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INFLUENCE OF GENETIC DIVERSITY AT INDIVIDUAL AND GROUP LEVEL ON THE HEALTH OF GROWING RABBITS

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ABSTRACT

This study investigates the impact of genetic diversity at both individual and group levels on the health of 1,038 growing rabbits raised without antibiotics during the post-weaning period. By increasing diversity at the individual level (crossbreeding) and at the group level (cross-fostering), our aim is to reduce the dependance on antibiotics in industrial farming systems. The survival, the visual health score, and the white blood cell counts were monitored. We compared purebred and crossbred rabbits, as well as two cross-fostering strategies: between- and within-genotypes. Results show that crossbreed rabbits exhibit better visual health scores at 64 days, indicating a positive effect of genetic diversity at the individual level. However, increasing genetic diversity at the group level through cross-fostering did not yield favorable outcomes, with more rabbits in the between-genotype strategy classified as diseased. Further investigation into the effects of genetic diversity at the herd level is recommended to understand its potential benefits on the farm health. Overall, this study underscores the complex interplay between genetic diversity and health outcomes in industrial rabbit farming systems.

Key words: Genetic diversity, cross-fostering, white blood cell count, crossbred, health.

INTRODUCTION

Our study is part of the quest for alternative solutions to reduce the dependence of antibiotics in rabbit farming. Building on the findings of King and Lively (2012), which demonstrate that the genetic diversity of host populations can offer protection against disease or parasites, our study focuses on the benefits of genetic diversity at individual and group levels on rabbit health during the post-weaning period. For the individual-related genetic diversity analysis, we compared purebred and crossbred rabbits. To evaluate genetic diversity at the group level, we compared two cross-fostering strategies: between- and within- genotype. The genetic diversity at the group level was maintained after weaning. Our objective was to evaluate the impact of genetic diversity on health and survival.

MATERIALS AND METHODS

Animals and experimental design

A total 1,038 growing rabbits born in four cohorts with a 42 days interval were monitored between 35 (weaning age) and 64 days of age. They were purebred 481 INRA-1777 kits (hereinafter INRA) and 557 Crossbreed kits (hereinafter Crossbreed) ¾ Fauve-de-Bourgogne and ¼ INRA. The Crossbreed were born from crossbreed ½ Fauve-de-Bourgogne × ½ INRA-1777 does inseminated with semen from purebred Fauve-de-Bourgogne males. The day after birth, rabbit kits were individually identified and two cross-fostering strategies were applied (Figure 1). At each birth cohort, half of the litters were assigned to the between-genotype cross-fostering strategy and the remain half were assigned to the within-genotype cross-fostering strategy. For each strategy, the average litter size at birth of each genotype was respected. We had four experimental groups: **IW**: INRA kits in the within-genotype cross-fostering strategy (n = 242), **CW**: Crossbreed kits in the within-genotype cross-fostering strategy (n = 295), **IB**: INRA kits in the between-genotype cross-fostering strategy (n = 239) and **CB**: Crossbreed kits in the between-genotype cross-fostering strategy (n = 262).

Figure 1: Representation of cross-fostering strategies. **IW**: INRA kits in the within-genotype cross-fostering strategy, **CW**: Crossbreed kits in the within-genotype cross-fostering strategy, **IB**: INRA kits in the between-genotype strategy and **CB**: Crossbreed kits in the between-genotype strategy.
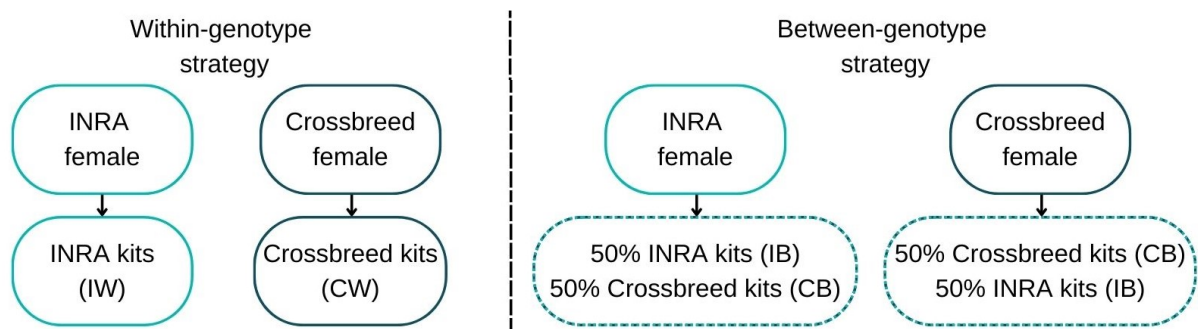
At weaning, the rabbit kits were placed in groups of five to six rabbits in wired cages (L×W×H: 90×46×60 cm). The genetic diversity at the group level (i.e. IW, CW, IB, and CB) was maintained after weaning. Rabbits were raised without antibiotics. They had free access to water and to a commercial feed (STABI-GREEN G, Terrya, Rignac, France) at all times.

