behavioral parameter changes after CD might be good indicators of resolution of clinical signs of metritis but not mastitis.

Key words: dairy cow, health monitoring, sensor, automation

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INTRODUCTION

The transition from a pregnant non-milk-producing to a nonpregnant milk-producing state is critical for dairy cows (Bell, 1995; Goff and Horst, 1997). During this transition, cows undergo metabolic and immune system challenges (Grummer, 1995; Sordillo, 2016; Horst et al., 2021) that increase the likelihood of suffering health disorders (**HD**). As a result, approximately 75% of HD affecting lactating dairy cows during lactation are observed in the first month after calving (LeBlanc et al., 2006; Pinedo et al., 2020). Among the most common HD that affect lactating cows are metabolic-digestive disorders, respiratory disease, metritis, and clinical mastitis (Ribeiro et al., 2013; Macmillan et al., 2021). Metritis and clinical mastitis are 2 disorders of special interest because of their substantial detrimental effects on overall cow health, milk yield, and welfare (Bareille et al., 2003; Pinedo et al., 2020; Pérez-Báez et al., 2021). Moreover, these HD cause economic losses due to treatment costs and the additional burden of cow health monitoring and management programs (Drillich et al., 2001; Mattachini et al., 2013).

To mitigate the detrimental effects of HD through medical or other management interventions, dairy farms implement health monitoring programs to identify cows with HD such as metritis and clinical mastitis as soon and as accurately as possible. Although a universal program to identify cows with HD is not used by all farms, many farms include a combination of methods for identifying clinical signs of disease. These might include visual inspection of body parts or bodily fluids, palpation, evaluation of body temperature, smell, and clinical tests (Espadamala et al., 2016). For many farms this is accomplished while cows are restrained in headgates, palpation lanes, chutes, or during and after milking (Espadamala et al., 2016). A caveat of traditional health monitoring programs is that the frequency, type, and effort dedicated to individual cow examinations might result in different levels of success for identifying cows with HD. Moreover, identification of a small proportion of cows affected by HD in a larger population of cows with no clinical disorders might be time consuming for farm personnel, costly, and disruptive of cow routines when implemented on large groups of cows in medium- to large-size farms (Mattachini et al., 2013).

Use of automated health monitoring systems (**AHMS**), including wearable sensors to monitor behavioral, physiological, and performance parameters, could help mitigate some of the problems of current health monitoring programs. Used alone or in combination with other methods to identify clinical signs of disease, AHMS might contribute to identify cows with HD such as metritis and clinical mastitis. Successful identification of cows with these HD depends on the ability of AHMS to monitor expected behavioral shifts in affected cows (Hart, 1988; Dantzer, 2006; Fogsgaard et al., 2012). In this regard, previous studies have documented that cows diagnosed with metritis and clinical mastitis fitted with wearable neck- or leg-attached sensors had reduced rumination time (**RT**) and physical activity (**PA**) and increased lying time (**LT**) before and after clinical diagnosis (**CD**) of these HD (Soriani et al., 2012; Liboreiro et al., 2015; Stangaferro et al., 2016c,b; Barragan et al., 2018) compared with cows not diagnosed with HD at the same range of DIM. A few studies with neck-attached sensors also suggested that the degree of alteration to cow behaviors monitored was associated with the severity of the disorder or the concomitant occurrence of another health disorder (Stangaferro et al., 2016a,b,c; Silva et al., 2021). This is relevant for cows affected by metritis and clinical mastitis because both HD can be accompanied by systemic signs of disease including pyrexia, reduced milk yield, dullness, inappetence, and anorexia (Drillich et al., 2001; Radostits et al., 2006; Sheldon et al., 2006). In addition, it is common for these HD to overlap with other clinical diseases that affect dairy cows in early lactation (Ribeiro et al., 2013). Thus, evaluating the timing and magnitude of alterations to behaviors monitored by sensors in cows with nonsevere cases of metritis and clinical mastitis versus cows with severe cases, and cows affected concomitantly by other HD, could help inform on-farm use of AHMS data and contribute to the development of AHMS algorithms for alerting farm personnel when cows are affected by HD.

Automated health monitoring systems based on ear-attached sensors that monitor behaviors including RT, PA, and LT are an option for health monitoring in commercial farms. Although highly dependent on the AHMS compared, ear-attached sensor-based AHMS may offer some benefits compared with other wearable sensor-based AHMS. Examples include monitoring behaviors that cannot be monitored by sensors placed on other cow body parts, not requiring readjustment of attachment systems across different stages of lactation, and smaller size. Unlike for AHMS including neck-attached sensors, for which some studies have evaluated the pattern of monitored parameters before, after, or both relative to CD of HD (Stangaferro et al., 2016b,c; Paudyal et al., 2018; Silva et al., 2021), information about the pattern of behaviors monitored by ear-attached sensors in lactating dairy cows affected by metritis and clinical mastitis is lacking. A few studies have documented behavioral parameters changes around CD of health events in the early postpartum period (Gusterer et al., 2020; Stevenson et al., 2020), but no specific information is available about behavioral patterns monitored by ear-attached sensors for cows affected by clinical mastitis and metritis. Data demonstrating an association between disease severity or occurrence of concomitant HD on ear-attached monitored sensor parameters are also not available.

We hypothesized that metritis and clinical mastitis would be associated with alterations to patterns of RT, PA, and LT as monitored by a commercially available AHMS based on an ear-attached sensor. Our secondary hypothesis was that more severe cases of metritis and clinical mastitis, or the concomitant occurrence of other clinical HD, would be associated with greater alterations to the patterns of the parameters of interest. Therefore, the objective of this observational cohort study was to characterize RT, PA, and LT immediately before, during, and after CD of metritis and clinical mastitis in dairy cows monitored with an AHMS that used an ear-attached sensor. The monitored behaviors were evaluated on the days preceding and following diagnosis of metritis and clinical mastitis and were compared with cows not diagnosed with these disorders or other relevant clinical metabolic-digestive disorders (i.e., displaced abomasum, clinical ketosis, and indigestion). Data for cows diagnosed with metabolic-digestive disorders as the primary disorder of interest are presented in a companion manuscript (Rial et al., 2023).

MATERIALS AND METHODS

All procedures performed with animals were approved by the Animal Care and Use Committees of Cornell University (protocol no. 2017-0024) and the University of Minnesota (protocol no. 1912-37705A).

Animals and General Management

Detailed descriptions of cows enrolled and herd management during this prospective cohort observational design study are presented in a companion manuscript (Rial et al., 2023). The study was conducted at a commercial farm in Long Prairie, Minnesota, from January to September of 2020. The farm housed an average of 1,259 (range 1,231 to 1,287) milking and 166 (range 139 to 203) dry Holstein cows during the study period. During the prepartum period, cows were housed in nulliparous and parous pens. Hourly, farm personnel monitored cows visually, and cows with signs of impending calving (i.e., observation of allantoic sac or calf, restlessness) were moved to a single-cow maternity pen bedded with straw. Immediately after calving, cows were milked once, and within approximately 3 to 12 h after calving, cows were transported to lactating pens. Milking occurred 3 times daily at ~8-h intervals in a double-18 parallel parlor equipped with individual stall milk meters (Dematron 75, GEA, Düsseldorf, Germany) for capturing milk weights at every milking.

Cows had ad libitum access to water, and a TMR was delivered twice a day and pushed every hour. Formulated feed ingredients and nutrient composition of the diets fed during the study are presented in a companion manuscript (Rial et al., 2023).

Study Design, Screening Procedures, and Clinical Examination

The study followed a prospective cohort observational design. All cows that calved and initiated a lactation during the study period were eligible for enrollment. No exclusion criteria were implemented.

In total, 871 Holsteins (314 primiparous and 557 multiparous) were enrolled at calving. Cows remained in the study until 21 DIM or until they exited the herd. Data on RT, PA, and LT were collected until 21 DIM or the day of herd exit, whichever occurred first. From 2 to 21 DIM, cow health was evaluated by 2 members of the research team in collaboration with a trained farm technician after the morning milking (~0600 to 0645 h).

From 2 to 10 DIM, a screening procedure was implemented in all cows to identify those that required extensive clinical examination. During this procedure cows were restrained in self-locking headgates with access to TMR. The screening procedure included visual observation, recording of rectal temperature using an electronic thermometer (GLA M700, GLA Agricultural Electronics, San Luis Obispo, CA), evaluation of levels of acetoacetic acid in urine (Ketostix, Ascensia Diabetes Care US Inc., Parsippany, NJ), and milk yield reduction between consecutive milking sessions. A member of the team positioned in front of cows conducted visual observation to determine general attitude (normal = alert, head and ears held up, eyes bright and no recession into the orbit; or depressed = unresponsive, droopy ears, sunken eyes, lethargic), nasal discharge (0 = normal serous discharge; 1 = minimal cloudy discharge; 2 = cloudy and excessive discharge; 3 = copious, bilateral mucopurulent nasal discharge), and apparent poor appetite (i.e., not eating TMR or evidence that cow did not eat TMR during clinical examination while restrained in self-locking headgates). Simultaneously, another technician observed cows from behind to evaluate the presence of fetal membranes, spontaneous vaginal discharge, fetid odor, presence of dry vaginal discharge in the perineum and tail, udder appearance (i.e., shape, color, and consistency to the touch), feet appearance (i.e., shape, signs of pain), and manure consistency for cows that defecated while standing (1 = watery, 2 = loose, 3 = thick porridge forming a pile of 2 to 3 cm, 4 = well-formed and stacks in rings, 5 = dry).

An extensive clinical examination was performed immediately on cows that presented at least one of the following outcomes of the screening procedure: depressed attitude; nasal discharge score >2; manure consistency scores of 1, 2, or 5; retained placenta; poor appetite; signs of inflammation or pain in the udder; rectal temperature >39.4°C; elevated acetoacetate levels in urine based on a Ketostix outcome different from negative (i.e., trace, small, moderate, or large); and milk yield reduction >15% between 2 consecutive milking sessions.

Clinical examination included abdominal auscultation to evaluate primary ruminal movements, abdominal finger percussion to detect resonant areas as evidence of abnormal gas accumulation, thoracic auscultation to evaluate the presence of abnormal lung sounds, and rectal palpation to evaluate rumen fill and obtain manure for determination of manure consistency, color, and odor. Cows that had a result different from negative (negative, trace, small, moderate, and large) for acetoacetate in urine had a blood sample collected for determination of circulating BHB concentrations. Palpation and milk forestripping (milk was stripped onto the floor) were used to evaluate conditions affecting the udder. Milk was considered abnormal if it was off-color or presented clots, flakes, or blood. Clinical mastitis monitoring was also conducted during milking by milkers trained to identify signs of mastitis. An aseptic milk sample was also collected for pathogen culture from individual affected quarters. Cows identified with clinical mastitis at milking underwent the complete clinical examination procedure after milking for confirmation of mastitis and determination of case severity. Cows with pyrexia, defined as rectal temperature ≥39.5°C during the cool season (January to April) and ≥39.7°C during the warm season of the year (May to September), had their uterine discharge evaluated (for consistency, color, and odor) after collection by transrectal uterine massage. At 10 DIM, uterine discharge was obtained by transrectal uterine massage and evaluated in all cows regardless of the outcome of the screening procedure. A watery, reddish, and fetid uterine discharge was considered evidence of metritis. In addition, the udder was evaluated as described, and lungs sounds were checked by thoracic auscultation.

