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Genetic and genomic dissection of dry matter intake at different lactation stages in primiparous Holstein cows

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ABSTRACT

Dry matter intake (DMI) and feed efficiency are economically relevant traits. Simultaneous selection for low DMI and high milk yield might improve feed efficiency, but bears the risk of aggravating the negative energy balance and related health problems in early lactation. Lactation stage-specific selection might provide a possibility to optimize the trajectory of DMI across days in milk (DIM), but requires in-depth knowledge about genetic parameters within and across lactation stages. Within the current study, daily heritabilities and genetic correlations between DMI records from different lactation stages were estimated using random regression models based on 910 primiparous Holstein cows. The heritability estimates from DIM 11 to 180 follow a slightly parabolic curve varying from 0.26 (DIM 121) to 0.37 (DIM 11 and 180). Genetic correlations estimated between DIM 11, 30, 80, 130, and 180 were all positive, ranging from 0.29 (DIM 11 and 180) to 0.97 (DIM 11 and 30; i.e., the correlations are inversely related to the length of the interval between compared DIM). Deregressed estimated breeding values for the same lactation days were used as phenotypes in sequential genome-wide association studies using 681 cows drawn from the study population and genotyped for the Illumina SNP50 BeadChip (Illumina Inc., San Diego, CA). A total of 21 SNP on 10 chromosomes exceeded the chromosome-wise significance threshold for at least 1 analyzed DIM, pointing to some interesting candidate genes directly involved in the regulation of feed intake. Association signals were restricted to certain lactation stages, thus supporting the genetic correlations. Partitioning the explained variance onto chromosomes revealed a large contribution of *Bos taurus* autosome 7 not harboring any associated marker in the current study. The results contribute to the knowledge about the genetic architecture of the complex phenotype DMI and might provide valuable information for future selection efforts.

Key words: dairy cow, dry matter intake, genetic parameters, genome-wide association study

INTRODUCTION

Dry matter intake is a trait of interest for dairy cattle breeding. Feed is a major component of the milk production costs and, therefore, it appears possible to improve economic efficiency by selecting for DMI. However, there has been a long-running debate whether and how DMI should be included in breeding programs (Van Arendonk et al., 1991; de Haas et al., 2012; Veerkamp et al., 2012; Berry and Crowley, 2013). This is a complicated task, as recording of DMI is difficult and expensive. Data are almost exclusively recorded in research herds, resulting in a small number of records (Vallimont et al., 2010) and a lack of reliable genetic parameters (Veerkamp et al., 2012). Another reason why an inclusion of DMI in breeding programs is not trivial is that the feed eaten by a cow is used for several other functions than milk production, such as maintenance, growth, and reproduction (Veerkamp, 1998). A reduction of DMI in early lactation leads to a more pronounced energy deficit postpartum (Spurlock et al., 2012). This, in turn, affects the constitution of the cow (Collard et al., 2000) and causes metabolic stress (Pryce and Løvendahl, 1999). Cows in a prolonged negative energy balance often fail to maintain functional fitness and, thus, the majority of metabolic and infectious diseases occur during early lactation (Goff and Horst, 1997). These diseases result in reduced milk yield, extra costs for drugs and veterinary treatments, additional labor, and involuntary culling and, thereby, cause economic loss (Heringstad et al., 2000). Moreover, several studies reported negative effects of an energy deficit on the reproductive performance of dairy cows (e.g., Reist et al., 2003), which is another limiting factor for profitability of milk production. Thus, breeding for economic efficiency of dairy cattle is difficult and requires in-depth knowledge of DMI genetics and genomics.

Published heritability estimates for DMI range from 0.04 to 0.54 (Veerkamp and Thompson, 1999; Coffey et al., 2001; Hüttmann et al., 2009; Buttchereit et al.,