Studied Variables

Kits survival. Kits survival from weaning to 64 days of age was monitored daily. Date and cause of death or culling were recorded. Survival data are presented as Kaplan-Meyer survival curves.

Visual health score. Each animal's health score was assessed visually based on the clinical signs of disease at 64 days of age. A total of 952 rabbits were recorded and classified as healthy or sick.

Hematological health score. Between 64 and 67 days of age, blood samples were taken on a representative subgroup of 850 rabbits. The differential count of white blood cells was performed using the MS9-5 Hematology Analyzer (Melet Schloesing Laboratoires). The literature provides reference values for the normal range of white blood cell counts in rabbits. However, they did not correspond to our populations. We therefore defined new normal values adapted to our genotypes. Box and whiskers plots for each white blood cell type were constructed for each genotype for all rabbits having an healthy Visual Health score at 64 days of age. Values falling outside the whiskers (whisker ends being calculated using 1.5 times the interquartile space according to Tukey, 1977), were considered outliers. The minimum and maximum values obtained after excluding outliers were kept as the new normal ranges (Table 1). On the basis of these new threshold values, we classified the rabbits into two classes for each white blood cell population: "normal" if the animal had values within the threshold values for its genotype, or "abnormal" otherwise.

Table 1: Normal white blood cells ($\times 10^9$/L) range from the literature (Fielder, 2022), or estimated from our data on healthy rabbits (visual health scores) at 64 days of age.

Hematological trait	Fielder, 2022	Genotypes	
		INRA	Crossbreed
Total White Blood Cell counts	6.0 - 12.0	3.6 - 12.8	1.9 - 12.3
Lymphocytes	1.6 - 10.6	1.2 - 3.9	0.6 - 4.8
Monocytes	0.05 - 0.5	0.3 - 1.1	0.3 - 0.9
Neutrophils	1.0 - 9.4	1.4 - 7.9	0.0 - 7.3
Eosinophils	0.05 - 0.5	0.0 - 0.2	0.1 - 0.1

Statistical Analysis

The statistical analyses was performed using the R statistical software version 4.2.2 (R CoreTeam, 2023). To analyze survival, a variable called Lifetime was set as the number of days between the weaning date and the date of death or culling. Kit survival was set as the

number of days between the weaning date and the date of death or culling. The model used to produce the Kaplan-Meier estimation of survival probability curves included the growing rabbit's cross-fostering strategy and their genotype. The model was implemented using the R-package {survival}. For the two binary traits: visual health score (healthy 0, sick 1) and hematological score (normal 0, abnormal 1), the data was analyzed using a general linear model. We analyzed the proportion of rabbits classified as 0 or 1 according to the cross-fostering strategy, the genotype and their interaction.

RESULTS AND DISCUSSION

Survival

The overall mortality rate (death or culling) between 35 and 64 days of age was 7.7%, with no significant difference between genotypes or cross-fostering strategies. Digestive syndromes were the main cause of death (66% of cases), followed by respiratory (15% of cases) and others syndromes (19%). Survival curves for the combination of genotype and crossbreeding strategy were statistically significant ($P<0.001$; Figure 2). The survival curve for the IW group differed from the others. The difference observed is related to the low survival probability observed in the IW group around 45 days of age. The INRA progeny seems to benefit from the between-genotype cross-fostering strategy.

Figure 2: Survival probability curves according to the genetic diversity at the individual (INRA or Crossbreed) or the group (within- and between- cross-fostering strategy) level
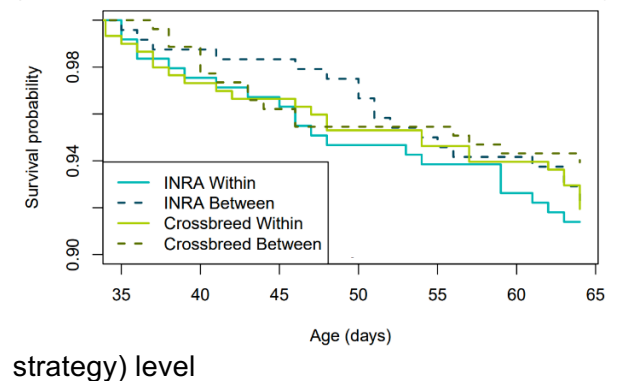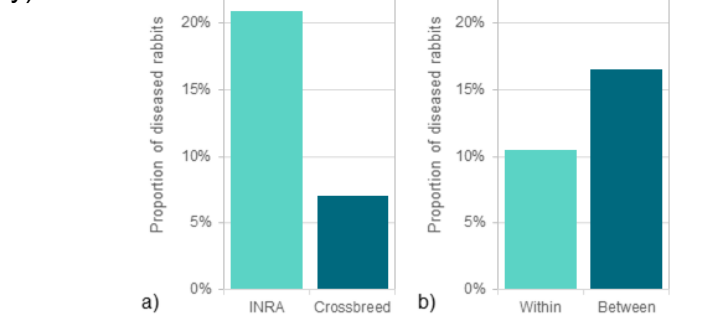
Figure 3. Proportion of rabbits classified as sick on the Visual Health Score according to the genetic diversity at (a) the individual (INRA or Crossbreed) or (b) the group (within- and between- cross-fostering strategy) level