All cows diagnosed with one or more HD were evaluated daily until resolution of clinical signs (**RCS**), defined as the first day at which no clinical signs of disease were observed during the clinical examination procedure conducted as described.

Cows remained in the fresh pen up to 15 to 21 DIM depending on health status (i.e., removed only if no evidence of clinical HD) and space constraints in the fresh pen. Cows that left the fresh pen were moved to high-lactating cow pens for primiparous or multiparous cows. Any cow that left the fresh pen before 21 DIM was under daily visual observation until 20 DIM and underwent a targeted visual observation evaluation at 21 DIM.

Cows that received antibiotic treatment or were diagnosed with clinical mastitis were moved immediately to a hospital pen, where cows had ad libitum access to water and a TMR delivered twice a day. Cows returned to their respective pens after milk tested negative for antimicrobial residues or when treatments were completed.

Health Disorder Definitions

Health disorder definitions were adapted from Stangaferro et al. (2016a,b,c). The following criteria were used to define HD of interest:

- Nonsevere metritis = watery, reddish, and fetid uterine discharge with or without pyrexia, as defined above;
- Severe metritis = watery, reddish, and fetid uterine discharge with pyrexia and at least 1 of the following systemic signs of disease: depressed attitude, anorexia, dehydration, decreased primary ruminal movements, and a reduction in milk yield >15% between 2 consecutive milking sessions;
- Nonsevere clinical mastitis = visibly abnormal milk secretion (i.e., off-color, presence of clots, or blood) with or without signs of udder inflammation, such as hardness, redness, and increased udder skin temperature to the touch;
- Severe clinical mastitis = visibly abnormal milk secretion with or without signs of udder inflammation, as described above, in addition to pyrexia and at least 1 of the systemic signs of disease described for severe cases of metritis;
- Pneumonia = rapid and shallow breathing, moist cough, nasal discharge, wheezing, depressed attitude, with or without pyrexia;
- Clinical ketosis = blood BHB concentration ≥1.2 mmol/L and at least 2 of the following clinical signs: anorexia, depressed attitude, decreased primary ruminal movements, >15% reduction in milk yield in 2 consecutive milking sessions, and altered manure (i.e., too dry or too loose);

- Displaced abomasum = abomasum in an abnormal position on the right or left side of the abdomen, detected by the presence of a metallic sound (i.e., "ping"), during simultaneous auscultation and finger percussion under an imaginary line traced from the tuber coxae to the elbow, and could extend from the 8th to the 12th intercostal space;
- Indigestion = either dry manure or diarrhea, lack of appetite, rumen and intestinal stasis (determined by presence of a dispersed metallic sound while simultaneously auscultating and percussion of either the right or left side of the abdomen) in absence of displaced abomasum and clinical ketosis.

In addition, the following criteria were used to define health conditions that were considered potential confounders for the evaluation of outcomes of interest (RT, PA, and LT). Even though some of these are clinical HD, hereafter, these conditions will be referred to as risk factors (**RF**) and were as follows:

- Retained placenta = failure to expel fetal membranes for up to 24 h after calving;
- Milk fever = inability to rise with or without low temperature, muscle tremors and decreased ruminal motility observed up to 3 DIM;
- Hyperketonemia = BHB concentration $\geq$1.2 mmol/L after a Ketostix outcome different from negative with no clinical signs of HD;
- Lameness = locomotion score $\geq$3 (1 = normal locomotion, 2 = mildly lame, 3 = moderately lame, 4 = lame, 5 = severely lame).

For data analysis, cows were grouped retrospectively based on diagnosis of HD. Cows in the no clinical health disorder (**NCHD**) group were not diagnosed with any of the clinical HD of interest (i.e., displaced abomasum, clinical ketosis, indigestion, metritis, and clinical mastitis) for which we aimed to characterize behavioral data generated by the AHMS used in this study. However, cows in the NCHD could have been diagnosed with the HD included in the RF group. Cows that presented at least 1 case of metritis were divided in 2 groups. Cows with a nonsevere case of metritis only and no other HD diagnosed within −7 to +7 d after CD of metritis were included in the metritis only (**MET**) group, whereas cows with a severe case of metritis (as defined in this study) or with metritis and another clinical HD diagnosed from −7 to +7 d after CD of metritis were included in the metritis plus (**MET+**) group. Cows diagnosed with at least 1 case of clinical mastitis were divided into a mastitis only (**MAST**) or mastitis plus (**MAST+**) group following the same criteria as for cows diagnosed with metritis. Cows in all groups may or may not have had RF recorded.

Automated Health Monitoring System

All cows were fitted with an ear-attached electronic accelerometer tag as part of an AHMS (Smartbow, Zoetis, Parsippany, NJ) a minimum of 2 mo before expected calving. The tag (52 × 36 × 17 mm and weight of 34.1 g) was attached approximately to the upper third of the inner surface of the outer left ear cartilage. Research personnel monitored sensor placement and functionality for individual cows at enrollment and twice weekly until the end of the study.

Data generated by the sensor were stored in the on-farm and cloud Smartbow system servers. At the end of the study, data were provided to researchers by Zoetis.

The health monitoring system recorded RT (min/h), LT (min/h), and PA. For PA, the total minutes of every hour of the day were split into 3 mutually exclusive possible states of PA: inactive, active, and high-active time. Thus, the system reported minutes of inactive, active, and high-active time per hour. For this study, PA was generated by the summation of total minutes of active time and high-active time per hour. Behavioral data (i.e., RT, PA, and LT) for each hour of the day were stored by the system software if at least 40 min of data per hour were available. Hourly periods that did not meet this criterion were included as missing data points for that hourly period. Failing to transfer data from the sensor to the system server was another reason for missing data. Altogether, the percentage of cow-days missing 1 or more hourly periods and removed from the data set was 9.4% (1,633/17,421).

For data analyses, hourly data for RT, PA, and LT were aggregated to generate a daily value in minutes per day for each behavioral parameter individually. Behavioral data were not available when cows where in the hospital pen, because the sensor was unable to communicate with the system reader for transferring data to the servers.

Validation of RT data from the Smartbow system has been reported elsewhere (Borchers et al., 2016; Reiter et al., 2018). Validation results for LT and PA data from the Smartbow system have not been reported in peer-reviewed publications and are not available from the manufacturer. Physical activity data created based on the combination of active and high-active, as used in this study, have been validated for monitoring estrous behavior in lactating dairy cows (Schilkowsky et al., 2021).

Blood Sample Collection and Estimation of Concentrations of Markers of Energy, Mineral, and Inflammation Status

Blood samples were collected for determination of plasma circulating concentrations of nonesterified fatty acids (**NEFA**), Ca, BHB, and haptoglobin (**Hp**) from a subgroup of cows in the NCHD group (n = 200), a subgroup of cows diagnosed with metritis (n = 21), and a subgroup of cows diagnosed with clinical mastitis (n = 20). Blood samples were collected by puncture of the caudal vein or artery using evacuated tubes containing sodium heparin (Vacutainer BD, Franklin Lakes, NJ). After collection, samples were placed in a cooler with ice packs until processing within 1 h of collection. Samples were centrifuged at 1,500 × g for 15 min at 4°C. Plasma aliquots were harvested and transferred to Eppendorf vials for storage at −20°C until assayed.

Blood was collected on the day of CD and on the day of RCS (as defined) for metritis or mastitis. For cows in the NCHD group (n = 200), blood was collected at 7, 14, and 21 DIM, but only the samples collected closest to the average DIM at which CD of metritis (CD = 7 DIM; RCS = 14 DIM) and cows with clinical mastitis (CD = 14 DIM; RCS = 21 DIM) were observed. Blood samples were collected, processed, and analyzed to determine plasma circulating concentrations of NEFA, Ca, BHB, and Hp as described in the companion manuscript (Rial et al., 2023).

Data Processing and Statistical Analysis

The number of cows available for inclusion in this study was based on the sample size estimation conducted for the study reported in the companion manuscript (Rial et al., 2023). All data analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Descriptive statistics and frequency distributions for daily values for the parameters of interest (RT, PA, and LT) were generated with PROC MEANS and PROC UNIVARIATE. The normality of continuous data was evaluated before statistical analysis using graphical methods (histogram) and the Shapiro-Wilk test of normality generated by PROC UNIVARIATE. In addition, normality of residuals and homogeneity of variance for all models with continuous outcomes were evaluated using residual plots. We used univariate analysis to evaluate associations between covariates and outcomes of interest. Covariates explored were season of calving (cold = January to April, vs. warm = May to September) and RF (i.e., no RF or at least 1 RF). A confounder was offered to multivariable statistical models if for the univariate analysis $P < 0.10$.

Behavioral parameter data generated by the AHMS for cows with clinical mastitis were available only until the day of CD because cows were moved to a hospital pen where the sensor was unable to communicate with the system reader to transfer data to the servers, resulting in missing data. Therefore, the daily pattern of RT, PA, active time, high-active time, LT, and milk yield (**MY**; kg/d) were evaluated from 7 d before until the day of CD (d 0) of events of clinical mastitis diagnosed during the study period. In contrast, for cows diagnosed with metritis, behavioral parameters from the AHMS were evaluated from −4 to 7 d after CD because data from earlier than −4 d of CD were altered by the effects of calving on parameters of interest.

Patterns of Behavioral Parameters Relative to CD

Two events of the same disorder were considered different events when diagnosed at least 7 d apart. For cows in the NCHD group, the average DIM at CD for cows in the MET/MET+ or MAST/MAST+ group was considered d 0. Data for the patterns of RT, PA, and LT were analyzed by ANOVA with repeated measurements using PROC MIXED. Models for each outcome of interest included group, day (i.e., days relative to CD), and the group by day interaction as fixed effects. Calving season and records of the occurrence of at least 1 RF were offered as covariates. Parity (primiparous vs. multiparous) was forced in all models. Cow within group was included as a random effect in all models, and cow was the subject of repeated measurements. Different covariance structures (i.e., compound symmetry, autoregressive order 1 with and without random effects, Toeplitz, and unstructured) were fitted to models for each response of interest. In all cases, Toeplitz minimized the Akaike information criterion and, thus, was selected as the covariance structure for all models. All final models included group, time, the group by day interaction, and parity, whereas other covariates were removed by manual backward elimination if $P > 0.10$. A similar analysis was conducted to determine the interval in days between nadir (RT and PA) or peak (LT) and the CD of disorders of interest. Models were developed and selected as described, including only day as fixed effect, using data for cows with the disorders of interest only.

Absolute and Relative Changes for Behavioral Parameters and Milk Yield

Analyses were conducted to compare absolute daily mean values in units of measurement and relative (%) differences for mean daily values for parameters of interest (i.e., RT, PA, LT, and MY) between 3 or

5 d before CD for metritis and mastitis, respectively, and the day of their nadir or peak for the respective parameters. Because cows in the NCHD group did not have a true nadir or peak, the value for d 0 was used as the equivalent to the day of the nadir or peak for cows with metritis and clinical mastitis. Moreover, we compared the interval in days between the nadir or peak daily value for the parameters of interest and the day of CD. The day of the nadir or peak for cows with mastitis was truncated to the day of CD because data were not available beyond that time point. For analysis of changes relative to CD, an interval of 3 d was used for the MET and MET+ groups and 5 d in the MAST and MAST+ groups, to avoid the effect of calving on the parameters of interest. The absolute change was calculated by subtracting the absolute mean daily value for RT, PA, LT, and MY at 3 or 5 d before CD for cows with metritis or mastitis, respectively, from the mean daily value observed on the day of the nadir or peak for the parameter. For relative changes, the absolute difference between the mean daily value on day of the nadir was divided by the mean daily value for RT, PA, LT, and MY observed 3 or 5 d before CD for cows with metritis or mastitis, respectively, and then multiplied by 100. The same procedures were used for estimating absolute and relative changes for cows in the NCHD group but using the average DIM at diagnosis of metritis or clinical mastitis as the day of CD. All analyses were conducted by ANOVA using PROC MIXED. Different models were run for each outcome of interest to compare cows with no clinical health disorders with cows in the MET/MET+ or MAST/MAST+ groups. Thus, all models included group of interest and parity, whereas calving season and RF were offered as covariates.

