Resistance to infectious diseases is a heritable trait in rabbits

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Resistance to infectious diseases is a heritable trait in rabbits[1]

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ABSTRACT: Selection for disease resistance is a powerful way to improve the health status of herds and to reduce the use of antibiotics. The objectives of this study were to estimate 1) the genetic parameters for simple visually assessed disease syndromes and for a composite trait of resistance to infectious disease including all syndromes and 2) their genetic correlations with production traits in a rabbit population. Disease symptoms were recorded in the selection herds of 2 commercial paternal rabbit lines during weighing at the end of the test (63 and 70 d of age, respectively). Causes of mortality occurring before these dates were also recorded. Seven disease traits were analyzed: 3 elementary traits visually assessed by technicians on farm (diarrhea, various digestive syndromes, and respiratory syndromes), 2 composite traits (all digestive syndromes and all infectious syndromes), and 2 mortality traits (digestive mortality and infectious mortality). Each animal was assigned only 1 disease trait, corresponding to the main syndrome (N = 153,400). Four production traits were also recorded: live weight the day before the end of test on most animals (n = 137,860) and cold carcass weight, carcass yield, and perirenal fat percentage of the carcass on a subset of slaughtered animals (n = 13,765). Records on both lines were analyzed simultaneously using bivariate linear animal models after validation of consistency with threshold models applied to logit-transformed traits. The heritabilities were low for disease traits, from 0.01 ± 0.002 for various digestive syndromes to 0.04 ± 0.004 for infectious mortality, and moderate to high for production traits. The genetic correlations between digestive syndromes were high and positive, whereas digestive and respiratory syndromes were slightly negatively correlated. The genetic correlations between the composite infectious disease trait and digestive or respiratory syndromes were moderate. Genetic correlations between disease and production traits were favorable. Our results indicate that it is possible to select rabbits using visually assessed disease syndromes without the need for a trade-off between health and production traits. Using a composite criterion that includes all infectious syndromes is easy to implement and heritable and is, therefore, a promising way to improve the general disease resistance in livestock species.

Key words: disease resistance, general resistance, genetic parameters, heritability, infectious diseases, rabbit

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INTRODUCTION

Since the 1990s, international organizations have been expressing concern about the development of antibiotic resistance and have developed guidelines for the monitoring of antibiotic resistance and antibiotic use in human and veterinary medicine. In 2012, a French action plan for "the reduction of the risks of antibiotic resistance in veterinary medicine" was published. The plan aims to reduce the quantity of antibiotics used in animal production by 25% within 5 yr and to promote alternative methods to maintain health in breeding farms (French Ministry of Agriculture, 2012). Genetic selection for disease resistance is such an alternative method, which allows slow but progressive, cumulative, and long-lasting improvement.

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Some selection programs that include disease resistance have been successfully implemented in rabbits (Garreau et al., 2012). Previous studies showed that it is possible to select rabbits for their resistance to bacterial infectious diseases caused by *Pasteurella* spp. and *Staphylococcus* spp. (Eady et al., 2007) as well as their resistance to digestive disorders by using simple records of disease syndromes (Garreau et al., 2008). However, little is known about the genetic correlations among various disease traits and between disease and production traits. The possibility to select livestock for general resistance or general immunity has been widely discussed (Guy et al., 2012), but until now, no study on this topic has been conducted in rabbits.

The main aim of this study was to estimate the genetic parameters for simple visually assessed disease syndromes and for a composite trait of resistance to any infectious diseases, which included all infectious disease syndromes. The secondary aim was to estimate the genetic correlations between disease resistance and production traits, to check whether it would be possible to select both in a compatible way.

MATERIALS AND METHODS

Data were collected in accordance with the national regulations of agriculture in the framework of selective breeding schemes of the HYPHARM breeding company.

Animals

The study was undertaken on data collected in the selection nucleus of 2 meat rabbit lines (AGP39 and AGP59) belonging to the HYPHARM breeding company (Roussay, France). Both lines are paternal lines, reared in 2 different rooms in the same building, and selected on production traits. Records on 85,502 rabbits from line AGP39 and on 67,898 rabbits from line AGP59 were analyzed. All rabbits were born between 1998 and 2014. Does were inseminated every 42 d (42-d reproductive cycle) and had an average of 3.8 parities. Kits in line AGP39 were weaned at 31 d and tested until 63.16 ± 0.87 d (hereafter 63 d of age) and kits in line AGP59 were tested until 70.04 ± 0.37 d (hereafter 70 d of age). All the kits were housed in collective cages and were subject to a restricted feeding program, except for 9% of them that were individually housed. The kits in each of the collective pens were from the same litter.

