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INBREEDING DEPRESSION ON GROWTH AND PROLIFICACY TRAITS

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ABSTRACT

This research aims at estimating inbreeding depression for growth and prolificacy traits in a rabbit population selected for growth rate for 60 generations. Data corresponded to 173,485 individuals of the Caldes line founded in 1983. The effects of old, intermediate and new inbreeding (Fold, Fint, Fnew), as well as classical (i.e. total cumulated) inbreeding (F) and 3 measures of ancestral inbreeding (AHC, Fa.K and Fa.B) were estimated for average daily gain (ADG), slaughter weight (SW), number of kits born alive (NA), total number of kits (NT) and number of weaned kits (NW). For growth traits the effect of inbreeding was estimated with a model that included the fixed effects of year of birth, parity order and litter size as well as the corresponding inbreeding coefficient as a covariate (or alternatively the addition of Fold, Fint, Fnew covariates), plus the random effects of litter, batch and additive genetic effects. For the analysis of prolificacy traits, the model included the fixed effects of year of birth, physiological status of the female at mating in addition to the covariate corresponding to the inbreeding coefficient, as for growth traits, and the random effects of dam, batch and additive genetic effects. There was a clear inbreeding depression for all growth and prolificacy traits (-10 g/d, -506 g, -7.4 kits, -6.2 kits and -6.2 kits for ADG, SW, NA, NT and NW, respectively on F). Ancestral inbreeding coefficients Fa.K and Fa.B had also a negative effect on all traits, and results were not significantly different to those obtained with F. However, the effect of Fold and Fint was null whereas it was negative for Fnew, on growth traits but not on prolificacy traits. Similar results to those obtained for Fint and Fold were also observed using AHC, suggesting the possibility of purging by selection of deleterious recessive alleles affecting growth.

Key words: inbreeding depression, cumulative inbreeding, ancestral inbreeding, selection

INTRODUCTION

Inbreeding depression is the loss in performance associated with the increase of homozigosity that results from matings between related individuals. Its level depends, among other factors, on the genetic load of an individual, which refers to the amount of deleterious recessive alleles this individual carries. Inbreeding usually increases in small populations subjected to selection. Successive generations of inbreeding may result in a rebound of performance due to the reduction of the frequency of deleterious alleles. This purging of deleterious alleles may shift towards zero the estimates of inbreeding depression obtained from a regression of performance on inbreeding (Holt et al. 2005). However, providing statistical significance of purging is not straightforward (Crnokrak and Barrett 2002).

The aim of this research was to quantify inbreeding depression on growth and prolificacy traits in a population of rabbits selected for growth for 60 generations and also to find some possibility of purging of deleterious alleles by selection.

MATERIALS AND METHODS

Animals

Data corresponded to 173,485 individuals of the Caldes selection line belonging to IRTA. This line was founded in 1983 by crossing animals from five New Zealand White lines and a California × New Zealand synthetic line. It has been selected for litter weight and individual growth rate until 1992, for growth rate until 2011, and currently for feed efficiency after 3 generations without selection. Management of rabbits was performed in overlapping generations (0.05 and 0.95 quartiles of the absolute value of the age difference between dam and sire were 1 and 310 days, respectively, being the mean generation interval 292 d). Matings between animals with common grandparents were avoided. This line is currently in its 60th generation. The average number of animals per generation was 2,928. The average number of does and sires per generation was 179 and 60, respectively.

Statistical Analysis

Following Ragab et al. (2015), we defined F_u^t as the inbreeding of an animal from generation u considering generation t as base generation, being $t < u$. For $t = 0$, F_u^0 represents the inbreeding accumulated since the foundation of the line, which is divided into several components that account for the inbreeding accumulated during different periods of time. Thus, for two given generations t_1 and t_2, being $0 < t_1 < t_2 < u$, we define the inbreeding accumulated until generation t_1 as $F_{0.t1}^0$, the inbreeding accumulated from generation t_1 to generation t_2 as $F_{t1.t2}^0$ and the inbreeding accumulated from generation t_2 to generation u as $F_{t2.u}^0$. These components are computed from formulas (Ragab et al. 2015) derived from the equation for inbreeding in hierarchically structured populations (Wright 1922; Hinrichs et al. 2007). Three periods of 20 generations were considered, and $t_1 = 20$ and $t_2 = 40$. We name Fnew the inbreeding accumulated in the period immediately preceding individual birth, Fint the inbreeding accumulated during the 20 generations period before this, and as Fold the inbreeding accumulated during the first 20 generations period of time. An animal born before generation 20 has only accumulated Fnew, whereas Fint and Fold are set to 0. An animal born between generations 20 and 40 has accumulated Fnew and Fint, whereas Fold is set to 0. An individual born after generation 40 has accumulated Fnew, Fint and Fold. Classical (i.e. total cumulated) inbreeding (F) and ancestral inbreeding coefficients were also computed. Ancestral inbreeding coefficients were computed using the ancestral history coefficient (AHC; Baumung et al. 2015) following Kalinowski’s method (Fa.K; Kalinowski et al. 2000) and Ballou’s approach (Fa.B; Ballou 1997). The AHC (i.e. the number of times that a random allele had been identical by descent (IBD) during pedigree segregation) indicates that alleles which have experienced inbreeding more often in the past are less likely to be deleterious than alleles which have undergone inbreeding less often, because they have survived to purging. The Fa.K represents the probability that any allele in an individual is currently IBD and has been IBD in previous generations at least once. Finally, Fa.B can be defined as the probability that any allele in an individual has been IBD in previous generations at least once. Ancestral inbreeding coefficients were computed using gene dropping with the R package GRAIN (Baumung et al. 2015).