Differences for Sensor Data, Milk Yield, and Blood Parameters on the Day of CD and RCS and Changes from the Day of CD to RCS

Behavioral parameters, MY, and blood parameters (NEFA, Ca, Hp, and BHB) were compared on the day of CD and RCS for cows diagnosed with metritis or clinical mastitis and the NCHD group. Data for the day of RCS were available from 16 cows with clinical mastitis that had already returned to pens in which sensors were able to transfer data to Smartbow servers. Data were analyzed by ANOVA with repeated measurements using PROC MIXED with models that included group (NCHD, metritis, and mastitis) and day relative to CD (i.e., day of CD and RCS) as fixed effects. Cow was the subject of repeated measurements. The covariance structure used was heterogeneous Toeplitz because this method does not assume equal variance among repeated measurements. Parity was forced in all models, and season of calving and RF were offered as covariates and removed by backward stepwise elimination as described above.

All explanatory variables and their interactions were considered significant if $P \leq 0.05$, whereas $0.05 < P \leq 0.10$ were considered marginally significant. When appropriate, the least significant difference post hoc mean separation test was used to determine differences between groups of means. Unless otherwise stated, all results are least squares means ± standard error of the mean.

RESULTS

Proportion of Cows with Clinical Health Disorders and Risk Factors

From a total of 871 cows enrolled, 51 were excluded from data analyses: 10 cows were sold or died before 2 DIM, and 41 cows had incomplete data due to sensor malfunction (n = 6) or did not have a sensor tag up to the end of the study period (n = 35). Data from 34 cows that were sold or died were included in analyses until the day of herd exit (mean days to herd exit and SD = 11.1 ± 8.5 DIM). Out of the remaining 820 cows, 75.1% (n = 616/820) were not diagnosed with any of the clinical HD of interest (i.e., displaced abomasum, clinical ketosis, indigestion, metritis, and clinical mastitis) for which we aimed to characterize behavioral data. In all, 32% (n = 199/616) of the cows in the NCHD group presented at least 1 RF: hyperketonemia (n = 161), lameness score ≥3 (n = 17), milk fever (n = 3), retained placenta (n = 7), or more than 1 of these disorders (n = 11). On the other hand, 24.9% of the cows (n = 204/820) had at least 1 clinical HD of interest for this study recorded up to 21 DIM, and out of these cows 53.4% (n = 109/204) had at least 1 RF. Out of all cows with at least 1 clinical HD diagnosed, 46.1% (n = 94/204) had at least 1 event of metritis, and 25.0% (n = 51/204) had 1 event of clinical mastitis. The proportions of cows diagnosed with metritis and clinical mastitis out of all cows included for data analysis were 11.4% (94/820) and 6.2% (51/820), respectively. Out of all cases of metritis diagnosed, 73.4% (n = 69/94) met the criteria to be classified as nonsevere and therefore were included in the MET group. The remaining 26.6% (n = 25/94) were either classified as severe or had another HD within 7 d of CD of metritis and therefore were included in the MET+ group. Out of all cases of clinical mastitis diagnosed, 70.6% (n = 36/51) met the criteria to be assigned to the MAST group and 29.4% (n = 15/51; Table 1) to the MAST+ group following the defined criteria. None of the cows

Table 1. Number and proportion of cows diagnosed with metritis and clinical mastitis and DIM at clinical diagnosis for 820 lactating Holstein cows evaluated from 2 to 21 DIM

Health disorder group	Cows (n)	Cows[1] (%)	DIM at CD[2] (mean ± SD)
All metritis[3]	94	—	6.1 ± 1.8
MET[4]	69	73.4	5.8 ± 1.8
MET+[5]	25	26.6	6.9 ± 1.6
All mastitis[6]	51	—	11.2 ± 5.0
MAST[7]	36	70.6	11.5 ± 5.4
MAST+[8]	15	29.4	10.3 ± 4.0

[1]Proportion of the disorders.

[2]CD = clinical diagnosis.

[3]Cows diagnosed with at least 1 event of metritis during the period of interest.

[4]Cows diagnosed with nonsevere metritis and no other clinical health disorder.

[5]Cows diagnosed with severe metritis or metritis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, mastitis, pneumonia).

[6]All mastitis = cows with at least 1 event of mastitis.

[7]Cows diagnosed with nonsevere mastitis and no other clinical health disorder.

[8]Cows diagnosed with severe mastitis or mastitis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, metritis, pneumonia).

presented more than 1 event of the metritis or clinical mastitis up to the end of the study period.

Data for cows (n = 58) diagnosed with metabolic-digestive disorders only are presented in a companion manuscript (Rial et al., 2023).

Rumination Time, Physical Activity, and Lying Time

Metritis. We observed an interaction between group and day ($P < 0.001$) for RT, whereby cows in the MET group had less RT than cows in the NCHD group from −3 to +2 d relative to CD (Figure 1A). Cows in the MET+ group had less RT than the NCHD group from −4 to +5 d relative to CD, except for d +4, and had less RT than the MET group from −4 to −2 d and at +5 d relative to CD. Primiparous cows had less RT ($P < 0.001$) than multiparous cows, and cows that calved during cool season had less RT ($P < 0.001$) than cows that calved during warm season (Supplemental Table S1, https://hdl.handle.net/1813/113442).

An interaction between group and day ($P < 0.001$) was observed for PA (active time + high-active time), whereby the MET group had less PA than the NCHD group from −4 to +4 d relative to CD (Figure 1B). The MET+ group had less PA than the NCHD from −4 to +7 d relative to CD and less PA than the MET group from −4 to −3 d, at d +3, and at +5 to +7 relative to CD. Cows that calved during cool season had lower PA ($P < 0.001$) than those that calved during warm season, and cows with RF had a marginally significant reduction in PA ($P = 0.09$) than cows with no RF in this analysis (Supplemental Table S1).

For LT, an interaction occurred between group and day ($P < 0.001$) whereby the MET group had greater LT than the NCHD group from −4 to +7 d relative to CD (Figure 1C). Cows in the MET+ group had greater LT than the NCHD group from −4 to +7 d relative to CD and had greater LT than the MET group from −4 to −2 d and at d +5 relative to CD. Primiparous had lower LT than multiparous ($P < 0.001$), and cows with RF had a marginally significant increase in LT than those with no RF ($P = 0.09$) in this analysis (Supplemental Table S1).

Clinical Mastitis. We detected an interaction between group and day ($P < 0.001$) for RT, whereby the MAST group had less RT than the NCHD group from −4 to 0 d relative to CD (Figure 2A). In addition, the MAST+ group had less RT than the NCHD and MAST groups from −6 to 0 d relative to CD and at −6, −5, −1, and 0 d relative to CD, respectively. Primiparous cows had lower RT ($P < 0.001$) than multiparous cows, and cows that calved during cool season had lower RT ($P < 0.001$) than cows that calved during warm in this analysis (Supplemental Table S1).

For PA, an interaction between group and day ($P < 0.001$) was observed because the MAST group had less PA the NCHD group from −3 to 0 d relative to CD (Figure 2B). Cows in the MAST+ group had lower PA than the NCHD group from −6 to 0 d relative to CD and lower PA than the MAST group from −6 to −4 and at −1 and 0 d relative to CD. Cows that calved during cool season had lower PA ($P < 0.001$) than cows that calved during warm season, and cows with RF had lower PA ($P = 0.006$) than those with no RF in this analysis (Supplemental Table S1).

For LT, we observed an interaction between group and day ($P < 0.001$) whereby the MAST+ group had greater LT than the NCHD and MAST groups at d −1 and 0 relative to CD (Figure 2C), but no difference was detectable between the NCHD and MAST groups

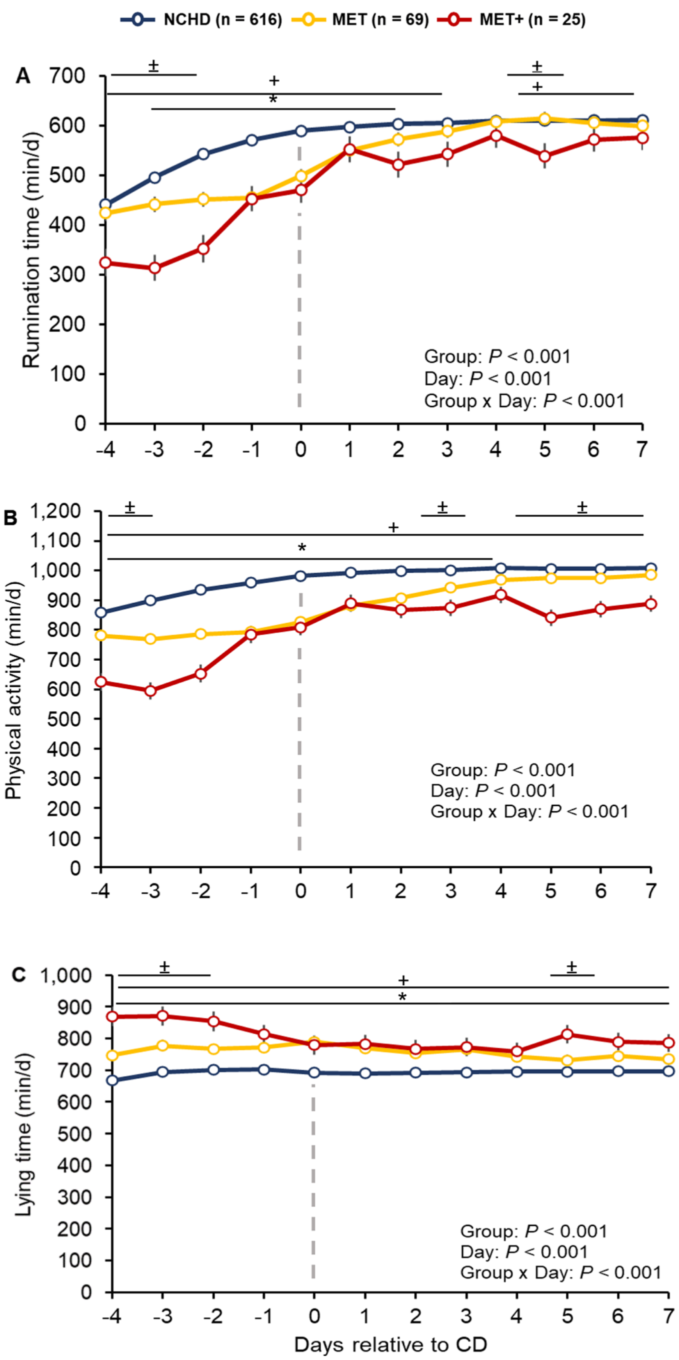

Figure 1. Patterns of daily rumination time (A), physical activity (B), and lying time (C) from 4 d before to 7 d after clinical diagnosis (CD) of metritis for cows diagnosed with nonsevere cases of metritis and no other clinical health disorder (MET; n = 69), cows with a severe case of metritis or metritis with at least 1 other health disorder (MET+; n = 25), and cows with no clinical health disorders diagnosed (NCHD; n = 616). For the NCHD group, the average DIM at CD for all cows with metritis (i.e., 6 DIM) was considered d 0 (vertical dashed lines). Values are LSM ± SEM. Within a day, differences between groups based on the LSD test are represented as follows: * MET different from NCHD; + MET+ different from NCHD; ± MET different from MET+.