Visual health score

The proportion of sick rabbits at 64 days old (Figure 3) was significantly higher for INRA than for Crossbreed rabbits (20.9% vs. 7.0%, respectively; $P<0.001$), and significantly higher for the for the between-genotypes compared to the within-genotype cross-fostering strategy (16.5% for vs. 10.5%, respectively, $P<0.01$). No significant interactions between kit genotype and cross-fostering strategy was observed for this trait. Live animals at 64 days old being classified as sick using the visual health score had respiratory syndromes in 95% of the cases.

Hematological health score

The percentage of rabbits with white blood cell populations outside the normal range (here defined: Table 1) is shown in Table 2. Overall, the proportion of rabbits with abnormal values was less than 6% for total white blood cells, lymphocytes, monocytes and neutrophils. For eosinophils, between 11.2% and 26.3% of all rabbits had values outside the normal range. A genotype effect was identified for eosinophils, linked to a high percentage of Crossbreed rabbits in the within-genotype cross-fostering strategy showing eosinophil values outside the normal range compared to other groups (on average, 26.3% vs. 13.5%; $P<0.05$). Interactions between genotype and cross-fostering strategy were also observed for lymphocytes and neutrophils.

Table 2: Effect of genetic diversity at the individual (INRA or Crossbreed genotype) or group (within- or between- cross-fostering strategy) level on the percentage of rabbits with hematological values out of the normal range.

Genotype (G)	INRA		Crossbreed		*P*-values[1]		
Cross-fosterig strategy (CS)	Within	Between	Within	Between	G	CS	G×CS
Total white blood cells	2.54	2.51	3.39	1.37	0.90	0.31	0.32
Lymphocytes	0.50	4.02	2.11	0.46	0.30	0.40	<0.01
Monocytes	4.06	4.02	5.08	4.13	0.68	0.71	0.76
Neutrophils	4.56	0.50	2.11	2.29	0.73	0.08	0.03
Eosinophils	11.2[a]	15.1[a]	26.3[b]	14.2[a]	<0.01	0.07	0.04

[1]*P*-values of the main effects Genotype (G), Cross-fostering Strategies (CS) and their interaction (G×CS): type II analysis of variance.
[a-b] Percentages having different superscripts differ at *P*<0.05.

Genetic diversity at the individual, group or herd level
We observed a favorable effect of genetic diversity at the individual level on the visual health score, where a higher proportion of Crossbreed rabbits were classified as healthy at 64 days compared to INRA rabbits. This could be explained by the heterosis effect of Crossbreed rabbits. Heterosis has a highly positive effect on health (Blasco et al., 1993). On the opposite, we observed an unfavorable effect of genetic diversity at group level. Rabbits in the within-genotype cross-fostering strategy showed a significantly higher proportion of healthy visual health scores at 64 days compared to rabbits in the between-genotype cross-fostering strategy. Cross-fostering within a single genotype is a common practice in rabbit breeding that tends to increase pre-weaning survival (Heim et al., 2012). Is worth noting that throughout the experimental period (four consecutive cohorts), more than 91% of rabbits (independent on the genotypes and cross-fostering strategies), were classified as health at age 64 days without any antibiotic use. We can hypothesize that individual genetic diversity, and perhaps group genetic diversity may have had a positive effect at herd level. Further studies need to be carried out, for example comparing single-breed herds with herds using a mixture of breeds, to demonstrate the potential benefits of increased genetic diversity at the herd level on health traits.

CONCLUSIONS
We studied the influence of genetic diversity at individual and group level on the health of rabbits during the post-weaning growth period. Crossbreed rabbits showed better visual health scores at 64 days, indicating a positive effect of genetic diversity at the individual level. However, increasing genetic diversity at group level through cross-fostering strategies did not appear to have a favorable effect, with more rabbits in the between-genotype cross-fostering classified as sick for the visual health scores at 64 days. No difference in mortality was observed between groups.

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