The effect of the three components of inbreeding on average growth traits at fattening (i.e. ADG: average daily gain in g/d and SW: slaughter weight in g) was estimated using the following model:

$$y_{ijklmn} = Batch_i + P_j + LS_k + \beta_1 Fold_l + \beta_2 Fint_l + \beta_3 Fnew_l + a_l + c_m + e_{ijklmn}$$

where y_{ijklmn} is the ADG or SW of individual l ; $Batch_i$, P_j and LS_k are the systematic effects of batch (294 levels), parity order (4 levels: 1st, 2nd, 3rd , 4th and posterior) and litter size (7 levels: <6, 6, 7, 8, 9, 10, >10), respectively; $Fold_l$, $Fint_l$ and $Fnew_l$ are the three components of F_u^0 for animal l and β_1, β_2 and

β_3 the corresponding regression coefficients; a_l is the additive genetic effect; c_m is the litter effect (22,982 levels); e_{ijklmn} is the residual. A total of 151,263 records were used for the analysis.

The model for prolificacy traits was:

$$y_{ijklm} = Batch_i + PS_j + \beta_1 Fold_k + \beta_2 Fint_k + \beta_3 Fnew_k + a_k + p_l + e_{ijklm}$$

where y_{ijklm} is the NA, NT or NW of individual *k* and PS_j is the physiological status of the female (5 levels: 1, for nulliparous does; 2, and 3 for primiparous does in or not in lactation at mating, respectively; 4 and 5 for multiparous does in or not in lactation at mating); p_l is the permanent effect of female and all the other terms are as defined above. There were 26,256 prolificacy data from 8,575 does, and the pedigree has 10,312 individuals. For prolificacy traits, only the inbreeding coefficient of the doe was included in the model.

The aforementioned models include Fold, Fint and Fnew in the same model. However, these three inbreeding coefficients were replaced by F, AHC, Fa.K or Fa.B to obtain the corresponding regression coefficients for each inbreeding coefficient, separately. A total of 5 models (Fold+Find+Fnew, F, AHC, Fa.K and Fa.B) were run for each trait. A favourable regression coefficient significantly different from zero suggests the occurrence of purging of inbreeding depression for the trait under investigation, while an unfavourable regression coefficient significantly different from zero indicates inbreeding depression of the trait (Mc Parland et al. 2009). Analyses were performed using airemlf90 from BLUPf90 family programs (Misztal, 2002).

RESULTS AND DISCUSSION

Cumulated inbreeding coefficient was in this population 0.074 on average (mean in generation 60th = 0.17) which represents an increase of 0.3% per generation and 0.5% per year. Correlations between parts of cumulated inbreeding were small in absolute value: 0.20 and 0.02 between Fold and Fint, and between Fold and Fnew, respectively, and -0.11 between Fint and Fnew. Therefore, we do not expect collinearity prevents differentiation of their effects on the analyzed traits. Table 1 shows the regression coefficients for growth and prolificacy traits for the different inbreeding coefficients. For prolificacy traits, there was not a significant change in the regression coefficients. Therefore, the entire inbreeding coefficient has a negative effect on prolificacy traits.

For ADG (the selection criteria) and SW inbreeding depression was observed for F, Fnew, Fa.K and Fa.B. For example, Fnew is the responsible of a reduction of 21% and 25% of the mean for ADG and SW, respectively. Accordingly, an increased trend from negative to null in the regression coefficients from Fnew to Fold was observed, but the regression coefficients were not significantly different from zero for Fint, Fold and AHC (except for ADG). These results may suggest the possibility of purging of alleles with deleterious effects due to the selection process.