Production Traits

Live weight (**LW**) was recorded at the end of the test on 137,860 animals. The day after weighing, one-third of the kits from the first delivery of the does, as well as some kits from the second and the third delivery (about 10% of the animals with LW records), were slaughtered in a commercial slaughterhouse. Twenty-four hours after slaughter, the cold carcass weight (**CW**) was measured. Carcass yield (**CY**; CW/LW just before slaughter) and perirenal fat percentage (**FAT%**; perirenal fat weight/CW) were also recorded. The descriptive statistics on these traits are listed in Table 1.

Table 1. Descriptive statistics for production traits: number of animals per trait, means, SD, minimum, and maximum values

Trait[1]	Unit	No.	Mean	SD	Minimum	Maximum
CY	%	13,765	57.692	1.915	46.360	69.850
FAT%	%	13,764	1.577	0.444	0.280	3.570
LW	kg	137,860	2.878	0.385	1.100	4.385
CW	kg	13,765	1.713	0.226	0.670	2.540

[1]CY = carcass yield; FAT% = perirenal fat percentage; LW = live weight; CW = carcass weight.

Disease Traits

When weighing the carcasses at 63 or 70 d of age, the technicians recorded the health status of each individual rabbit. They monitored rabbits for digestive and respiratory syndromes and other infectious syndromes that occur naturally at the breeding farm. The probable cause of death of rabbits that died before weighing, which concerns 4.7% of the rabbits, was also recorded. The causes of infectious death were diarrhea (60%), various digestive syndromes (36%), respiratory syndromes (2%), and other infections (2%). If a rabbit had more than 1 disease syndrome, only the predominant one was recorded. All the animals (153,400) in the data set had disease records. The disease traits observed are listed in Table 2. They were recorded as 0 (absence) or 1 (disorder). Elementary disease traits were morbidity or mortality from diarrhea (**DIARR**), from various digestive syndromes (**VARDIG**), and from various respiratory syndromes (**RESPI**). Composite disease traits were all digestive syndromes (**ALLDIG**; DIARR + VARDIG) and a trait of mortality or morbidity from infectious syndromes (**INFECT**; ALLDIG + RESPI + other infectious syndromes). Other infectious syndromes accounted for only 1% of the troubles; they included abnormal low weights, skin infections, and other syndromes of infectious origin. All the abovementioned traits included mortality or disease syndromes. Two other mortality traits were also taken into consideration: digestive mortality (**DIGMORT**) and infectious mortality (**INFMORT**). In this case, the numeral 1 denoted an animal that died before the end of the test. In the full population of 153,400 young rabbits,

Table 2. Description of disease traits observed in 153,400 young rabbits during the postweaning period

Trait	Abbreviation	Signs observed in rabbits	Percent observed
Diarrhea	*DIARR*	Morbidity or mortality from diarrhea	3.2
Various digestive syndromes	*VARDIG*	Morbidity or mortality from bloated abdomen and various digestive syndromes (excluding diarrhea)	3.9
All digestive syndromes	*ALLDIG*	DIARR + VARDIG. Morbidity or mortality from diarrhea, bloated abdomen, and any form of digestive syndrome	7.1
Digestive mortality	*DIGMORT*	Mortality from any digestive syndrome	4.5
Respiratory syndromes	*RESPI*	Morbidity or mortality from nasal discharge, lung lesion, eye infection, and wry neck	4.0
Infectious syndromes	*INFECT*	ALLDIG + RESPI + other infectious syndromes. Morbidity or mortality from all digestive or respiratory syndromes, abnormally low weight, abscesses, and any other form of infection	12.1
Infectious mortality	*INFMORT*	Mortality from any infectious syndrome	4.7

12.1% showed INFECT and 4.7% died of infectious syndromes (INFMORT). Most of the rabbits showing disease syndromes were not sent to the slaughterhouse. Therefore, in the subpopulation of 13,765 rabbits that had slaughter measurements (CY, FAT%, and CW), 2.8% showed only INFECT and none died of infectious syndromes (INFMORT).