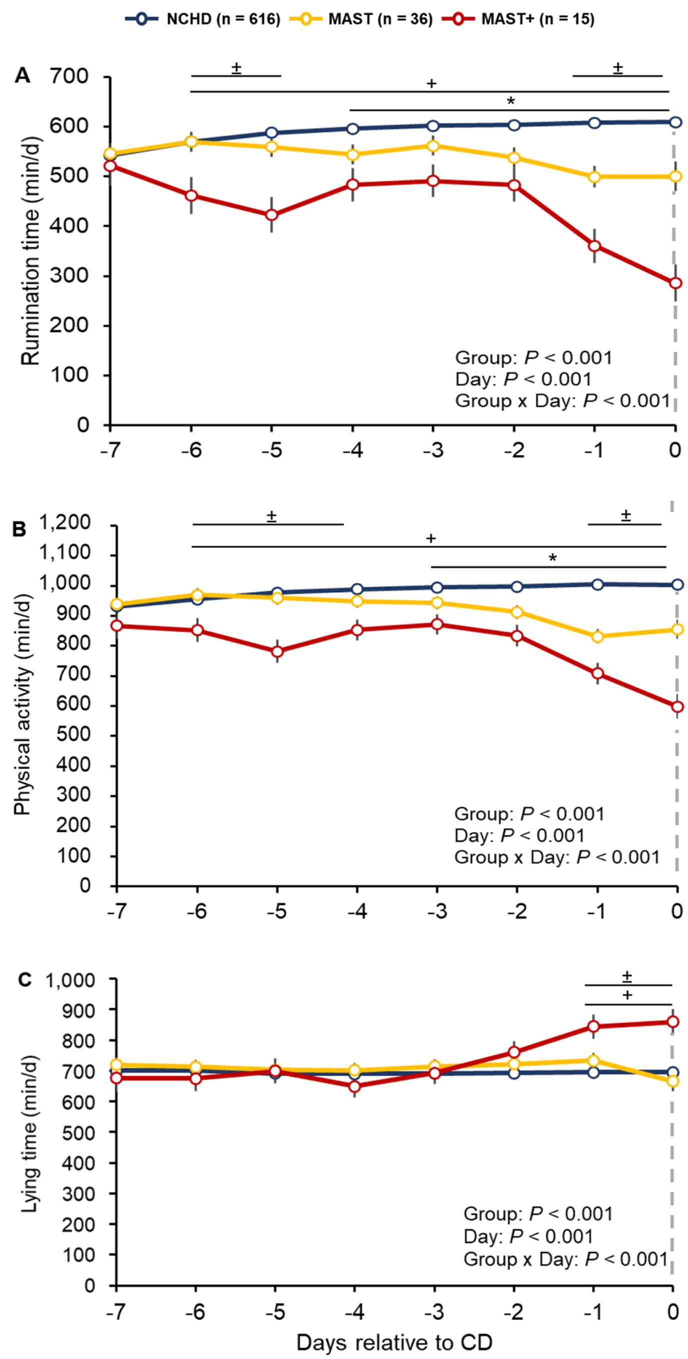

Figure 2. Patterns of daily rumination time (A), physical activity (B), and lying time (C) from 7 d before to the day of clinical diagnosis (CD) of mastitis for cows diagnosed with nonsevere cases of mastitis and no other clinical health disorder (MAST; n = 36), cows with a severe case of mastitis or mastitis with at least 1 other health disorder (MAST+; n = 15), and cows with no clinical health disorders diagnosed (NCHD; n = 616). For the NCHD group, the average DIM at CD for all cows with mastitis (i.e., 11 DIM) was considered d 0 (vertical dashed lines). Values are LSM ± SEM. Within a day, differences between groups based on the LSD test are represented as follows: * MAST different from NCHD; + MAST+ different from NCHD; ± MAST different from MAST+.

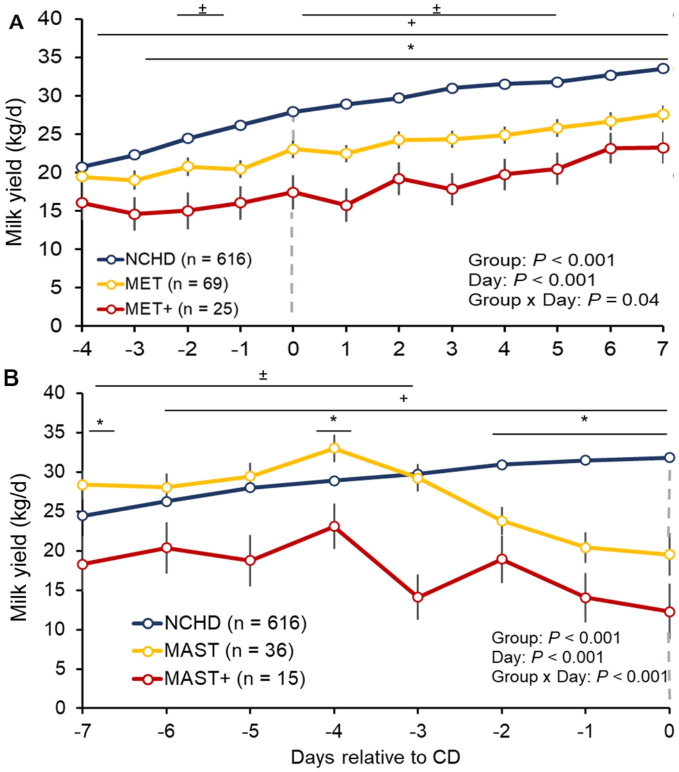

Figure 3. Daily milk yields for cows with nonsevere cases of metritis (MET, A) or nonsevere mastitis (MAST, B) and no other clinical health disorder; cows with severe cases of metritis (MET+) or mastitis (MAST+) plus another health disorder; and cows with no clinical health disorders diagnosed (NCHD). For cows in the NCHD group, the average DIM at day of clinical diagnosis (CD) for all cows with metritis or mastitis was considered d 0 (vertical dashed lines). Values are LSM ± SEM. Within a day, differences between groups based on the LSD test are represented as follows: * MET or MAST different from NCHD; + MET+ or MAST+ different from NCHD; ± MET or MAST different from MET+ or MAST+.

($P = 0.45$). Primiparous cows had lower LT ($P < 0.001$) than multiparous (Supplemental Table S1).

Milk Yield Relative to Clinical Diagnosis

Metritis. We observed an interaction between group and day ($P < 0.001$) for MY because the MET group produced less milk than NCHD group from −3 to +7 d relative to CD (Figure 3A). The MET+ group produced less milk than the MET and NCHD groups at d −2, from 0 to +5 d, and from −4 to +7 relative to CD, respectively. Primiparous cows produced less milk ($P < 0.001$) than multiparous, and cows with RF produced more milk ($P < 0.001$) than cows with no RF in this analysis (Supplemental Table S1).

Clinical Mastitis. We observed an interaction between group and day ($P < 0.001$), as the MAST group produced more milk on d −7 and −4, and then less milk from d −2 to 0 relative to CD, than the NCHD group (Figure 3B). The MAST+ group produced less milk than the NCHD from −6 to 0 d relative to CD. Compared with the MAST group, the MAST+ group produced less milk from −7 to −3 relative to CD. Primiparous cows produced less milk ($P < 0.001$) than multiparous, and cows with RF produced more milk ($P < 0.001$) than cows with no RF (Supplemental Table S1).

Absolute and Relative Changes in Rumination Time, Physical Activity, and Milk Yield Up to the Day of Nadir or to the Day of Peak for Lying Time

The absolute and relative changes from 3 d before CD to the day of the nadir for RT, PA, and MY, or the day of the LT peak for cows with metritis, are presented in Table 2. Cows in the MET and MET+ group had greater ($P < 0.001$) absolute and relative changes compared with cows in the NCHD group for all behavioral parameters and MY, except for relative changes for PA and LT. Conversely, no differences ($P > 0.10$) were observed between the MET and MET+ group. The associations for covariates was consistent regardless of the analysis. Both parity and season of calving were associated with RT outcomes ($P < 0.05$). Parity and season of calving ($P < 0.05$) were associated with PA outcomes, whereas LT and MY outcomes were associated with parity only ($P < 0.05$).

Absolute and relative change data for cows with clinical mastitis are presented in Table 3. For all comparisons, we found an association between group ($P < 0.001$) and outcomes of interest because cows in the MAST and MAST+ group differed from cows in the NCHD group. Except for LT, for which cows in the MAST+ group had a greater ($P < 0.05$) change than cows in the MAST group, no differences were detectable between these 2 groups. The associations between covariates and outcomes were consistent regardless of the analysis. Season of calving was associated ($P < 0.05$) with RT outcomes. Physical activity was not associated ($P > 0.1$) with parity, season of calving, or RF. Parity was associated ($P < 0.05$) with LT and MY outcomes.

The difference in interval in days between the nadir for RT, PA, and MY and the peak for LT with the day of CD for cows with metritis (MET vs. MET+) and clinical mastitis (MAST vs. MAST+) are shown in Table 4. Negative values indicate that the nadir or peak was observed before the day of CD, whereas positive values indicate that the nadir or peak was observed after the day of CD. There was no statistically significant difference ($P > 0.10$; Table 4) between groups for

Table 2. Absolute values and percent change from 3 d before clinical diagnosis of the disorders of interest to the day of the nadir for daily rumination time, physical activity, milk yield, or peak daily lying time for cows in MET and MET+ groups from 2 to 21 DIM

	Health disorder group			
Item[1]	NCHD[2] (n = 616)	MET[3] (n = 69)	MET+[4] (n = 25)	P-value
Rumination time				
Absolute change (min)	130.9 ± 7.0[a]	−60.9 ± 21.5[b]	−76.3 ± 36.6[b]	<0.001
Relative change (%)	35.5 ± 2.2[a]	−4.2 ± 6.9[b]	−4.5 ± 11.7[b]	<0.001
Physical activity				
Absolute change (min)	112.6 ± 7.4[a]	−106.5 ± 22.9[b]	−173.6 ± 37.7[b]	<0.001
Relative change (%)	24.2 ± 7.1	−10.5 ± 23.9	−29.3 ± 39.6	0.17
Lying time				
Absolute change (min)	31.8 ± 5.2[b]	87.8 ± 17.7[a]	81.8 ± 30.4[ab]	<0.001
Relative change (%)	8.3 ± 0.9	13.3 ± 3.0	13.9 ± 5.2	0.18
Milk yield				
Absolute change (kg)	7.0 ± 0.3[a]	−2.9 ± 1.0[b]	−4.6 ± 1.7[b]	<0.001
Relative change (%)	36.9 ± 1.8[a]	−21.7 ± 6.1[b]	−45.5 ± 11.4[b]	<0.001

[a,b]Different superscripts within a row indicate differences ($P \leq 0.05$) between means based on the LSD post hoc test.

