CANALISING SELECTION ON WITHIN LITTER VARIABILITY OF BIRTH WEIGHT IN RABBITS: RESPONSES TO SELECTION AND CHARACTERISTICS OF THE UTERUS OF THE DOES

Bolet G.[1]*, Garreau H.[1], Hurtaud J.[2], Saleil G.[1], Esparbié J.[1], Falieres J.[1], Theau-Clément M.[1], Bodin L.[1]

[1]INRA, SAGA, BP 52627, F31326 Castanet-Tolosan, France
[2]Grimaud Frères Sélection, La Corbière F49450 Roussay, France
*Corresponding author : gerard.bolet@toulouse.inra.fr

ABSTRACT

A divergent selection experiment on within litter homogeneity of birth weight in rabbits was carried out at INRA. The two lines have been created by selecting breeding does and bucks from the female strain AGP22 bred at the Grimaud Frères Sélection Company. This involved a new model incorporating a genotypic value for the mean and a genotypic value for the environmental variance. There was a favourable selection response with a significant difference in within-litter standard deviation of birth weight between the lines selected for increasing (HOM) or decreasing (HET) the homogeneity. In generation 7, the difference between lines reached 1.6 g, i.e. 19% of the mean of this standard deviation. The standard deviation of weaning weight diverged in generation 7 by 9 g, i.e. 12% of the mean standard deviation. There was a favourable correlated response for the young survival from birth to weaning and litter size at weaning, and no effect of selection for variability on individual weight of the young at birth. At the end of the 3rd and the 6th generation, after the weaning of their last litter, females were sacrificed to collect the uterine horns and measure their initial length and their length after elongation with a weight of 50 g and then 70 g. The length and the elongation in the homogeneous line were significantly higher, whatever the weight added. It is the first time that a positive response to a canalising selection, acting on variability and not on the mean of a trait, was observed in domestic mammals. Given this significant result, the breeding company associated with this work implemented this method of selection in one of its selected strains. At INRA, this experiment continues for better understanding the physiological mechanisms and looking for the genes implied in this response.

Key words: Rabbit, Canalising selection, Homogeneity, Birth weight, Uterus.

INTRODUCTION

The birth weight of young rabbits is very heterogeneous (Bolet *et al.*, 1996). The lightest ones are likely to die very quickly or, if they survive, to be more sensitive to diseases (Poignier *et al.*, 2000). So, a selection to reduce the within litter variability of the weight at birth would be an attractive challenge, provided that it does not contribute to reduce the average weight. The objective is thus to act by selection on the variability of a character, and not on its average. It is what is called the "canalising" selection (Hill, 2002). In quantitative genetics, models were developed with the assumption that, in addition to the environmental effects, genetic effects can modify the environmental variability of a character (San Cristobal *et al.*, 1998). The additive genetic determinism of this variability is generally low (Bodin *et al.*, 2002), and the effectiveness of this method was never checked in experiments. This is why a divergent selection experiment on the homogeneity of the birth weight of the young rabbits was undertaken in 2001 by INRA and Grimaud Frères Selection. We present here the results after 7 generations of divergent selection. In addition, we compared the characteristics of the uterus of the does, to check if they had evolved differently in the divergent lines.

MATERIALS AND METHODS

Animals and selection of the divergent lines

The two divergent lines were created starting from 193 females and 108 males of line AGP22 (Grimaud Frères Selection). To constitute the first generation (G0) of the "homogeneous" line (HOM), the 15 females and 4 males having the lowest genetic values for the variability of the birth weight were retained. In the same way, 14 females and 5 males having the strongest genetic values were retained to constitute the G0 of the "heterogeneous" line (HET). The females were transferred to an INRA experimental unit (Auzeville), while the males remained in the farm of origin and were used through artificial insemination. At each generation, the genetic values of the males and females (approximately 60 per line) were estimated after 3 series of inseminations to select within each line the following generation.

Estimation of the genetic values

We used the model developed by San Cristobal-Gaudy *et al.* (1998) introducing a genetic value for the mean and a genetic value for the environmental variability, both associated with the phenotypic value. The analysed character, measured in the base population, was the individual weight of the alive young rabbits at birth, considered as a trait of the dam. We first estimated the genetic parameters of the mean of the trait. We then estimated the genetic parameters of a function of the residual, which contains information relating to environmental variability, using another model introducing environmental and genetic effects. For these 2 analyses the REML method was applied to an animal model, using VCE software (Neumaier and Groeneveld, 1998). These genetic parameters made it possible to calculate for each animal a BLUP genetic value of the variance of the weight at birth, by using the PEST software (Groeneveld and Kovac, 1990).

Characteristics of the genital tract of the females

After the weaning of their 3rd litter, the females of G3 (31 in line HOM and 33 in line HET) underwent a superovulation treatment and were sacrificed 72 hours after being inseminated. We recorded the number of corpora lutea and the weight of each ovary. Each uterine horn was separated from its conjunctive tissue, perfused to collect the embryos and weighed. Then, it was hung on a support and measured, after being ballasted for 1 minute with an initial weight of 5 g to ensure its tension, then a weight of 50 g, and finally a weight of 70 g. The objective was to measure its initial length and its elongation. The same measurements were made on 64 females at the end of G6 (33 in line HOM and 31 in line HET), 72 hours after insemination, without any superovulation treatment.