Statistical Analysis

Model. All traits were analyzed using a REML method, with ASReml 3.0 (Gilmour et al., 2009). Genetic and phenotypic variances or covariances were estimated using a pairwise bivariate animal model. The animal model included a random additive polygenic effect and a random common litter effect for all traits and a maternal genetic effect for LW and CW. The common litter effect is a nongenetic component that represents the common environment of all the kits of the same litter. Genetic and phenotypic parameter estimates and their SE were obtained by running bivariate analyses. First, analyses separately were run on each rabbit line (results not shown) and gave similar parameter estimates, with high SE for the rabbit line with fewer individuals. Consequently, to increase accuracy, both rabbit lines were simultaneously analyzed, simultaneously considering the 2 pedigrees. For the binary disease traits, a threshold model would theoretically be more exact than a linear model (Gianola and Foulley, 1983), especially for extreme incidence of the binary traits (Kadarmideen et al., 2003). The impact of non-normal distributions of the disease traits on their genetic parameter estimates depends on which estimation procedure is used. Preliminary univariate analyses with ASReml showed very similar heritability estimates between threshold models after a logit transformation and linear models, but genetic correlations could not be estimated with the threshold models with this software. The correlations between the EBV of the 2 models were above 0.93 for all disease traits. For that reason, only results from the linear model are presented here.

Fixed Effects. The significance of the fixed effects was determined for each trait using the Wald F statistic, which is similar to an ANOVA (Gilmour et al., 2009). All fixed factors were first tested together, and then a stepwise selection of the significant ones was applied. Significant fixed factors ($P < 0.05$) were maintained in the subsequent mixed model analyses and are summarized in Table 3. The fixed effects of the line (2 levels), the contemporary group within the line (146 levels for line AGP39 and 152 for line AGP59), and sex (3 levels) were fitted for all traits. The categories for sex were 1 for males, 2 for females, and 3 when the information was missing (for 11.8% of the animals). Sex was recorded at weighing and was missing for the rabbits that died before weighing. Other fixed effects were the parity of the dam (10 levels: 1 level for each parity up to 9 and 1 level for 10 parities and above) and litter size recorded 21 d after delivery (8 levels: 3 kits and below; 4, 5, 6, 7, 8, and 9 kits; and 10 kits and above). The cage effect covered both rabbits in collective cages with restricted feeding and rabbits fed ad libitum in individual cages. The age at weighing was significant only for LW. They were 5 classes: below 63 d, 63 d, 64 to 69 d, 70 d, and above 70 d. Interactions between the sex, parity of the dam, litter size, cage effects, and the line effects were fitted when significant.

RESULTS

Heritability Estimates

Direct and maternal heritabilities and ratio of the common litter effects variance to total variance for all traits are listed in Table 4. All disease traits exhibited a significant genetic component. Even if low, all heritabilities were significantly different from 0. Infectious mortality had the highest heritability among disease traits (0.043 ± 0.004). Heritabilities were moderate for LW, CW, and CY (ranging from 0.130 ± 0.009 to 0.243 ± 0.026) and very high for FAT% (0.608 ± 0.033). The

Table 3. Significant fixed and random effects included in the mixed model for the analysis of disease and production traits

	Fixed effects											Random effects		
Trait[1]	Line	Contemporary group	Sex	Parity	Cage	Litter size	Age	Sex × line	Parity × line	Cage × line	Litter size × line	Animal genetic	Litter	Maternal genetic
ALLDIG	x	x	x	x	x			x		x		x	x	
DIGMORT	x	x	x	x	x	x		x		x	x	x	x	
DIARR	x	x	x	x	x	x		x		x	x	x	x	
VARDIG	x	x	x	x	x			x		x		x	x	
RESPI	x	x	x	x	x			x				x	x	
INFECT	x	x	x	x	x			x		x		x	x	
INFMORT	x	x	x	x	x	x		x		x	x	x	x	
CY	x	x	x		x	x		x		x	x	x	x	
FAT%	x	x	x			x						x	x	
LW	x	x	x	x	x	x	x	x	x	x	x	x	x	x
CW	x	x	x	x		x					x	x	x	x

[1]ALLDIG = all digestive syndromes; DIGMORT = digestive mortality; DIARR = diarrhea; VARDIG = various digestive syndromes; RESPI = respiratory syndromes; INFECT = infectious syndromes; INFMORT = infectious mortality; CY = carcass yield; FAT% = perirenal fat percentage; LW = live weight; CW = carcass weight.

common litter effect was moderate but higher than the heritability of disease traits. This effect was especially high for DIARR and DIGMORT, which suggests contamination between littermates sharing the same cage.