[1]Data presented include the absolute difference or the relative change between 5 d before clinical diagnosis and the day of the nadir for rumination time, active time, and milk yield, or the peak for lying time. Values are LSM ± SEM.

[2]NCHD = no clinical health disorders. Cows not diagnosed with clinical health disorders during the period of interest.

[3]MET = cows diagnosed with nonsevere metritis and no other clinical health disorder.

[4]MET+ = cows diagnosed with severe metritis or metritis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, mastitis, pneumonia).

most of the comparisons. We only observed that the nadir for PA was earlier ($P < 0.001$) for cows in MET+ than for those in the MET group, and the nadir for MY was earlier ($P = 0.03$) for cows in the MAST+ than for those in the MAST group. Season was marginally significantly associated ($P < 0.10$) with RT outcomes for cows with metritis. Parity ($P < 0.05$) was associated with MY outcomes for cows with clinical mastitis.

Table 3. Absolute values and percent change from 5 d before clinical diagnosis of the disorders of interest to the day of the nadir for daily rumination time, physical activity, milk yield, or peak daily lying time for cows in the MAST and MAST+ groups diagnosed from 2 to 21 DIM

	Health disorder group			
Item[1]	NCHD[2] (n = 616)	MAST[3] (n = 36)	MAST+[4] (n = 15)	P-value
Rumination time				
Absolute change (min)	18.2 ± 7.4[a]	−126.5 ± 28.0[b]	−203.8 ± 52.4[b]	<0.001
Relative change (%)	6.7 ± 1.4[a]	−19.4 ± 5.3[b]	−36.6 ± 9.9[b]	<0.001
Physical activity				
Absolute change (min)	25.9 ± 7.3[a]	−402.7 ± 28.7[b]	−362.3 ± 51.5[b]	<0.001
Relative change (%)	4.5 ± 1.6[a]	−40.6 ± 7.2[b]	−38.7 ± 13.0[b]	<0.001
Lying time				
Absolute change (min)	3.9 ± 4.8[c]	107.2 ± 20.3[b]	261.3 ± 38.1[a]	<0.001
Relative change (%)	2.1 ± 0.7[c]	16.8 ± 3.2[b]	43.0 ± 6.1[a]	<0.001
Milk yield				
Absolute change (kg)	3.1 ± 0.4[a]	−11.0 ± 1.5[b]	−7.4 ± 3.0[b]	<0.001
Relative change (%)	14.4 ± 1.5[a]	−29.2 ± 6.0[b]	−49.5 ± 14.1[b]	<0.001

[a–c]Different superscripts within a row indicate differences ($P \leq 0.05$) between means based on the LSD post hoc test.

[1]Data presented include the absolute difference or the relative change between 5 d before clinical diagnosis and the day of the nadir for rumination time, active time, and milk yield, or the peak for lying time. Values are LSM ± SEM.

[2]NCHD = no clinical health disorders. Cows not diagnosed with any clinical health disorder.

[3]MAST = cows diagnosed with nonsevere mastitis and no other clinical health disorder.

[4]MAST+ = cows diagnosed with severe mastitis or mastitis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, metritis, pneumonia).

Table 4. Interval in days between clinical diagnosis (CD) and the nadir or peak for daily rumination time, physical activity, milk yield, and lying time for cows diagnosed with metritis or clinical mastitis between 2 and 21 DIM

	Interval in days from nadir or peak to CD[1]					
Parameter	MET[2] (n = 69)	MET+[3] (n = 25)	P-value	MAST[4] (n = 36)	MAST+[5] (n = 15)	P-value
Rumination time	−1.2 ± 0.2	−0.4 ± 06	0.23	−2.5 ± 0.2	−2.1 ± 0.5	0.51
Physical activity	−1.2 ± 0.3	1.0 ± 0.5	0.001	−1.1 ± 0.2	−1.7 ± 0.6	0.38
Lying time	0.07 ± 0.3	−0.9 ± 0.7	0.21	−2.8 ± 0.2	−2.0 ± 0.4	0.16
Milk yield	−0.1 ± 0.4	0.8 ± 1.1	0.41	−3.2 ± 0.3[b]	−2.0 ± 0.5	0.03

[1]Days from the day of the nadir for daily rumination time, physical activity, milk yield, or peak daily lying time to the day of clinical diagnosis of the disorder of interest.

[2]MET = cows diagnosed with nonsevere metritis and no other clinical health disorder.

[3]MET+ = cows diagnosed with severe metritis or metritis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, mastitis, pneumonia).

[4]MAST = cows diagnosed with nonsevere mastitis and no other clinical health disorder.

[5]MAST+ = cows diagnosed with severe mastitis or mastitis and at least 1 other clinical health disorder (i.e., any metabolic-digestive disorder, metritis, pneumonia).

Differences in Behavioral Parameters and Milk Yield Between the Day of Clinical Diagnosis and Resolution of Clinical Signs

Metritis. For RT, an interaction ($P < 0.001$) was detectable for group and day, whereby cows with metritis had less RT (Figure 4A) than cows in the NCHD group on the day of CD (metritis: 498.9 ± 12.5 min/d; NCHD: 570.1 ± 5.1 min/d) but not on the day of RCS (metritis: 594.9 ± 12.1 min/d; NCHD: 602.0 ± 4.8 min/d). For both the NCHD group and for cows with metritis, RT was greater ($P < 0.05$) on the day of RCS than on the day of CD. Rumination time was greater ($P < 0.001$) for multiparous than for primiparous cows and greater ($P < 0.001$) for cows that calved during the warm than the cool season.

For PA, there was an interaction ($P < 0.001$) between group and day, as cows with metritis had less PA than cows in the NCHD group on the day of CD (metritis: 825.9 ± 14.3 min/d; NCHD: 957.3 ± 6.0 min/d) and RCS (metritis: 956.1 ± 12.7 min/d; NCHD: 997.6 ± 5.4 min/d), and PA increased for both groups from the day of CD to the day of RCS (Figure 4B). Physical activity was greater ($P < 0.001$) for cows that calved during the warm than the cool season and was less ($P = 0.02$) for cows with than without RF.

For LT, an interaction between group and day ($P = 0.03$) was observed because cows with metritis had more LT than cows in the NCHD group on the day of CD (metritis: 792.3 ± 14.6 min/d; NCHD: 709.3 ± 6.3 min/d) and on the day of RCS (metritis: 756.9 ± 13.9 min/d; NCHD: 701.6 ± 6.0 min/d), and cows with metritis had lesser LT on the day of RCS than CD (Figure 4C). Lying time was greater ($P < 0.001$) for multiparous than primiparous cows and greater ($P = 0.02$) for cows that calved during the cool than the warm season. Marginal significance was detectable ($P = 0.07$) for an association between RF and LT, whereby cows with RF had greater LT than cows without RF.

Finally, cows with metritis had reduced ($P < 0.001$) MY (Figure 4D) compared with cows in the NCHD group on the day of CD (metritis: 21.9 ± 0.8 kg/d; NCHD: 27.5 ± 0.3 kg/d) and RCS (metritis: 24.8 ± 0.9 kg/d; NCHD: 31.4 ± 0.3 kg/d). Milk yield was greater ($P < 0.001$) for multiparous than primiparous cows, greater ($P = 0.02$) for cows that calved during the warm than the cool season, and greater ($P < 0.001$) for cows with than without RF.

Clinical Mastitis. Cows with clinical mastitis (444.8 ± 26.5 min/d) had less ($P < 0.001$) overall RT than cows in the NCHD group (605.7 ± 4.5 min/d; Figure 5A) at both time points. Rumination time was greater ($P < 0.001$) for multiparous than for primiparous cows and greater ($P < 0.001$) for cows that calved during the warm than the cool season.

Cows with clinical mastitis (817.0 ± 26.6 min/d) had less ($P < 0.001$) overall PA than cows in the NCHD group (1,017.7 ± 4.6 min/d), and overall, we found marginal significance ($P = 0.06$) for PA to be greater on the day of RCS (933.1 ± 17.5 min/d) than CD (901.6 ± 14.5 min/d; Figure 5B). Physical activity was greater ($P < 0.001$) for multiparous than for primiparous cows, and greater ($P = 0.004$) for cows that calved during the warm than the cool season.

Cows with clinical mastitis (769.6 ± 31.1 min/d) had greater LT ($P = 0.009$) than cows in the NCHD group (688.0 ± 4.8 min/d; Figure 5C). Lying time was greater ($P < 0.001$) for multiparous than for primiparous cows.

Finally, cows with clinical mastitis (19.3 ± 1.9 kg/d) had less ($P < 0.001$) MY than cows in the NCHD group (33.6 ± 0.3 kg/d), and overall MY was greater ($P = 0.03$) on the day of RCS (27.8 ± 1.2 kg/d) than

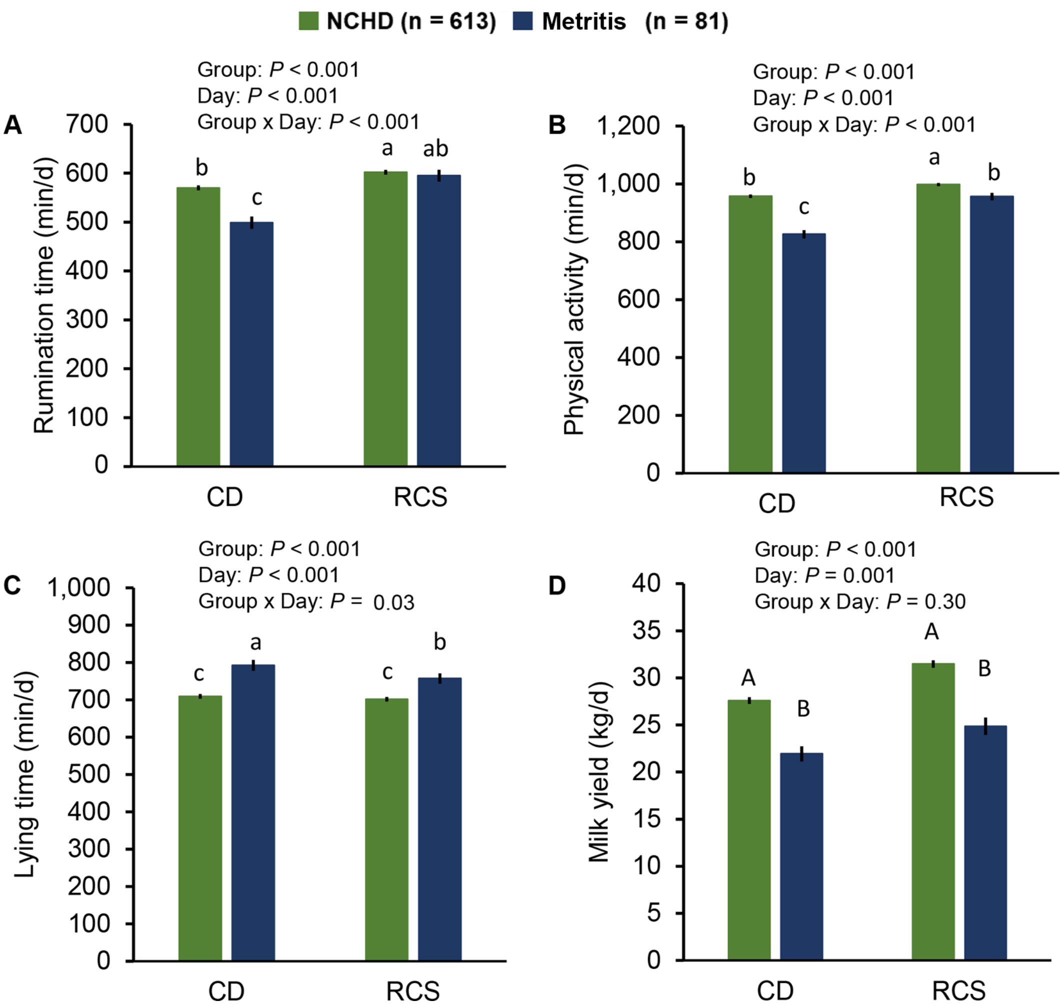

Figure 4. Median rumination time (A), physical activity (B), lying time (C), and milk yield (D) average values on the day of clinical diagnosis (CD) and the day of resolution of clinical signs (RCS) for cows diagnosed with nonsevere metritis (n = 81) and cows with no clinical health disorders diagnosed (NCHD, n = 613). For cows in the NCHD group, values for the day of CD and RCS were for the average DIM at CD (i.e., 5 DIM) and RCS (i.e., 9 DIM) for cows with metritis. Values are LSM ± SEM. Within a day, differences between groups based on the LSD test are represented by uppercase letter differences; the interactions are represented by lowercase letter differences.

