Genomic merit for reproductive traits: Selecting for improved estrous characteristics and pregnancy in Holstein cattle

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Introduction

Efficient reproduction of dairy cows is necessary for maximum profitability (Giordano et al., 2012). Some factors that can affect reproductive outcomes directly or indirectly are reproductive management, nutrition, health, and genetics. Prior to the early 2000s the focus of genetic selection was on production traits, with little to no attention was placed on selection for reproduction traits (Lucy 2001). Many have hypothesized that because productive and reproductive traits are not correlated or even negatively correlated the focus on productive traits resulted in selection of cattle with reduced estrous expression (Lopez et al., 2005). Cattle with reduced or no estrous expression at the time of insemination have reduced pregnancy per artificial insemination (AI) even when they are submitted to fixed-time insemination (Lima et al., 2013). Regulation of the intensity of estrous behavior has a genetic component (Kommadath et al., 2010, 2011, 2013; Woelders et al., 2014), suggesting it is a trait that can be selected for. Little is known, however, about association between reproduction traits and estrous expression and characteristics.

Despite reported correlations between estrous expression and increased fertility and decreased pregnancy losses following timed artificial insemination and embryo transfer (Pereira et al., 2016), consistent means to measure estrus are difficult. Automated estrous detection monitoring devices (**AED**) have become more accurate and affordable over the years. They indirectly detect estrus according to changes in walking, activity, and rumination patterns (Fricke et al., 2017). The systematic use of such devices allows for the evaluation of estrous characteristics (duration, intensity, and so on) from a large number of animals in a uniform manner.

Since the mid-2000s when dairy breeders realized importance of selecting cattle for both production and reproduction traits, genetic selection has included reproduction traits such as daughter pregnancy rate (**DPR**), introduced in 2003 (VanRaden et al., 2003), and heifer conception rate (**HCR**), introduced in 2013 (Council on Dairy Cattle Breeding, 2018). Heifer conception rate is a measure of the likelihood of pregnancy following AI of a bull's daughter compared with the contemporaneous population, whereas DPR is a measure of the hazard of pregnancy after calving (21-d pregnancy rate, days open) of a bull's daughters compared with the contemporaneous population. The hypothesis of this study was that genomic merit for DPR (**GDPR**) is associated with estrous characteristics, metabolic responses, and pregnancy establishment in Holstein females.

Animals, Materials, and Methods

In the *study 1*, Holstein heifers (n = 1,005) genotyped within two months of birth were classified into quartiles (Q1 = lowest, Q4 = highest) according to the GDPR and GHCR values of the study population. At 10 to 11 months of age, heifers were fitted with a collar (Heat Rumination Long Distance, SCR Inc., Netanya, Israel) that recorded activity and rumination and determined the occurrence of estrus according to changes in activity and rumination compared with the individual's baseline values. Based on the intensity of changes in activity and rumination, an internal algorithm (DataFlow2) calculated the heat index (0 = no estrus to 100 = maximum heat index). Heifers with heat index ≥ 70 were considered to be in estrus. In the first 30 d after fitting the collars, characteristics of spontaneous estruses (**SPE**; estruses occurring before the start of the reproductive program) were recorded. Heifers then had their estrous cycle synchronized with $PGF_{2\alpha}$ and characteristics of $PGF_{2\alpha}$-synchronized estruses (**PGSE**; estruses occurring after the

start of the reproductive program) were recorded. Following detection of estrus received either artificial insemination or embryo transfer (ET) according to the herd's genetic selection program (first service: AI = 495 and ET = 510; second service: AI = 280 and ET = 338).

In *study 2*, 831 of the heifers used in *study 1* were used to determine the associations between GDPR and genomic milk yield (GMY) and estrous characteristics, metabolic responses postpartum, and pregnancy outcomes. Genomic merit for milk yield reflects the genomic estimate of a bull's daughter production compared with the contemporaneous population. At approximately 30 d before expected calving date, an automated estrus-detection device mounted on a collar was fitted on the left cranial area of the neck of all heifers. A sub-sample of cows (n = 499) had blood sampled at 7, 14, 21, and 28 DIM. Samples were analyzed for insulin like growth factor-1 (IGF-1), glucose, non-esterified fatty acid (NEFA), and beta-hydroxybutyrate (BHB). Cows were monitored for signs of estrus based on the automated estrus-detection device, visually (standing to be mounted, mounting other cows, bellowing, increased nervousness and activity, walking fence line, swelling and reddening of the vulva, and vaginal mucous discharge), and a mount detection device applied to the tail-head (Estrotect; Rockway Inc., Spring Valley, WI). Cows determined to be in estrus were serviced (n = 398) and those not detected in estrus were enrolled in an ovulation synchronization protocol (Ovsynch – n = 373) for first service. The Ovsynch (GnRH, PGF2α 7 d later, GnRH 2.5 d later, and timed AI 16 h later) started at 75 DIM.