Both AHC and the partition of inbreeding moving the base generation (Ragab et al. 2015) may provide a worth representation of the possibility of purging. The rationale behind AHC is that the probability of purging increases with the number of times the alleles have been IBD. Consequently, an allele that has been IBD several times in an individual's pedigree is more likely to have a neutral or favorable effect on traits under selection, compared to an allele that has been IBD only once or never before (Doekes et al. 2019). Accordingly, Ragab et al. (2015) with the partition of inbreeding approach observed the same results as those obtained in the present study for prolificacy traits in four rabbit lines selected for prolificacy. Finally, there was strong and positive correlation (0.99 – 1.00) between Fnew and Fa.K, F and Fnew, F and Fa.K, and between AHC and Fa.B, whereas it ranged from -0.11 to 0.38 for all the other pairs of inbreeding coefficients. This means that the partition of inbreeding seems a reliable alternative to evaluate inbreeding depression and purging and it could provide complementary information to other indexes.

Table 1: Regression coefficients (S.E.) of growth and prolificacy traits on: classical (F), new (Fnew), intermediate (Fint), old (Fold) inbreeding coefficients, ancestral history coefficient (AHC), and ancestral inbreeding as defined by Kalinowski et al. (Fa.K) or Ballou (Fa.B)

Trait[1]	F	Fnew	Fint	Fold	AHC	Fa.K	Fa.B
ADG (g/d)	-9.73 (1.67)	-10.05 (1.73)	-7.66 (4.39)	2.24 (6.11)	-2.95 (1.16)	-13.86 (2.47)	-13.26 (3.92)
SW (g)	-505.86 (65.23)	-533.68 (67.37)	-318.80 (166.97)	77.36 (224.15)	-35.69 (44.06)	-715.90 (96.25)	-604.03 (149.25)
NA	-7.35 (1.34)	-6.54 (1.42)	-9.06 (2.33)	-12.12 (2.62)	-0.60 (0.13)	-9.76 (1.70)	-2.67 (0.48)
NT	-6.20 (1.24)	-5.79 (1.31)	-7.47 (2.23)	-8.54 (2.55)	-0.46 (0.13)	-8.05 (1.60)	-2.07 (0.48)
NW	-6.24 (1.20)	-5.13 (1.31)	-8.53 (2.06)	-9.27 (2.29)	-0.54 (0.10)	-8.80 (1.45)	-2.53 (0.37)

[1] ADG: average daily gain, SW: slaughter weight, NA: number of kits born alive; NT: total number of kits; NW: number of weaned kits

CONCLUSIONS

Results confirm the existence of inbreeding depression on growth and prolificacy traits in rabbit and suggest the possibility of purging of deleterious recessive alleles involved in growth, but not in prolificacy traits, by selection for growth rate.

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Inbreeding depression

- **What is it?**

  is the **loss in performance** associated with the **increase of homozygosity** that results from mattings between related individuals

- **what does it depend on?**

  Its level depends on **the genetic load** of the individual

- **Where does it happen?**

  In small populations subjected to **selection**

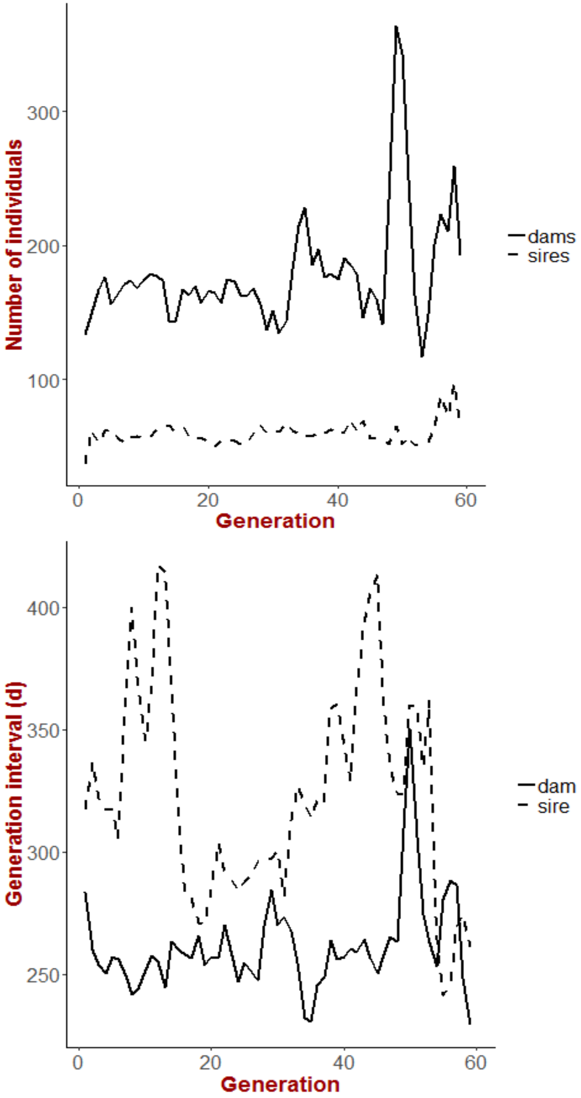
BUT successive generations of inbreeding may result in **purging of deleterious alleles**

⇩

rebound of performance

OBJECTIVE

To quantify **inbreeding depression on growth and prolificacy traits** and to find some evidence of **purging of deleterious alleles by selection**.



ANIMALS

173,485 individuals (**60 generations**) of the **Caldes line**

- Founded in 1983 by crossing animals from 5 NZW lines and a California × NZ synthetic line.

- Selected for:
  - 1983 to 1992: litter weight and individual growth rate
  - 1992 to 2011: individual growth rate
  - 2011 to 2014: No selection
  - 2014 to 2021: feed efficiency at growing

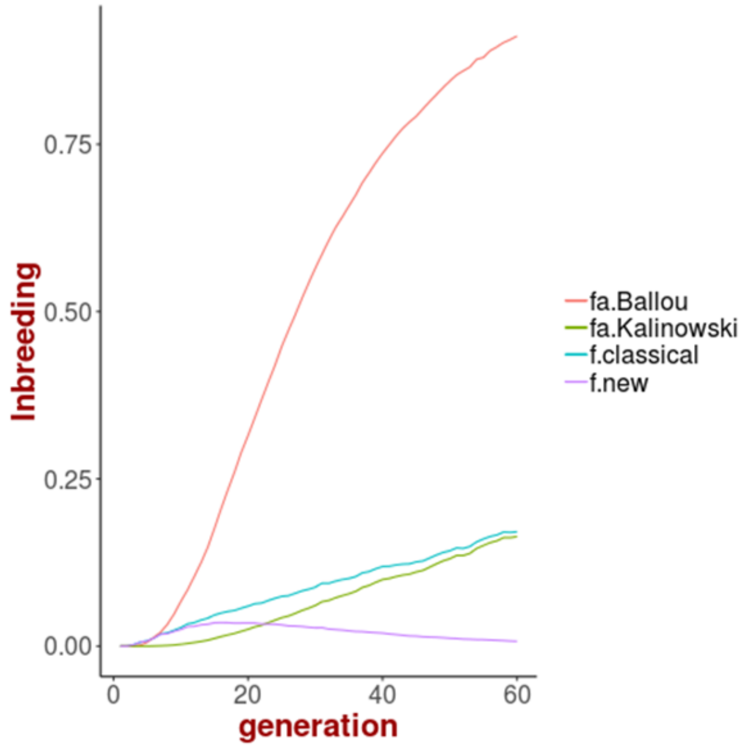
- Overlapping generations
- Animals per generation = 2,928
- Does per generation = 179
- Bucks per generation = 60
- Generation interval = 292 d

PARTITIONED INBREEDING

inbreeding of animal *i* from generation *u* > *40*

$F_{0,20}^0$	**F-old**	Inbreeding accumulated until generation 20
$F_{20,40}^0$	**F-int**	Inbreeding accumulated from generation 20 to generation 40
$F_{40,60}^0$	**F-new**	Inbreeding accumulated from generation 40 to generation u

CLASSICAL & ANCESTRAL INBREEDING



- f = Total cumulated inbreeding
- AHC = Ancestral history coefficient (Baumung et al. 2015)
- fa.K = Ancestral inbreeding following Kalinowski's method (Kalinowski et al. 2000)
- fa.B = Ancestral inbreeding following Ballou's method (Ballou 1997).

f.classical = mean in generation 60th = 0.17
+ 0.3% per generation and + 0.5% per year.