Statistical analyses

Response to the selection

The traits analyzed were: the within litter standard deviation of the weight of the young rabbits at birth and at weaning, the number of young rabbits born and weaned by litter, the individual weight of the young rabbits at birth, the stillbirth rate and the mortality rate from birth to weaning. Analyses of variance were carried out with the SAS software. All the models included the fixed effects of the generation, batch and line within generation and parity. For individual birth and weaning weights, the random effect of the dam within line x generation was added, using the MIXED procedure of SAS.

Measurements of the genital tract

An analysis of variance with the fixed effects of the line (HOM and HET), the side (right and left) and other fixed effects (batch, physiological state, size of the preceding litter) was performed (see Bolet *et al.*, 2007). The traits analyzed were the number of corpora lutea, the weight of the ovary and the uterine horn, the length at each measurement and the elongation.

RESULTS

Responses to selection

For all traits, there was a significant effect of the line within generation, and thus significant direct and indirect responses to selection. The within litter standard deviation of birth weight diverged between the two lines as soon as G0 (Figure 1a). The line difference in standard deviation units was then approximately 0.6 g. In G7, the difference between lines reached 1.6 g, i.e. 19% of the standard deviation mean (7.7 g in G7).

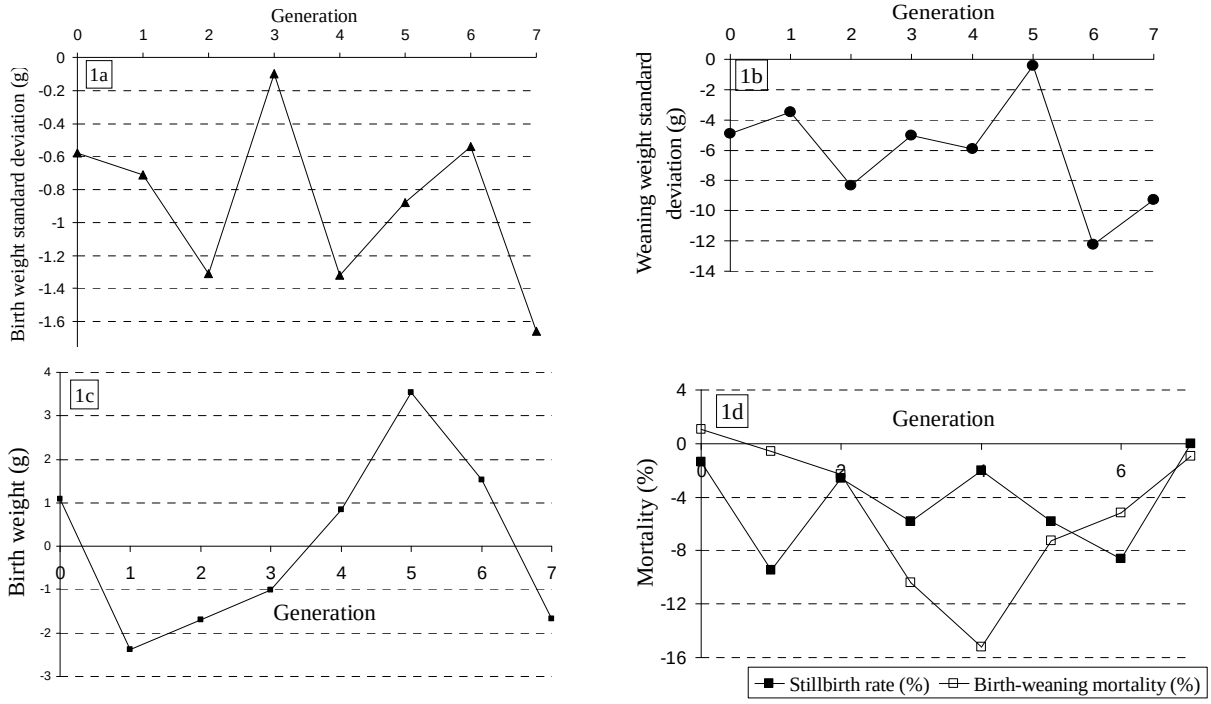

Figure 1: Difference between the "homogeneous" and the "heterogeneous" lines from generation 0 to 7 for the within litter standard deviation of birth weight (1a), of weaning weight (1b), for individual birth weight (1c) and for the mortality rate from birth to weaning (1d)

There was a significant correlated response for the within-litter standard deviation of the weight at weaning, since the difference between lines went from 5 g in G0 to 9 g in G7 (12% of the mean of this standard deviation) (Figure 1b). Selection had no effect on the mean weight of the young rabbits at birth, which did not diverge between lines (Figure 1c). We also observed a correlated response on the mortality of the young rabbits: the rate of stillbirth was lower in the homogeneous line, the difference appearing as soon as G0 and varying from 1,4 to 9,5%, except in G7. The birth to weaning mortality rate was also significantly lower in the HOM line in most generations (Figure 1d). This explained the favourable effect of selection for homogeneity on litter size at weaning, whereas there was no significant effect on litter size at birth.