Results and Discussion

Among the study population, the GDPR ($\pm$SD) = 1.65 $\pm$ 1.29 (range: −1.8 to 5.9), GHCR ($\pm$SD) = 1.34 $\pm$ 1.11 (range: −2.1 to 5.5), GMY ($\pm$SD) = 988.4 $\pm$ 504.7 kg (range: -531 to 2,544 kg).

Study 1 – Heifer Results. Genomic merit for DPR was not ($P = 0.24$) associated with the duration of the SPE. Conversely, heifers in Q2 for GHCR tended ($P = 0.10$) to have longer SPE than heifers in Q4, whereas heifers in Q1 and Q3 did not ($P \geq 0.21$) differ from each other or from heifers in Q2 and Q4 (Figure 1). Both the interval from onset of estrus to peak of activity and rumination nadir on the day of SPE were not associated with GDPR, GHCR, and the interaction between GDPR and GHCR. An interaction between GDPR and GHCR was detected ($P = 0.04$) for the likelihood of activity peak $\geq$ 80. Among heifers in Q3 and Q4 of GHCR, those in Q1 of GDPR were less likely to have activity peak $\geq$ 80. Genomic merit for DPR was ($P = 0.01$) associated with the hazard of estrus within 7 d of the first PGF$_{2\alpha}$ treatment. Heifers in Q4 of GDPR had a shorter interval from the first PGF$_{2\alpha}$ treatment to the first detected estrus compared to heifers in Q1, Q2, and Q3 of GDPR (Figure 2). The median intervals from the first PGF$_{2\alpha}$ treatment to the first detected estrus: Q1 = 62.5, Q2 = 62, Q3 = 61, and Q4 = 52 h. The percentage of heifers not detected in estrus 7 d after the first PGF$_{2\alpha}$ treatment were: Q1 = 25.3, Q2 = 25.1, Q3 = 17.3, and Q4 = 14.4%. Additionally, GDPR was (P = 0.02) associated with the duration of the PGSE because heifers in Q1 had (P $\leq$ 0.05) shorter PGSE than heifers in Q2 and Q4 and tended (P = 0.09) to have shorter PGSE than heifers in Q3 (Figure 3). Finally, there was an association between GDPR and rumination nadir on the day of PGSE because heifers in Q1 had (P = 0.02) greater rumination nadir on the day of PGSE than Q4 heifers (Figure 4). The interaction between GDPR and GHCR was (P = 0.04) associated with the likelihood of activity peak $\geq$80 at PGSE. The likelihood of activity peak $\geq$80 at PGSE tended to increase for heifers in Q2 and Q3 for GDPR as GHCR increased, but the opposite trend was observed for heifers in Q1 and Q4 for GDPR. This demonstrates that heifers with higher GDPR displayed estrus faster and more

intense estrus than heifers with lower GDPR. Interestingly, having a higher GHCR was associated with less intense signs of estrus.

Genomic merit for DPR was associated with the likelihood of pregnancy 38 ± 3 and 73 ± 3 d after the first AI. Heifers in Q4 for GDPR had a greater percentage of pregnancies per AI at 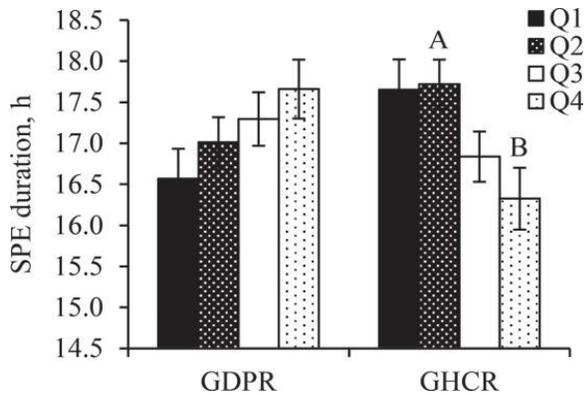38 and 73 d after the first AI compared to heifers in Q1, Q2, and Q3. On the other hand, GHCR was associated with the likelihood of pregnancy 38 ± 3 and 73 ± 3 d after the second AI. Heifers in Q3 and Q4 for GHCR had a greater percentage of pregnancies per AI at 38 and 73 d after the second AI compared to heifers in Q1 and Q2.