Phenotypic and Genetic Correlations

Table 5 lists the genetic and phenotypic correlations, including direct genetic effects and maternal genetic effects for LW and CW (**LWdir**, **CWdir**, **LWmat**, and **CWmat**, respectively).

Disease Traits. The genetic correlations among the 4 disease traits related to digestive syndromes (ALLDIG, DIARR, VARDIG, and DIGMORT) were very high and positive (varying from 0.71 ± 0.06 to 0.99 ± 0.01). The corresponding phenotypic correlations were generally lower but showed the same trend (ranging from 0.33 ± 0.00 to 0.73 ± 0.00) except the one between VARDIG and DIARR, which was slightly negative (–0.14 ± 0.00). Phenotypically, the 4 digestive disease traits were not correlated with the respiratory syndrome trait (correlations ranged from –0.03 ± 0.00 to –0.01 ± 0.00), whereas genetically, they were slightly negatively correlated with it (correlations ranged from –0.26 ± 0.06 to –0.14 ± 0.09). Concerning the 2 composite traits (INFMORT and INFECT), INFECT was moderately phenotypically and genetically correlated with all the other disease traits (0.42 ± 0.00 to 0.72 ± 0.06) whereas INFMORT showed a high positive phenotypic correlation with DIGMORT and a genetic correlation equal to 1 with DIGMORT and DIARR.

Production Traits. Live weight and CW were phenotypically and genetically highly correlated for both their maternal effects and their direct effects. Within and between these weight traits, the genetic correlations between direct and maternal effects were slightly negative (ranging from –0.04 ± 0.07 to –0.39 ± 0.12). The 2 weight traits were moderately positively phenotypically correlated with CY and FAT% (ranging from 0.15 ± 0.01 to 0.41 ± 0.01). Genetically, except for the slight positive correlation (0.25 ± 0.05) between FAT% and LWmat, all correlations between weight traits and FAT% were null. The genetic correlations between CY and the weight traits were the reverse: a positive correlation with LWmat and CWdir and a negative correlation with LWdir and CWmat. Genetic and phenotypic correlations between FAT% and CY were not significantly different from 0.

Disease and Production Traits. Nearly all the phenotypic correlations between disease traits and production traits were null or moderately negative, meaning that an unhealthy animal exhibited lower weight, CY, and perirenal fat (Table 5).

Genetic correlations between disease traits and CY were also negative, that is, favorable, and of higher magnitude than phenotypic correlations. Genetic correlations between disease traits and FAT% or CW (direct and maternal) were not significantly different from 0. Most of the genetic correlations between disease traits and LW were not significantly different from 0, except for DIGMORT and LWmat, INFMORT and LWmat, and VARDIG and LWdir, which were moderate and positive, and for INFECT and LWmat, which was moderate and negative.

To summarize our findings, all disease traits were heritable and genetically positively correlated with each other, except RESPI, which was slightly negatively correlated with the digestive disease traits. Genetic correlations between disease and production traits were mostly favorable or null.

Table 4. Estimates of direct heritability (h^2), common litter effect (c^2), and maternal heritability (m^2) and SE (in parentheses) of estimates for disease and production traits

Trait[1]	h^2	c^2	m^2
ALLDIG	0.034 (0.003)	0.090 (0.002)	
DIGMORT	0.041 (0.004)	0.133 (0.003)	
DIARR	0.018 (0.003)	0.124 (0.003)	
VARDIG	0.011 (0.002)	0.060 (0.002)	
RESPI	0.041 (0.004)	0.057 (0.002)	
INFECT	0.030 (0.003)	0.076 (0.002)	
INFMORT	0.043 (0.004)	0.127 (0.003)	
CY	0.243 (0.026)	0.098 (0.012)	
FAT%	0.608 (0.033)	0.060 (0.011)	
LW	0.130 (0.009)	0.137 (0.003)	0.136 (0.008)
CW	0.205 (0.032)	0.163 (0.014)	0.108 (0.022)

[1]ALLDIG = all digestive syndromes; DIGMORT = digestive mortality; DIARR = diarrhea; VARDIG = various digestive syndromes; RESPI = respiratory syndromes; INFECT = infectious syndromes; INFMORT = infectious mortality; CY = carcass yield; FAT% = perirenal fat percentage; LW = live weight; CW = carcass weight.