INBREEDING EFFECTS ON GROWTH TRAITS

$$\mathrm{y} = \mathrm{YOB} + \mathrm{Batch} + \mathrm{Parity} + \mathrm{Litter\ size} + \boldsymbol{\beta_1} \times \mathbf{f.old} + \boldsymbol{\beta_2} \times \mathbf{f.int} + \boldsymbol{\beta_3} \times \mathbf{f.new} + \mathrm{additive} + \mathrm{litter} + \mathrm{e}$$

Posterior Mean [HPD95%] of regression coefficients of average daily gain (ADG), weaning weight (WW) and slaughter weight (SW) on partitioned inbreeding coefficients

Trait	f.new	f.int	f.old
ADG (g/d)	-7.60 [-11.71, -3.73]	-5.49 [-13.43, 2.88]	7.97 [-3.60, 19.77]
WW (kg)	-0.28 [-0.37, -0.17]	-0.10 [-0.31, 0.12]	0.02 [-0.22, 0.30]
SW (kg)	-0.48 [-0.64, -0.33]	-0.24 [-0.57, 0.11]	0.33 [-0.10, 0.77]

INBREEDING EFFECTS ON GROWTH TRAITS

$$y = \text{YOB} + \text{Batch} + \text{Parity} + \text{Litter size} + \beta \times \text{IC} + \text{additive} + \text{litter} + e$$

Inbreeding coefficient:

- *f.Classical*
- *Fa.Kallinowski*
- *Fa.Ballou*
- *AHC*

Posterior Mean [HPD95%] of regression coefficients of average daily gain (ADG), weaning weight (WW) and slaughter weight (SW) on different inbreeding coefficients

Trait	f.classical	fa.Kallinowski	fa.Ballou	AHC
ADG (g/d)	-7.19 [-11.01, -3.35]	-10.60 [-17.05, -3.83]	-0.21 [-5.04, 5.34]	0.06 [-2.06, 2.40]
WW (kg)	-0.25 [-0.34, -0.15]	-0.41 [-0.58, -0.24]	-0.04 [-0.11, 0.04]	0.06 [0.03, 0.10]
SW (kg)	-0.45 [-0.60, -0.30]	-0.73 [-0.98, -0.48]	-0.29 [-0.52, -0.14]	-0.003 [-0.08, 0.06]

INBREEDING EFFECTS ON PROLIFICACY TRAITS

$$y = \mathrm{YOB} + \mathrm{Batch} + \mathrm{Phisiological\ status} + \beta_1 \times \mathrm{f.old} + \beta_2 \times \mathrm{f.int} + \beta_3 \times \mathrm{f.new} + \mathrm{additive} + \mathrm{permanent} + e$$

Regression coefficients of prolificacy traits on partitioned inbreeding coefficients

Trait	f.new	f.int	f.old
Born Alive	-6.51 [-10.30, -2.79]	-2.39 [-9.02, 4.08]	2.52 [-6.93, 11.35]
Stillborn	1.78 [-0.04, 3.67]	-1.09 [-4.57, 2.15]	3.03 [-1.35, 7.78]
Total Born	-4.60 [-8.19, -1.19]	-3.18 [-9.35, 2.58]	5.41 [-2.63, 13.99]
Weaned	-4.07 [-7.63, -0.50]	-1.69 [-8.04, 4.71]	5.18 [-4.19, 14.45]

INBREEDING EFFECTS ON PROLIFICACY TRAITS

$$y = \text{YOB} + \text{Batch} + \text{Phisiological status} + \underset{\uparrow}{\beta} \times \text{IC} + \text{additive} + \text{permanent} + e$$

Inbreeding coefficient:

- *f.Classical*
- *Fa.Kallinowski*
- *Fa.Ballou*
- *AHC*

Regression coefficients of prolificacy traits on different inbreeding coefficients

Trait	f.classical	fa.Kallinowski	fa.Ballou	AHC
Born Alive	-5.94 [-9.70, -2.52]	-9.11 [-15.18, -3.36]	0.41 [-2.47, 3.75]	-0.13 [-1.24, 1.08]
Stillborn	1,23 [-0.53, 2.99]	2.89 [-0.05, 5.75]	**1.68 [0.52, 3.08]**	**1.07 [0.62, 1.58]**
Total Born	-4.48 [-7.73, -1.17]	-5.73 [-11.24, -0.15]	3.40 [-0.70, 7.38]	**1.39 [0.12, 2.75]**
Weaned	-3.79 [-7.01, -0.43]	-7.02 [-12.21. -1.55]	-4.06 [-7.01, -0.96]	-1.06 [-2.09, 0.007]

TO TAKE HOME MESSAGE

The partition of inbreeding in new, intermediate and old inbreeding, and the ancestral history coefficient (AHC)

may provide a worth representation of the possibility of purging of deleterious alleles because of selection

Same results for growth and prolificacy traits

Caldes line is selected for growth traits but probably some selection is being also performed on prolificacy traits

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