on the day of CD (25.0 ± 1.0 kg/d; Figure 5D). Multiparous cows produced more milk ($P < 0.001$) than primiparous cows, and cows with RF produced more milk ($P < 0.001$) than cows without RF.

Plasma Concentrations of Ca, NEFA, BHB, and Hp on the Day of Clinical Diagnosis and Resolution of Clinical Signs

Metritis. For Ca concentrations, we detected no association for group ($P = 0.99$), day ($P = 0.72$), or group by day interaction ($P = 0.76$; Figure 6A). We found that NEFA concentrations were greater ($P = 0.008$) for cows with metritis (0.7 ± 0.1 mEq/L) than for cows in the NCHD group (0.5 ± 0.1 mEq/L) and were also greater on the day of CD (0.7 ± 0.1 mEq/L) than at RCS (0.5 ± 0.1 mEq/L), but no group by day interaction was detectable ($P = 0.70$; Figure 6B). Cows with RF had greater ($P = 0.04$) concentrations of NEFA than cows without RF. An interaction between group and day ($P < 0.001$) was observed for BHB (Figure 6C) because cows with metritis had greater concentrations of BHB than cows in the NCHD group on the day of CD (metritis: 1.2 ± 0.07 mmol/L; NCHD: 0.9 ± 0.06 mmol/L) but had reduced concentrations of BHB on the day of RCS (metritis: 0.8 ± 0.06 mmol/L; NCHD: 1.0 ± 0.02 mmol/L). Moreover, cows in the NCHD group had the same concentrations of BHB on the day of CD and RCS, whereas cows with metritis had greater concentrations of BHB on the day of CD than on the day of RCS. Concentrations of BHB were greater ($P < 0.001$) for cows with

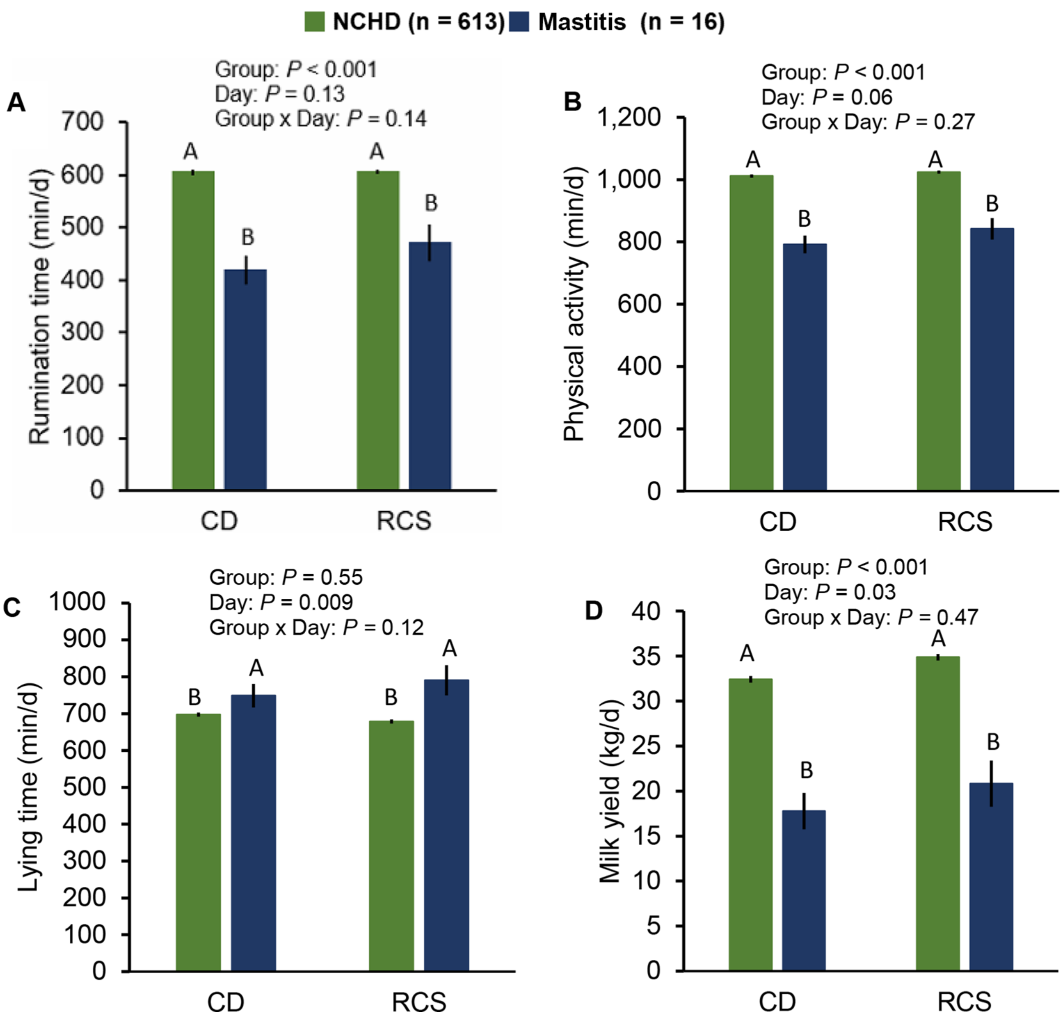

Figure 5. Median rumination time (A), physical activity (B), lying time (C), and milk yield (D) on the day of clinical diagnosis (CD) and the day of resolution of clinical signs (RCS) for cows diagnosed with mastitis (n = 16) and cows with no clinical health disorders diagnosed (NCHD, n = 613). For cows in the NCHD group, values for the day of CD and RCS were for the average DIM at CD (i.e., 10 DIM) and RCS (i.e., 15 DIM) for cows with mastitis. Values are LSM ± SEM. Within a day, differences between groups based on the LSD test are represented by uppercase letter differences; the interactions are represented by lowercase letter differences.

than without RF and were marginally significantly greater ($P = 0.08$) for multiparous than primiparous cows. For concentrations of Hp (Figure 6D), we found an association with group ($P < 0.001$), as cows with metritis (2.6 ± 0.1 mg/mL) had greater Hp concentrations than cows in the NCHD group (0.6 ± 0.05 mg/mL) on both days. There was also an effect of day ($P < 0.001$) because concentrations of Hp were greater on the day of CD (1.9 ± 0.1 mg/mL) than at RCS (1.2 ± 0.1 mg/mL).

Clinical Mastitis. Concentrations of Ca did not differ ($P = 0.86$) between groups or days ($P = 0.53$), and there was no group by day interaction ($P = 0.88$; Figure 7A). Concentrations of NEFA were greater ($P = 0.001$) for cows with clinical mastitis (0.7 ± 0.1 mEq/L) than for cows in the NCHD group (0.4 ± 0.07 mEq/L) on both days, and overall concentrations of NEFA were greater ($P = 0.02$) on the day of CD (0.6 ± 0.08 mEq/L) than at RCS (0.5 ± 0.09 mEq/L; Figure 7B). Multiparous cows had greater ($P = 0.005$) concentrations of NEFA than primiparous cows, and cows that calved during the warm season had marginally significantly ($P = 0.08$) greater concentrations of NEFA than cows that calved during the cool season. Marginal significance ($P = 0.07$) was detected for an interaction for concentrations of BHB, because cows with clinical mastitis had greater BHB than cows in the NCHD group on the day of CD (mastitis: 1.2 ± 0.07 mmol/L; NCHD: 1.0 ± 0.02 mmol/L), but no difference was found on the day of RCS (mas-