DISCUSSION

This study established that additive genetic variation for resistance to any infectious disease or respiratory or digestive disease syndromes exists in rabbit. Selection for resistance to diseases syndrome could, therefore, be successful.

Selection for Disease Syndromes

Visually assessed disease syndromes were heritable and can, therefore, be used to select rabbits for improved disease resistance.

Our results are in accordance with those of previous studies in commercial meat rabbits. These studies showed that disease traits grouping digestive syndromes on the one hand (Garreau et al., 2008) and bacterial infectious syndromes (from *Pasteurella multocida* or *Staphylococcus aureus*) on the other hand (Eady et al., 2004, 2007) are heritable. A heritability of 0.08 ± 0.02 was found for ALLDIG in the AGP39 rabbit line with 53,222 records analyzed from 1999 to 2007 with a threshold model (Garreau et al., 2008). Heritability of bacterial infectious syndromes at 9 or 10 wk of age estimated with a linear model was 0.04 ± 0.01 in French meat rabbit populations (Eady et al., 2004) and 0.06 ± 0.02 in Australian meat rabbit populations (Eady et al., 2007).

The efficiency of selection for ALLDIG has already been demonstrated by an experimental inoculation with *Escherichia coli* O 103 (Garreau et al., 2012): mortality was significantly lower in the group of rabbits with the lowest EBV for ALLDIG (i.e., the most resistant rabbits) compared with the group with the highest EBV.

Table 5. Estimates of genetic (above diagonal) and phenotypic (below diagonal) correlations and their SE (in parentheses) of estimates between disease and production traits[1]

	ALLDIG	DIGMORT	DIARR	VARDIG	RESPI	INFECT	INFMORT	CY	FAT%	LWdir	LWmat	CWdir	CWmat
ALLDIG		0.91 (0.01)	0.96 (0.02)	0.96 (0.02)	–0.18 (0.07)	0.65 (0.04)	0.92 (0.02)	–0.40 (0.07)	–0.09 (0.06)	0.11 (0.07)	–0.11 (0.06)	–0.21 (0.11)	0.05 (0.12)
DIGMORT	0.73 (0.00		0.99 (0.01)	0.71 (0.06)	–0.26 (0.06)	0.53 (0.05)	1.00 (0.00)	–0.18 (0.08)	–0.04 (0.06)	0.03 (0.07)	0.17 (0.06)	–0.12 (0.11)	0.14 (0.12)
DIARR	0.58 (0.00	0.65 (0.00)		0.84 (0.08)	–0.21 (0.09)	0.72 (0.06)	1.00 (0.01)	–0.02 (0.11)	–0.01 (0.08)	0.09 (0.10)	0.00 (0.09)	0.09 (0.14)	–0.05 (0.16)
VARDIG	0.72 (0.00	0.33 (0.00)	–0.14 (0.00)		–0.14 (0.09)	0.69 (0.06)	0.69 (0.06)	–0.49 (0.10)	–0.05 (0.08)	0.23 (0.09)	–0.16 (0.09)	–0.21 (0.14)	0.12 (0.15)
RESPI	–0.03 (0.00	–0.01 (0.00)	–0.01 (0.00)	–0.03 (0.00)		0.61 (0.04)	–0.27 (0.06)	–0.10 (0.08)	0.04 (0.06)	0.01 (0.06)	–0.06 (0.06)	–0.08 (0.10)	0.05 (0.11)
INFECT	0.71 (0.00	0.52 (0.00)	0.42 (0.00)	0.51 (0.00)	0.60 (0.00)		0.52 (0.05)	–0.35 (0.08)	–0.04 (0.06)	0.06 (0.07)	–0.25 (0.06)	–0.18 (0.11)	0.04 (0.12)
INFMORT	0.70 (0.00	0.97 (0.00)	0.63 (0.00)	0.32 (0.00)	0.02 (0.00)	0.54 (0.00)		–0.18 (0.08)	–0.06 (0.06)	0.00 (0.07)	0.14 (0.06)	–0.12 (0.11)	0.17 (0.12)
CY	–0.20 (0.01	–0.09 (0.01)	0.09 (0.01)	–0.19 (0.01)	–0.02 (0.01)	–0.05 (0.01)	–0.08 (0.01)		0.12 (0.06)	–0.21 (0.06)	0.23 (0.06)	0.50 (0.08)	–0.28 (0.11)
FAT%	–0.13 (0.01	–0.05 (0.01)	0.07 (0.01)	–0.09 (0.01)	0.00 (0.01)	–0.01 (0.01)	–0.05 (0.01)	0.14 (0.01)		0.08 (0.05)	0.25 (0.05)	0.09 (0.08)	–0.01 (0.10)
LWdir	–0.34 (0.00	–0.06 (0.00)	–0.21 (0.00)	–0.29 (0.00)	–0.04 (0.00)	–0.31 (0.00)	–0.13 (0.00)	0.15 (0.01)	0.32 (0.01)		–0.10 (0.06)	0.93 (0.01)[2]	–0.13 (0.06)
LWmat												–0.04 (0.07)	1.00 (0.00)[2]
CWdir	–0.33 (0.01	–0.11 (0.01)	0.17 (0.01)	–0.28 (0.01)	–0.02 (0.01)	–0.06 (0.01)	–0.11 (0.01)	0.41 (0.01)	0.28 (0.01)	0.96 (0.00)			–0.39 (0.12)
CWmat													