Characteristics of the genital tract

For the two generations (G3 and G6), there was no significant effect of the side on the traits analysed. There was no significant effect of the line on the number of ova shed (counted by the number of corpora lutea). There was a significant effect of the line on the length and extensibility of the uterine horns. Whatever the generation and the elongation to which it was subjected, the uterine horn of line HOM was longer and more extensible in HOM line (Figure 2).

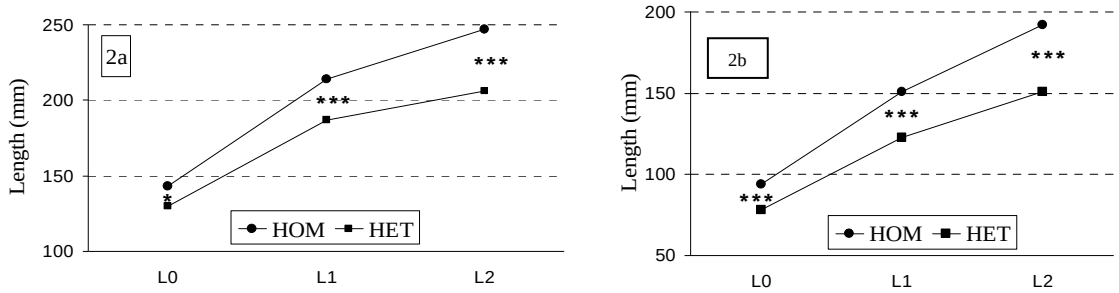

Figure 2: Length of the uterine horn in the "homogeneous"(HOM) and in the "heterogeneous"(HET) line in generation 3 (2a) and 6 (2b) according to the weight added (L0: + 5 g, L1: +50 g, L2: +70 g)

DISCUSSION

The aim of the canalising selection is to modify the variability and not the mean of the selected traits. Its theoretical effectiveness had already been shown (Bodin *et al.*, 2002), but it is the first time that a positive response is evidenced in domestic mammals. Although the selection was not directly based on the standard deviation of the weight, but on a more complex criterion (Garreau *et al.*, 2004), the difference between lines reaches 19% of the standard deviation mean after 7 generations. It should however be noted that a large part of the line difference was established as soon as the first generation, because the selection intensity was much more important in G0, the two lines having been made up starting from a large population, than in the following generations. Although the correlations between the direct and indirect responses could not be estimated, a certain number of points deserve to be underlined:

- the trend observed for the variability of the weight at weaning was similar to that observed at birth tends to indicate that the correlation between these two parameters is positive.
- the lack of trend for the mean weight at birth shows that it is possible to modify the variability of a character independently from its mean. The basic assumption of the method employed is that there are genes acting on the variability of a trait and that these genes are, at least partially, independent from those acting on the mean. Our results would confirm this assumption, although it is not very likely that there is a total genetic independence between the mean and the variance. Indeed, in pigs, Damgaard *et al.*. (2003) showed a positive genetic correlation between the mean and the standard deviation of birth weight. Ros *et al.* (2004) provided a strong indication of a positive genetic correlation between additive genetic values affecting the mean and those affecting environmental variation of adult body weight in the snail *Helix Aspersa*.
- an indirect response was observed on the viability of the young rabbits at birth and from birth to weaning, in favour of the line selected for an increased homogeneity. This result is in agreement with the genetic correlations calculated in pigs by Damgaard *et al.*. (2003). In pigs, Milligan *et al.* (2002) observed that a strong variability of the weight at birth is associated with a low survival rate, independently from the size of the litter.

Our results show that the length and the extensibility of the uterine horns are significantly larger in the homogeneous line. This observation was made in the very first days of gestation, but affects the continuation of gestation. Bolet *et al*. (1996) highlighted that the elongation of the uterus made it possible to compensate for the overcrowding of a uterine horn without major effect on the average weight of the young rabbits. Argente *et al.* (2003, 2004) compared the characteristics and the irrigation of the horns uterine in two lines diverging for their uterine capacity, and did not highlight important differences. In pigs, Chen and Dziuk (1993) observed that average space available had more influence on prenatal survival than on the weight or the length of the foetuses. Lebas (1982) showed that the site of the foetus in the uterine horn had an effect on its weight, those located at the ends being heavier. Did the divergent selection act by reducing this phenomenon in the homogeneous line, or by other mechanisms relating to the metabolism of the uterine horn?

CONCLUSIONS

It is the first time that a positive response to a canalising selection, acting on variability and not on the mean of a trait, was observed in domestic mammals. This significant reduction in the variability of the weight of young rabbits at birth was accompanied by favourable correlated responses on the viability of the young rabbits, litter size at weaning and within litter variability of weight at weaning. This result is sufficiently significant so that this method of selection was implemented by the breeding company associated with this work in one of its selected strains. At INRA, this experiment continues for better understanding the physiological mechanisms and looking for genes implied in this response.

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