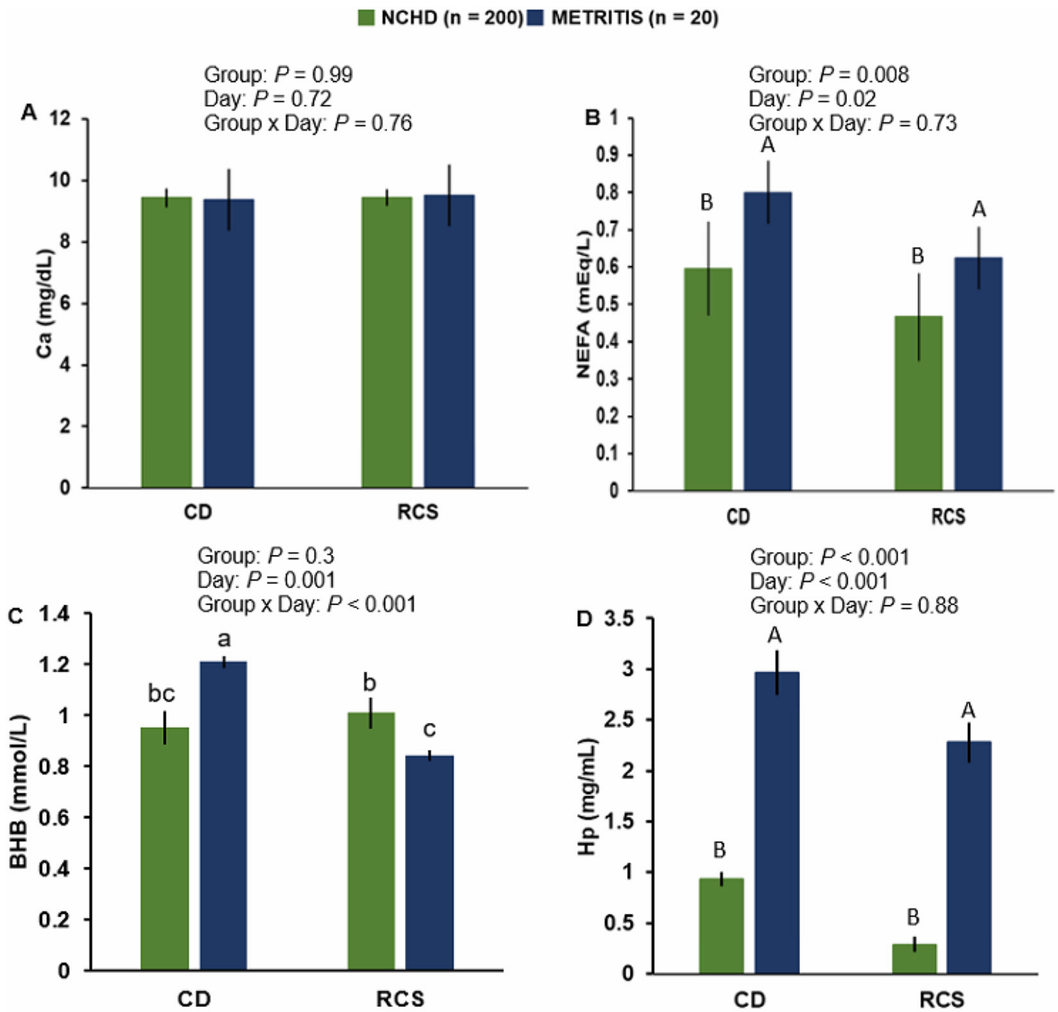

Figure 6. Circulating concentrations of Ca (A), nonesterified fatty acids (NEFA, B), BHB (C), and haptoglobin (Hp, D) on the day of clinical diagnosis (CD) and the day of resolution of clinical signs (RCS) in a subset (n = 20) of cows diagnosed with metritis and a subset of cows with no clinical health disorders diagnosed (NCHD, n = 200). For cows in the NCHD group, values for the day of CD and RCS were values for the average DIM at CD (i.e., 7 DIM) and RCS (i.e., 14 DIM) for cows with metritis. Values are LSM ± SEM. Uppercase letter differences represent overall effects of group, and lowercase letters indicate results of interactions based on the LSD post hoc median separation test.

titis: 1.0 ± 0.1 mmol/L; NCHD: 1.0 ± 0.02 mmol/L; Figure 7C). Concentrations of BHB were greater ($P < 0.001$) for cows with than without RF and were marginally significantly greater ($P = 0.09$) for multiparous than for primiparous cows. For concentrations of Hp, an interaction occurred between group and day ($P < 0.001$), whereby cows with clinical mastitis had greater plasma concentrations of Hp than cows in the NCHD group both on the day of CD (mastitis: 2.9 ± 0.1 mg/mL; NCHD: 0.2 ± 0.03 mg/mL) and at RCS (mastitis: 0.7 ± 0.1 mg/mL; NCHD: 0.2 ± 0.03 mg/mL), and cows with clinical mastitis had greater concentrations of Hp on the day of CD than at RCS (Figure 7D). Primiparous cows had marginally significantly ($P = 0.08$) greater concentrations of Hp than multiparous cows.

DISCUSSION

General Findings for Cows Diagnosed With Metritis or Clinical Mastitis

In support of our primary hypothesis, cows affected by metritis and clinical mastitis presented alterations of their patterns of RT, PA, and LT several days before and after (metritis only) CD of these disorders. Moreover, the behavioral parameters monitored presented distinct trajectories depending on the disease and behavior evaluated. Specifically, we observed a smaller rate of increase in RT and PA and a slower rate of decline for LT on the days leading to CD of metritis compared with cows in the NCHD group. For cows with severe metritis, or metritis and a concomi-

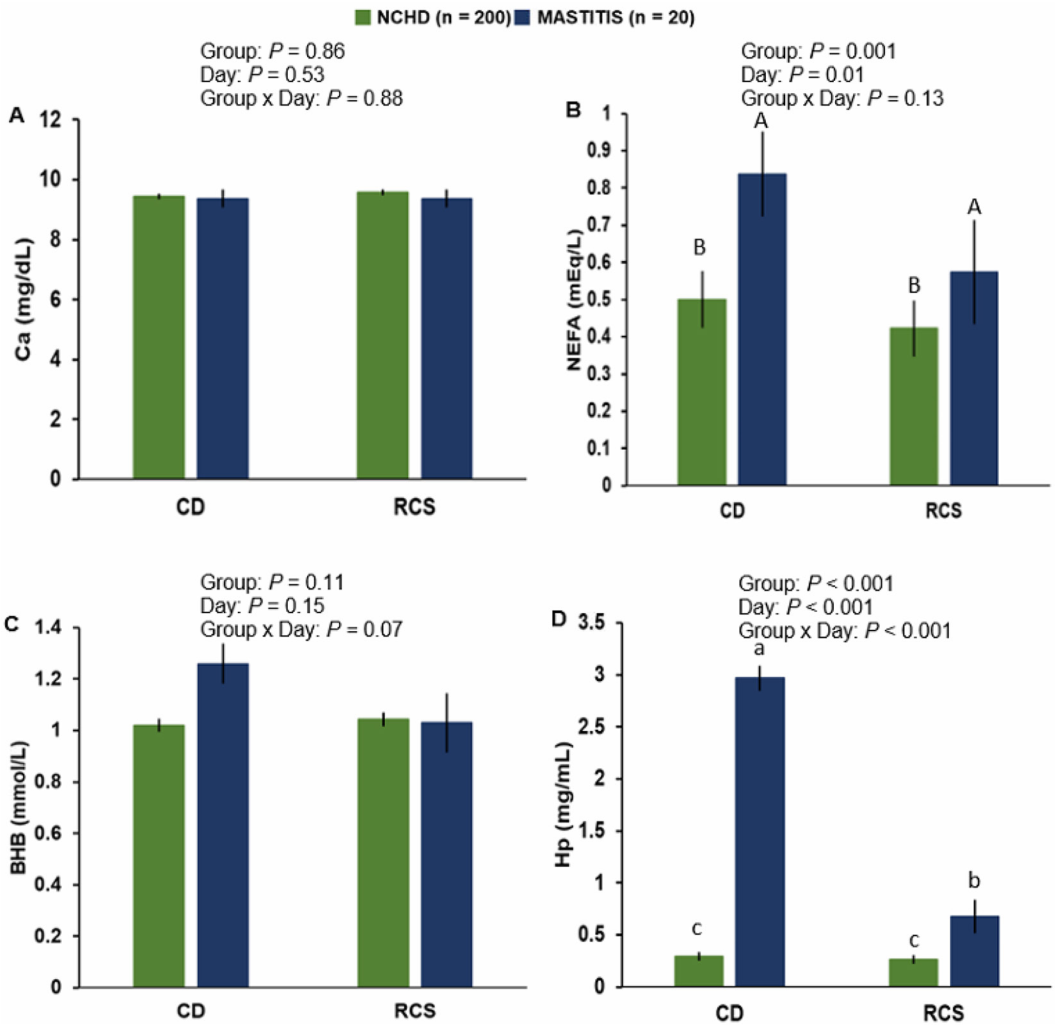

Figure 7. Circulating concentrations of Ca (A), nonesterified fatty acids (NEFA, B), BHB (C), and haptoglobin (Hp, D) on the day of clinical diagnosis (CD) and the day of resolution of clinical signs (RCS) in a subset (n = 20) of cows diagnosed with mastitis and a subset of cows with no clinical health disorders diagnosed (NCHD, n = 200). For cows in the NCHD group, values for the day of CD and RCS were values for the average DIM at CD (i.e., 14 DIM) and RCS (i.e., 21 DIM) for cows with metritis. Values are LSM ± SEM. Uppercase letter differences represent overall effects of group, and lowercase letters indicate results of interactions based on the LSD post hoc median separation test.

tant disorder, RT and PA were already lesser compared with cows in the NCHD group as early as 4 d before metritis diagnosis. The latter suggested that behavior for these cows might have diverged from that of cows not affected by metritis earlier than 4 d before CD. The characteristic pattern for the sensor parameters for cows with metritis and the NCHD group was the result of the early stage of lactation at which metritis was diagnosed. For cows with clinical mastitis, RT and PA were lesser than for cows in the NCHD group starting 3 (i.e., PA) or 4 d (i.e., RT) before CD for cows with nonsevere clinical mastitis and 6 d before CD for cows with severe clinical mastitis or a concomitant health disorder, respectively. Moreover, the nadir for RT and PA in cows with clinical mastitis was observed on the day of CD. On the other hand, LT was greater than for cows in the NCHD group than for cows affected by severe clinical mastitis or a concomitant disorder only, and peaked on the day of CD.

Data partially supported our secondary hypothesis because, compared with cows in the NCHD group, cows with a severe case of metritis or clinical mastitis, or cows affected by a concomitant HD, had the largest differences and for the longest duration in RT, PA, and LT. However, compared with cows with nonsevere cases of metritis and clinical mastitis, cows with severe cases of metritis and clinical mastitis, or a concomitant HD, had lesser RT and PA or greater LT only for a few days relative to CD. Moreover, these differences were of smaller magnitude compared with those observed for cows in the NCHD group. Also, despite relative differences between cows in the MET and MET+ group greater than 100% for PA, and greater than 50% in RT for cows in the MAST and MAST+ groups, we only observed a statistically significant reduction in LT for cows in the MAST+ compared with the MAST group. Thus, the degree of alteration of sensor parameter patterns and relative changes before CD of metritis and clinical mastitis depended on the severity of the disorder, or the concomitant occurrence of another HD for some but not all sensor parameters. Taken together, these data demonstrated that lactating dairy cows diagnosed with spontaneous cases of metritis and clinical mastitis had differences in behavioral parameters monitored by an ear-attached AHMS, compared with cows not affected by these disorders. Moreover, for RT and PA, cows affected by severe cases of metritis or clinical mastitis, or cows with concomitant HD (as defined in this study), presented greater and earlier differences compared with cows not affected by metritis and mastitis or than cows affected by nonsevere cases of these disorders.

Metritis

A better understanding of sensor parameter patterns in cows affected by HD is necessary to provide a framework for the development of data analytical tools and management strategies for identifying cows affected by diseases. We observed substantial alterations to the pattern of RT, PA, and LT that might enable identification of cows with metritis using these sensor-monitored parameters. The timing at which most cases of metritis are observed in dairy herds and the effects of this disease on cow behavior, however, might pose some challenges. As most cases of metritis were observed before 10 DIM, sensor data were analyzed for only 4 d before CD to mitigate part of the confounding effect of calving-related physiological and behavioral changes on sensor data (Soriani et al., 2012; Liboreiro et al., 2015). Despite this adjustment, cows with metritis presented a different RT and PA dynamic around CD than cows affected by clinical mastitis or metabolic-digestive disorders (Stangaferro et al., 2016a,b). Unlike for cows grouped based on diagnosis of clinical mastitis and metabolic-digestive disorders (Rial et al., 2023), which already reached the postcalving plateau by the time of CD, cows diagnosed with metritis continued to have an increase in RT and PA on the days leading to CD. This was because the postcalving plateau was not yet reached by the time of metritis diagnosis. This observation agreed with our previous study (Stangaferro et al., 2016c) in which, rather than a sharp decline with nadir on the day of or immediately around diagnosis, cows with metritis presented reduced RT and PA as early as 5 d before CD. Cows with metritis also presented a smaller rate of increase of these parameters than cows not diagnosed with metritis (Stangaferro et al., 2016c). In contrast, others have observed a decline in RT before CD, but neither DIM at diagnosis nor the dynamic of daily differences were reported (Paudyal et al., 2016). Our observations are not surprising because, in previous studies, cows diagnosed with metritis at either 7 ± 3 or 14 ± 3 DIM presented reduced RT from 2 to 9 d and reduced PA from 2 to 5 d after calving (Liboreiro et al., 2015). In our study, metritis detection at earlier DIM was the most likely reason for the contrasting dynamics of RT and PA for cows diagnosed with metritis versus clinical mastitis or metabolic-digestive disorders (Rial et al., 2023). A slower rate of increase was observed for cases of metritis, as opposed to a marked decline before CD for cows diagnosed with clinical mastitis and metabolic-digestive disorders. When RT and PA are evaluated for groups rather than individual cows in early lactation, the expected RT and PA decline can be overridden by the normal trajectory of these behavioral parameters in the early postpartum period. Despite this, the average differential for RT and PA relative changes for individual cows with metritis (MET and MET+) and cows without metritis was in a similar range (i.e., 40 to 50%) to that of cows affected by metabolic-digestive disorders (Rial et al., 2023). This comparable dynamic demonstrated that, in relative terms, metritis caused alterations to these sensor parameters similar to those of metabolic-digestive disorders. Therefore, analytical approaches to identify cows with metritis might not only benefit by adjusting for stage of lactation, but also might be most accurate if comparisons with previous days for the same cow, or referent values for a population of healthy herdmates, or healthy cow data sets are used. This approach could adjust for the normal trajectory of sensor parameters immediately after calving, as observed in previous studies (Paudyal et al., 2016).