[1]ALLDIG = all digestive syndromes; DIGMORT = digestive mortality; DIARR = diarrhea; VARDIG = various digestive syndromes; RESPI = respiratory syndromes; INFECT = infectious syndromes; INFMORT = infectious mortality; CY = carcass yield; FAT% = perirenal fat percentage; LWdir = direct genetic effects for live weight; LWmat = maternal genetic effects for live weight; CWdir = direct genetic effects for carcass weight; CWmat = maternal genetic effects for carcass weight.

[2]Reached the limits of the parameter space.

Low Observed Heritability of Disease Traits

The estimated heritability of disease resistance traits is generally low (Bishop and Woolliams, 2014). Lipschutz-Powell et al. (2012) demonstrated that low estimates of heritability may be caused by a failure to capture all the relevant genetic variance in disease resistance, by not taking into account the genetic variation in infectivity. Bishop and Woolliams (2010) also demonstrated that incomplete exposure to infection and imperfect diagnostic test sensitivity and specificity lead to underestimation of the heritability of disease resistance. Specificity is the probability that a healthy individual is classified as healthy by the diagnostic test, whereas sensitivity measures the probability that a diseased individual is classified as diseased by the test. With diagnosis of diseases by visual appraisal, we would expect both sensitivity and sensibility to be imperfect. We would also expect exposure to the disease to be incomplete, implying that the observed phenotypes are imperfect and that heritabilities of resistance to diseases are likely underestimated. Nucleus herds are generally highly protected and benefit from a very high sanitary status, whereas disease occurrences at the commercial level are higher due more open herds and less stringent sanitary barriers. Heritability and correlation estimates would probably not be the same in such environment. The "true" heritability for disease resistance is likely to be much higher than our estimates. Under experimental infection of rabbits with epizootic rabbit entheropathy, Garreau et al. (2006) estimated heritability for diarrhea (presence of at least 1 diarrhea symptom during 33 d after inoculation) of 0.21 ± 0.16, which may be closer to the true heritability of the trait than our estimations under natural infection and incomplete exposure to pathogens.

Genetic Correlations between Disease Traits

No other study in rabbits has described the genetic correlations between disease traits. The genetic correlations between digestive disease traits were high, even among traits such as VARDIG and DIARR. This result suggests a common genetic determinism between the 2 traits. Conversely, there was almost no genetic correlation between digestive and respiratory disease traits. This result can be partly explained by the fact that only 1 syndrome was recorded per animal but also by the genetic independent genetic susceptibility to digestive and respiratory diseases. Similar genetic independence has been observed in pigs (Henryon et al., 2001).

The composite INFECT trait was genetically correlated with all traits. A similar trend was observed by Henryon et al. (2001) in pigs with favorable and moderately strong correlations between the composite trait "resistance to any clinical or subclinical disease" and respiratory diseases or diarrhea. The composite INFECT trait could, therefore, be a good indicator trait to improve general disease resistance and to reduce the sensitivity of rabbits to digestive or respiratory infections.

Favorable Correlations between Disease and Production Traits

We showed that genetic correlations between disease and production traits were mostly favorable in an environment with moderate infectious challenge.