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2011; Spurlock et al., 2012). Heritability of DMI is shown to vary across lactation, but uncertainty exists about the trajectory. The same applies to the genetic correlations between DMI observations across lactation. Several authors found low (Veerkamp and Thompson, 1999; Berry et al., 2007; Hüttmann et al., 2009) to negative (Koenen and Veerkamp, 1998; Coffey et al., 2001; Buttchereit et al., 2011) correlations between DMI measurements from early and mid lactation, whereas Spurlock et al. (2012) reported that genetic correlations between DMI in early and mid lactation remained above 0.70. In addition, Coffey et al. (2001) found highly positive correlations between DMI records from early and late lactation, which was in contrast to the results of Berry et al. (2007). Those authors, studying the first 305 DIM, observed the weakest genetic correlation between DMI at 8 DIM and 305 DIM. Most estimates for genetic correlations, however, originate from small data sets and either no standard errors were provided or the majority of the genetic correlations was not significantly different from zero ($P > 0.05$) because of large standard errors. Therefore, there is a lack of reliable estimates, leading to several gaps in knowledge. For example, it is unknown whether selection for efficient cows with a low DMI in mid or late lactation would have implications on early lactation DMI. A reduction in DMI during the initial lactation period could have severe consequences on fertility and health due to the detrimental effects of a pronounced energy deficit. Thus, the use of an inclusion of DMI in breeding goals depends strongly on genetic interrelationships across lactation. In this context, it is quite interesting that results from previous studies indicate that DMI might be influenced by different genes at different stages of lactation (Koenen and Veerkamp, 1998; Berry et al., 2007). Recently, Veerkamp et al. (2012) performed a genome-wide association study (**GWAS**) for DMI and identified potential candidate genes. The average DMI for wk 3 to 15 of lactation was used as phenotype in their study. However, if DMI is controlled by different genes at different lactation stages, GWAS for DMI at different DIM are needed to gain a better insight into the genetic architecture of this trait.

The objectives of the current study were to quantify the degree and change in heritability of DMI across lactation and to estimate genetic correlations between DMI records from different DIM. Furthermore, deregressed EBV for DMI were estimated using random regression methodology and the results for DIM 11, 30, 80, 130, and 180 were used as phenotypes for GWAS, with the aim of identifying genomic regions significantly associated with DMI at specific or multiple stages of lactation. The study was limited to first lactation, with emphasis on early and mid lactation.

MATERIALS AND METHODS

Data from primiparous Holstein Friesian cows were recorded between September 2005 and December 2012 on the dairy research farm Karkendamm of the Institute of Animal Breeding and Husbandry, Christian-Albrechts-University (Kiel, Germany). This farm runs a bull dam performance test and all Karkendamm bull dam candidates had to complete a test period under commercial conditions in a freestall barn until DIM 180. Nonqualified primiparous cows left the herd afterward. Therefore, only records between DIM 11 (start of feed intake recording) and DIM 180 were used in the present investigation.

Cows were milked twice per day and fed a TMR diet ad libitum. Daily TMR intake was recorded for each animal via single feeding troughs equipped with a weighing unit and automatic cow identification. As cows were generally housed separately during the first 10 DIM, no feed intake data were available for this period. Individual TMR intake was deleted for the first and last day with TMR intake information and if cows were separated for insemination or pregnancy testing. Values obtained for fresh TMR intake were discarded if they were among the 0.5% highest or 0.5% lowest values, resulting in a range of fresh TMR intake between 4.8 and 77.3 kg. Dry matter content of the TMR was analyzed twice weekly. The average NE_L of the TMR was 7.1 MJ/kg of DM. Fixed amounts of concentrates were dispensed via concentrate feeders. Primiparous cows in the first 180 DIM consumed an average of 2.26 kg of concentrate DM per day (SD = 0.49 kg of DM/d). Total mixed ration DM intake was 17.88 kg/d, on average (SD = 4.79 kg of DM/d).

Animals were excluded from all further analyses if the number of DMI observations per cow across the entire period was less than 4. This resulted in 910 primiparous cows and an average number of 103 DMI observations per cow (93,797 DMI observations, in total). The maximum number of DMI observations per cow was 165. The total DMI (concentrate and TMR intake) in this data set was 20.17 kg/d, on average, and ranged between 1.99 and 45.45 kg/d.

By tracing the pedigree of cows with observations 3 generations back, a pedigree file consisting of 5,683 animals was created. Data were analyzed using a random regression animal model considering the fixed effects test day, age at first calving, and stage of lactation. Age at first calving was divided into 5 classes (21 to 25, 26, 27, 28, and 29 to 38 mo). The general lactation curve was modeled by the function according to Ali and Schaeffer (1987), and random regression coefficients for permanent and additive genetic effects were modeled applying Legendre polynomials of 2 degrees: