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Genome-Wide Scan For Bovine Ovulation Rate Using A Dense SNP Map

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Introduction

Among the traits for which gene or marker-assisted selection will be the most useful are those that are expressed only in one sex or very costly to measure. This is precisely the reasons why finding genes or markers for twinning and ovulation could be useful to facilitate selection either for or against alleles conferring increased ovulation rate and twinning rate. To do so, the INRA twinning herd of the Maine-Anjou breed created in 1972 is a unique genetic resource whose twinning rate reached 25% in 2005, ie 5 times the level estimated in the French Maine-Anjou breed which is, however, one of the rare bovine breeds with a natural twinning rate surpassing 5% (Manfredi et al., 1990). Heritability of twinning rate is low (<0.10). Twinning rate is the product of ovulation rate, conception rate and embryo survival. Ovulation rate is an indirect predictor for twinning rate with an heritability estimate of 0.35 for the mean of six observations and a genetic correlation of 0.75 (Gregory et al., 1997). It has been suggested that twinning rate in cattle could be genetically determined by major genes (Morris and Day, 1990), but until now only putative QTL effects were identified on ovulation rate in the USDA MARC twinning herd (Kappes et al., 2000; Kirkpatrick et al., 2000; Allan et al., 2009), or on twinning rate in Norwegian cattle (Lien et al., 2000; Meuwissen et al., 2002) or in North American Holstein cattle (Cruickshank et al., 2004, Cobanoglu et al., 2005; Kim et al., 2009). The major focus has been on chromosome 5 where a putative QTL was detected in all three populations and a fine mapping which positionned the QTL within a 1-CM region was realized by Meuwissen et al. (2002) using linkage analysis (LA) and linkage disequilibrium (LD), accounting for unknown background genes and the cattle pedigree. The aim of the paper was to present preliminary results of a genome-wide scan for QTL fine mapping for ovulation rate in the INRA twinning herd using a similar LDLA approach.

Material and methods

Data. A total of 1,015 transrectal echographies performed on 150 heifers born between 2000 and 2008 in the INRA twinning herd were used for this analysis. These heifers were bred by 12 Maine-Anjou sires and 15 Maine-Anjou maternal grand sires, inclunding the 12 sires. A minimum of 5 successive oestrus cycles were observed for each heifer. The heifer ovulation

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rate was derived as the mean of the number of ovulations observed per ultrasound on average 12 days after observed oestrus.
The Illumina bovine SNP50K BeadChip was used to genotype 15 founder bulls and the 150 heifers. These SNPs were selected from across the genome, considering minor allele frequency above 4%. Genotypes were tested for Hardy-Weinberg equilibrium to identify possible typing errors. Physical locations of SNP markers were available from genome assembly v4.0. Finally, a total of 36181 SNP markers were used, the average density of informative SNP was 13.8 SNP per Mb.

Statistical Analyses. A polygenic animal model was used to analyse the polygenic genetic variance and the environnemental variance of ovulation rate using ASREML software developed by Gilmour et al. (2002). The age at first observed oestrus was the only significant fixed effect identified. Therefore the LDLA analysis was derived on ovulation rate corrected for this age effect using a methodological approach proposed by Druet et al. (2008) and Tarres et al. (2009) with a hidden Markov model proposed by Druet et al. (2010) for haplotype reconstruction. Identity by descent (IBD) probabilities were predicted using haplotypes with a window of six markers. Along each of the 29 autosomal chromosomes and at the midpoint position of the haplotype, the log-likelihood ratio of a model containing a QTL for ovulation rate and polygenic background genes was tested versus a model containing only background genes was derived. The distribution of this LRT is not exactly known, but a 2-d.f. chi-square distribution gave a conservative test for the assumption of no existing QTL (Druet et al., 2008).

Results and discussion

Phenotypic results. The average heifer ovulation rate was 1.30 with a raw standard deviation of 0.25, a minimum value of 1.00 and a maximum value of 2.50. Heifers having their first oestrus observed before 15 months had an average ovulation rate equal to 1.21, those with a first oestrus observed between 15 and 22 months had an average ovulation rate equal to 1.32 and the oldest heifers had an average ovulation rate equal to 1.38.

Polygenic results. Under an animal polygenic model, the heritability of ovulation rate was estimated to 0.39 and the environmental variance was 0.038. This result is very similar to previous results obtained from the USDA MARC twinning herd (Gregory et al., 1997).

QTL detection. Forty-three marker positions were suggestive of the existence of QTLs for ovulation rate with a significance level $P < 0.01$ (LRT > 9.2). These positions spanned chromosomes 1, 2, 4, 5, 8, 10, 20, 25 and 28. There were 4 positions among chromosomes 10 (Figure 1), 20 (Figure 2) and 28 (Figure 3) with a significance level $P < 0.001$ (LRT > 14) that still support strong evidence for the existence of QTLs for ovulation rate. As far as we have known until now, evidence of twinning or ovulation rate has been reported on chromosomes 5, 7, 8, 10, 12, 14, 19, 21, 23 and 29. Therefore, this analysis also reports strong evidence for QTLs on ovulation rate on chromosomes 20 and 28. For chromosome 10, Cobanoglu et al. (2005) located the position at 41.0 cM by interval mapping and genotyping

DNA pools of sons of extreme sires for twinning rates which is in the middle of the 2 LRT peaks in our analysis (Figure 1).

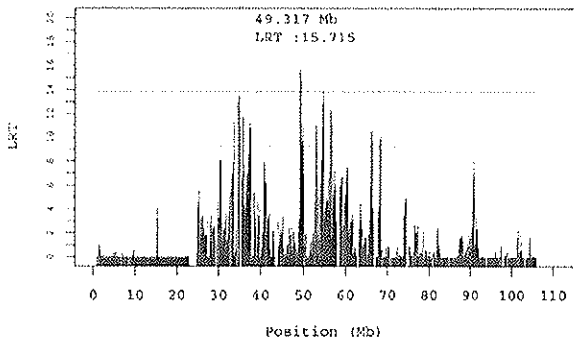

Figure 1: Log-likelihood ratio of LDLA analysis along chromosome 10

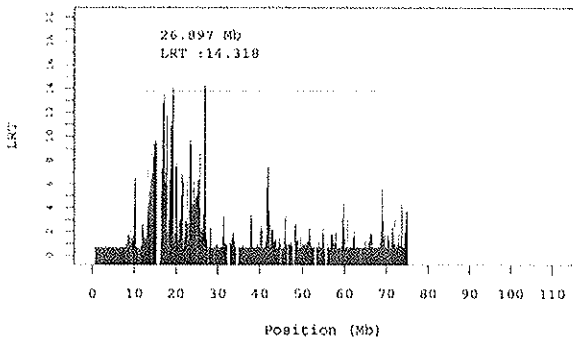

Figure 2: Log-likelihood ratio of LDLA analysis along chromosome 20

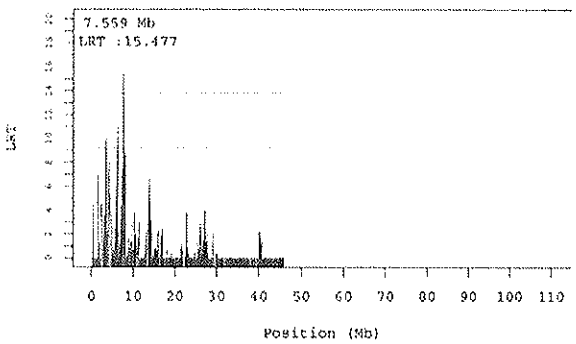

Figure 3: Log-likelihood ratio of LDLA analysis along chromosome 28

Conclusions

Ovulation rate is clearly under the control of at least a dozen QTLs. New evidence for QTLs on chromosomes 20 and 28 is given. Further investigation is needed to estimate the magnitude of these QTL effects and to find the main causative mutations.

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