Figure 1. Association between genomic merit for daughter pregnancy rate (GDPR) and genomic merit for heifer conception rate (GHCR) and duration of spontaneous estrus (SPE). Q = quartile (Q1 = lowest, Q4 = highest). [A, B]$0.05 < P \leq 0.10$.
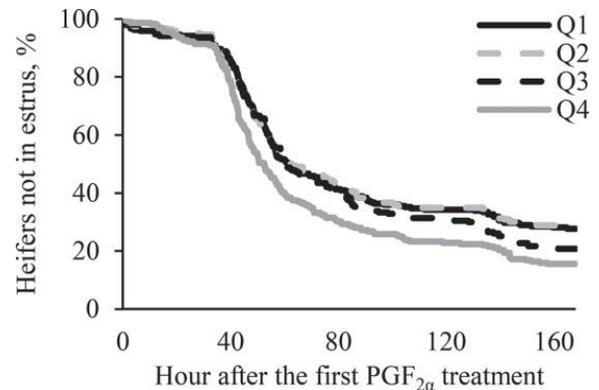

Figure 2. Association between genomic merit for daughter pregnancy rate (GDPR) and interval from the first PGF$_{2\alpha}$ treatment to the first estrus detected. Q = quartile (Q1 = lowest, Q4 = highest).
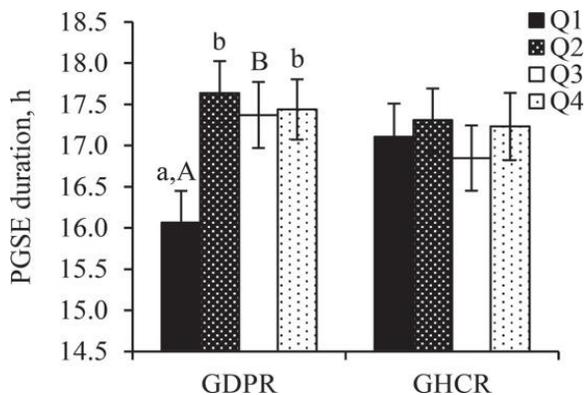

Figure 3. Duration of PGF$_{2\alpha}$-synchronized estrus (PGSE) according to genomic merit for daughter pregnancy rate (GDPR) and genomic merit for heifer conception rate (GHCR). Q = quartile (Q1 = lowest, Q4 = highest). [a, b]$P \leq 0.05$. [A, B]$0.05 < P \leq 0.10$.
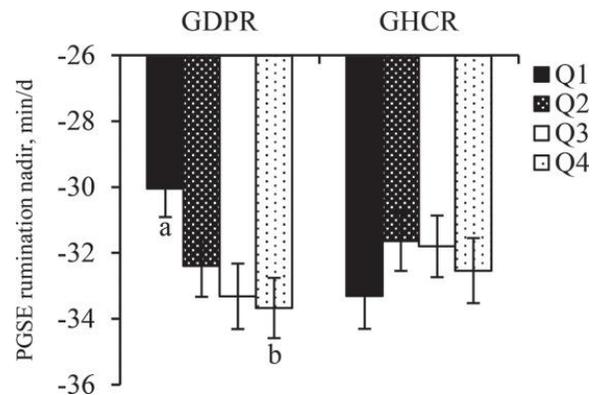

Figure 4. Rumination nadir at PGF$_{2\alpha}$-synchronized estrus (PGSE) according to genomic merit for daughter pregnancy rate (GDPR) and genomic merit for heifer conception rate (GHCR). Q = quartile (Q1 = lowest, Q4 = highest). [a, b]$P \leq 0.05$.

Study 2 – Cow Results.

There were no associations between GDPR and milk yield, which created the opportunity to investigate the associations between genomic merit for reproductive traits and phenotype. Cows with greater GDPR had ($P < 0.01$) greater BCS at 63 ± 3 DIM and lost less BCS from 3 to 63 ± 3 DIM. In addition, cows with higher GDPR had more favorable postpartum metabolism as they had ($P < 0.01$) greater concentrations of IGF-1 (Figure 5) and glucose (Figure 6) and reduced ($P \leq 0.03$) concentrations of NEFA and BHB.

Genomic merit for DPR was ($P < 0.01$) positively associated with the hazard of estrus within 62 DIM and the median intervals from calving to first estrus according to GDPR quartiles were: quartile $1 < 50\%$ of cows were detected in estrus ≤ 62 DIM; quartile $2 = 61$ d; quartile $3 = 51$ d; and quartile $4 = 51$ d. Genomic merit for DPR was positively associated with the number of estrus events up to 62 DIM ($P < 0.01$) and was ($P = 0.02$) negatively associated with the interval between recorded estruses (Figure 7). The duration of estrus was ($P = 0.02$) positively associated with GPDR (Figure 8). This demonstrates that selecting for Holstein cattle with higher GDPR will likely expedite the resumption of estrous cycles postpartum and result in stronger estrous characteristics.

Surprisingly, there were no associations between GDPR and pregnancy to first service, but there was a smaller risk of pregnancy loss from 38 to 87 d after the second service among cows with greater GDPR.
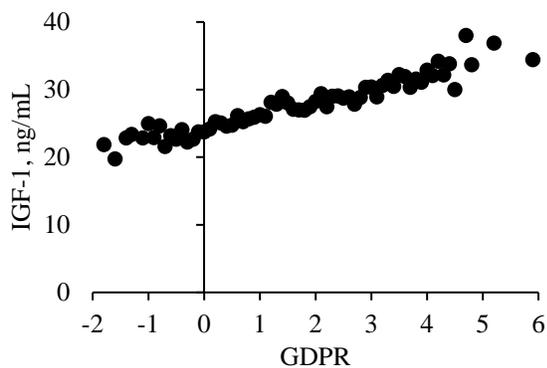

Figure 5. Association between genomic merit for daughter pregnancy rate (GDPR) and concentration of insulin like growth-factor 1 (IGF-1) from 7 to 28 DIM.
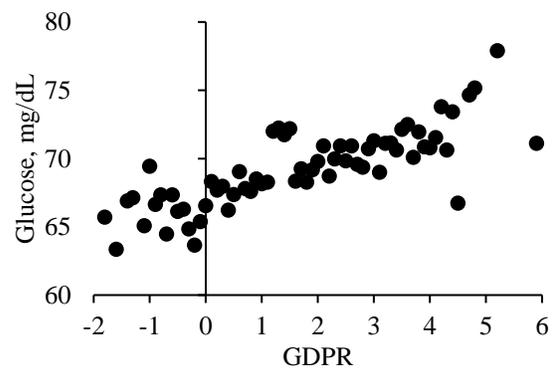

Figure 6. Association between genomic merit for daughter pregnancy rate (GDPR) and concentration of glucose from 7 to 28 DIM.
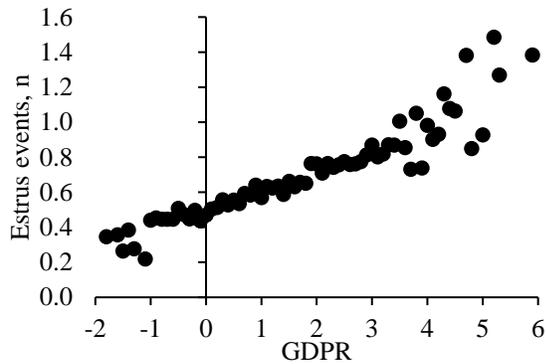
Figure 7. Association between genomic merit for daughter pregnancy rate (GDPR) and number of estrus events up to 62 DIM.
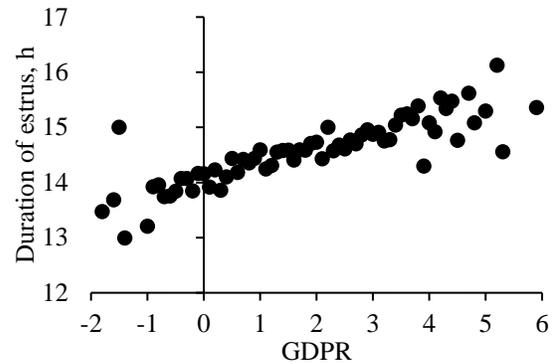

Figure 8. Association between genomic merit for daughter pregnancy rate (GDPR) and duration of estrus events recorded up to 62 DIM.

Conclusion

Selection of Holstein cattle for GDPR has the potential to significantly improve resumption of estrus cycles postpartum and the intensity of estrus. The physiological alterations associated with greater GDPR are likely to be associated with improved growth and estradiol production of the ovulatory follicle and improved metabolic status postpartum. Although the associations between GDPR and pregnancy establishment are not as evident, data from our group suggest that embryos from Holstein cattle with greater GDPR may grow faster, characterized by their greater production of pregnancy specific protein B and reduced risk of pregnancy loss. Considering the greater scrutiny of the public regarding the use of exogenous hormones in food producing animals, genomic selection of fertility traits such as GDPR may prove crucial to maintain the sustainability of Holstein herds.

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