A breeding objective could, therefore, include both production and disease resistance traits without the need for a trade-off. In the French commercial meat rabbit population, Garreau et al. (2008) reported nonsignificant negative genetic correlations between LW, CW, CY, FAT%, and ALLDIG, whereas Eady et al. (2004) reported a genetic correlation that was not significantly different from 0 between LW and a bacterial infection trait.

Correlation estimates between disease and slaughter traits could be improved. Only 10% of the rabbits had records on slaughter traits. Almost all of them were healthy, because sick rabbits were not sent to the slaughterhouse. This recording protocol could have biased the correlation estimates between disease and slaughter traits.

Genetic correlations between resistance and production traits can be favorable or unfavorable (Doeschl-Wilson et al., 2008; Stear et al., 2001). Genetic correlations depend on both the consequences of being infected as well as the costs of mounting or being able to mount appropriate immune responses (Bishopand Stear, 2003). The duration and the prevalence of the disease and the time of measurement (at the beginning of the infection, during the disease, or after recovery) affect the direction and the magnitude of the correlation between resistance and production traits. The genetic correlation estimates we obtained may be radically different in an environment with a higher or lower infectious challenge or with another disease recording method.

Breeding for General Disease Resistance

We have demonstrated that a composite trait grouping all disease syndromes was heritable. This is the first study to show that rabbits can be selected on general disease resistance. The simplicity of the recording process (a single record for each animal of a given age) means it can be used for a very large number of growing animals. In the future, it could be improved by assessing the multiple syndromes observed on each rabbit separately, to avoid possible underestimation of the correlation between diseases. In pigs, Henryon et al. (2001) estimated a heritability of 0.18 ± 0.05 for a trait of resistance to any clinical and subclinical disease based on

general syndromes. This trait included lameness, respiratory diseases, diarrhea, and reduced feed consumption. The authors used survival analysis and considered the time until the first diagnosis of the disease as the selection trait, which needs additional steps for proper interpretation but has been successfully implemented by some breeding companies for selection.

In rabbits, as in pigs and other livestock species, individuals in herd are exposed to a variety of pathogens that are not always identified, which makes this approach especially desirable. Except for our study and a study by Henryon et al. (2001), the main way to breed for nonspecific disease resistance has been to enhance immune response (Bishop and Woolliams, 2004). The feasibility of selecting for immune responsiveness has also been demonstrated in pigs (Wilkie and Mallard, 1999), chickens (Pinard-van der Laan, 2002), and cows (Heriazon et al., 2013). Immune response traits tend to be substantially heritable, for example, in pigs (Flori et al., 2011). Improved resistance to different diseases was the target of the search, unfortunately with contradictory results. Pigs selected for high antibody response, when infected with a mycoplasma, had less polyserositis but developed more severe arthritis (Wilkie and Mallard, 1999). Chicken selected for high antibody response were not significantly more resistant to Marek's disease than the control line (Pinard et al., 1993). On the opposite, cows classified as high cell or antibody mediated immune responses had lower occurrence of disease (Thompson-Crispi et al., 2012).

In Spain, a robust rabbit line founded by rabbits of high reproductive longevity showed higher leukocyte counts and better ability to confront digestive disorders (García-Quirós et al., 2014). So breeding for general disease resistance could indeed enhance the immune response.

Conclusion

Here we explored the genetic variability of disease syndromes recorded on the farm. Syndromes of respiratory or digestive diseases, as well as a composite trait of resistance to any infectious disease, are heritable traits. These disease traits are either not correlated or favorably genetically correlated with production traits. The results suggest that it is possible to select rabbits for disease resistance by using simple health records without causing negative effects on production, at least in environments with moderate infectious challenge. It also seems possible to select rabbits for general disease resistance based on syndromes of any infectious diseases. Breeding for general disease resistance based on the simple visual assessment of the presence of infectious diseases is very promising. Phenotyping costs are low, so the number of records can be high. Our results may also be relevant for other livestock species that are routinely exposed to a number of infectious pathogens. In a context of reduction of antibiotic treatments, the potential outcome of more resistant animals is of major importance for breeders. The present study paves the way for actual breeding for resistance to infectious diseases in rabbits. Comparing the immune response of extreme animals with the highest EBV for disease resistance and disease sensitivity would provide further insights into the immune mechanisms in play. Further studies would also be needed to investigate the genetic × environment effect in more details by studying disease records in farm with higher infectious disease challenge.

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