Lying time was also affected by metritis, but the pattern was characterized by presenting the same level of difference with the NCHD across the entire observation period. Cows in the MET+ group presented a decline before CD, but the magnitude of this decline was moderate. Conversely, for cows in the MET group LT remained mostly unchanged, and the differential for relative changes compared with cows in the NCHD group for both the MET and the MET+ group was rather small (i.e., $<5\%$). This dynamic for LT seemed to reflect minor changes for this behavior in cows with metritis and suggested that this parameter might have limited value as an aid for identifying cows with metritis for the AHMS used in this study. Others have also reported weak and inconsistent associations between metritis occurrence and the pattern of lying behavior in dairy cows. For example, Neave et al. (2018) reported no difference in LT per day between cows with no HD diagnosed and cows with metritis only, or metritis plus subclinical ketosis, within 3 d before diagnosis of metritis. Barragan et al. (2018) reported increased LT for up to 7 d after metritis diagnosis for primiparous but not for multiparous cows. Differences in herd management and facilities within and across herds and studies, and differences in cow grouping based on diagnosis of HD across studies is likely a contributor to these inconsistent observations for the association between LT and occurrence of diseases such as metritis. Indeed, lying behavior can be strongly influenced by management practices and facilities (Ito et al., 2009).

In partial support of our secondary hypothesis, we observed some differences in the pattern of behavioral parameters, relative changes around CD, and the day of the nadir for sensor parameters between cows in the MET and MET+ group. Most notable were the long duration and large magnitude of the differences for RT and PA between the MET+ and NCHD groups. In contrast, some of the differences observed between the MET and MET+ groups were short lived, of relatively small magnitude, and might have been confounded by the occurrence of concomitant disorders rather than being due to variation in severity of metritis. Large cow-to-cow variation or small sample size could have also explained some of the lack of statistically significant differences despite more than a doubling of the relative change up to the day of the nadir, as observed for PA and MY. Although we could not determine whether the lack of more substantial differences between the MET and MET+ groups was due to large sensor parameter alterations for cows in the MET group, versus lack of more substantial alterations for cows in the MET+ group, our findings suggest that it may not possible to differentiate cows with nonsevere metritis and cows with either severe metritis or metritis and a concomitant HD using behavioral parameters data from the AHMS used in this study. In contrast, Stangaferro et al. (2016c) reported that cows with metritis plus another HD were more likely to have health index score alerts than cows with metritis only. Moreover, cows with metritis and a health index score alert, which was considered an indication of severity of the disorder, had substantial differences in RT and PA compared with cows with metritis but no health index score alert. Although direct comparisons of results from different studies are challenging, due to different approaches to grouping cows and methods of diagnosing disease, collectively data from these studies support the hypothesis that severity of cases of metritis, and occurrence of concomitant disorders, influences some behavioral parameters that can be monitored by sensors.

As for cows with metabolic-digestive disorders (Rial et al., 2023), the dynamics of RT, PA, and LT from the day of CD to the day of RCS suggested that relative changes for these parameters might be more sensitive indicators of metritis recovery than MY. Unlike behavioral parameters monitored by the ear-attached sensor, MY did not differ between the day of CD and RCS, despite a small upward trend. Also, different from cows with metabolic-digestive disorders (Rial et al., 2023), the circulating concentration dynamics of markers of energy, inflammation, and metabolic status presented less notable changes from the day of CD to RCS, and the observed changes were not directly aligned with sensor parameter changes. Except for BHB, which presented a significant but small decline from the day of CD to RCS, all other markers remained unchanged and presented either no or small relative changes. Thus, RT, PA, and LT might be more sensitive indicators of recovery after metritis than MY and the blood markers evaluated in this study. Future studies should evaluate the use of behavioral data as diagnostic tools to complement or replace clinical examination for determination of RCS of metritis. Automated tools for accurate determination of RCS could contribute to the development of novel treatment and metritis management strategies aimed at reducing the burden and unintended consequences of antimicrobial use for metritis treatment.

Clinical Mastitis

Based on the known alterations to cow behavior caused by intramammary infections that lead to mastitis (Dantzer, 2006; Dantzer and Kelley, 2007; Fogsgaard et al., 2012) and previous studies that used automated sensors to monitor cow behavior (Paudyal et al., 2016; Stangaferro et al., 2016b,c), we hypothesized that cows affected by clinical mastitis would present alterations of RT, PA, and LT. In support of this hypothesis, cows with clinical mastitis presented clear reductions in RT and PA on the days leading to CD of clinical mastitis. As opposed to cows affected by metritis, diagnosis at later DIM removed the confounding effect of calving-related behavioral changes, which enabled observation of a clear divergence of monitored behaviors compared with cows not affected by clinical mastitis at the same range of DIM. Both parameters presented a decline on the days leading to CD with levels different from the NCHD group for up to 4 to 6 d before CD. Rumination time and PA declined at rates of 5.1% and 5.4% per day until the day of CD, when both parameters presented the smallest recorded value. Early, prolonged, and relatively large differences in the pattern of RT and PA between the MAST and MAST+ groups partially supported the hypothesis that a more severe case of clinical mastitis, or a concomitant disorder, would cause greater behavioral changes than nonsevere clinical mastitis, or a case of clinical mastitis alone. Although observed earlier than CD for both the MAST and MAST+ groups, the lack of differences for days to the RT and PA nadir did not support the hypothesis that greater alterations would be observed for cows affected by more severe cases of clinical mastitis or a concomitant disorder. Similar average relative RT and PA declines for individual cows on the days preceding the respective nadirs also suggested that differences in these behaviors between distinct types of cases of clinical mastitis might be less pronounced. Compared with cows not diagnosed with clinical mastitis, relative changes were substantial, but no differences were observed between the MAST and MAST+ groups. This was observed despite an almost doubling of the relative change for RT for cows in the MAST+ than the MAST group. Our observations agreed with the previously reported alterations to the patterns of RT and PA for cows diagnosed with clinical mastitis based on a neck-attached sensor tag (Paudyal et al., 2016; Stangaferro et al., 2016b,c). Of note, RT differences were more pronounced and were observed earlier in the current study than in Stangaferro et al. (2016c). In the latter study, all cows diagnosed with clinical mastitis, and cows diagnosed with clinical mastitis with a health alert presented differences in RT compared with cows not affected by clinical mastitis no earlier than 1 d before CD. Another contrasting difference between Stangaferro et al. (2016c) and the present study was that, in the previous study, cows with clinical mastitis had greater and more prolonged shifts for PA than RT. Conversely, RT seemed to be as sensitive as PA to cases of clinical mastitis in our study because differences in RT between cows with and without clinical mastitis were observed as early and for as long as for PA.

Contrary to our hypothesis, we observed no detectable alterations to the pattern of LT for cows in the MAST and NCHD groups, and differences between the MAST+ and NCHD group were observed only 1 d before CD of mastitis. This was in contrast with previous studies in which either a decrease (Siivonen et al., 2011) or an increase (Fogsgaard et al., 2012) in lying behavior was reported for dairy cows with induced mastitis. In the previous studies, changes in lying behavior were attributed to inflammation of the udder and pain caused by contact with the floor while lying (Siivonen et al., 2011). As lying behavior was only characterized in our study using the ear-attached sensor, it is not possible to determine whether cows with clinical mastitis presented less dramatic changes in lying behavior or whether LT, as measured by the ear-attached sensor, was less sensitive to changes in this behavior.

Unlike for cows affected by metabolic-digestive disorders (Rial et al., 2023) and cows with metritis, the dynamic of RT, PA, and LT from the day of CD to RCS of clinical mastitis did not reflect the improved health status of cows. Likewise, MY did not present a significant recovery. These data suggested that neither the dynamic of sensor parameters nor MY were strongly correlated with the evolution of clinical status in cows affected by clinical mastitis. The only exception to all the parameters measured was haptoglobin, which presented a large decline from the day of CD to RCS. The value of monitoring haptoglobin levels to evaluate RCS of clinical mastitis is likely limited because of the need to collect blood samples and the lack of a cowside test. Our findings deserve further exploration in larger studies because, although a small sample size could have been a factor for not detecting sensor parameter differences between the day of CD and RCS, the lack of pattern in the data was obvious.

Study Limitations

The study design and approaches used for data analyses had weaknesses. Most notable are limited generalizability, potential underdiagnosis of clinical HD, and confounding due to cow grouping strategies used. Generalizability was limited because the study was conducted at a single farm. The inability to conduct extensive clinical examination in all cows every day of the study period could have resulted in underdiagnosis of certain HD or clinical signs of interest. Including cows with RF (as defined in this study) in the NCHD could have confounded results by altering the magnitude of the differences between cows with and without metritis and clinical mastitis. Controlling for RF group in statistical models (term retained only when $P < 0.10$) likely reduced but did not fully eliminate the confounding effect of including cows with RF in the NCHD group.

This study did not provide evidence that the ear-attached based AHMS evaluated could be used to identify cows affected by or at risk of suffering metritis or clinical mastitis in real time under commercial farm conditions. All data comparisons were made retrospectively for groups of cows rather than for individual cows. Evaluating data for groups with tens or hundreds of cows makes patterns of sensor parameters obvious and increases the likelihood of detecting statistically significant differences and large effect sizes. Additional research evidence is needed to demonstrate that the AHMS used in this study can identify cows affected by or at risk of suffering metritis and clinical mastitis in real time under commercial farm conditions.

CONCLUSIONS

Cows diagnosed with metritis and clinical mastitis with or without another health disorder had differences in behavioral parameters captured by the ear-attached sensor compared with cows not affected by clinical health disorders. Before diagnosis of metritis and clinical mastitis, cows had lesser rumination time and physical activity as compared with cows not affected by these disorders. Lying time for cows diagnosed with metritis was greater and, for cows with clinical mastitis, increased on the days leading to clinical diagnosis. Based on the dynamic, magnitude, and timing changes for the monitored behavioral parameters observed around diagnosis of metritis and clinical mastitis, the AHMS evaluated might have potential value for identifying dairy cows with these disorders in early lactation.

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