Bayes factor analysis for the genetic background of physiological and vitality variables of F2 Iberian × Meishan newborn piglets

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ABSTRACT: The Bayes factor (BF) procedure was applied to examine the additive genetic component of several physiological and vitality variables for newborn pigs. Nine variables were studied: heart rate, arterial oxygen saturation, rectal temperature (all at birth and 60 min later), birth weight, interval between birth and first teats contact, and interval between birth and first colostrum intake. The available numbers of data ranged from 288 (heart rate at 60 min) to 839 records (birth weight) from F2 Iberian × Meishan newborn pigs. We compared a model with zero heritability (nonheritable) with the one where the additive genetic background was included. The BF was used to discriminate between both candidate models. Very strong evidence of genetic background was detected for heart rate 60 min after birth (BF = 48.90), and strong evidence was detected for rectal temperature at birth (BF = 13.82). Posterior modes (means) of heritabilities were 0.29 (0.32) and 0.40 (0.39), respectively. In addition, substantial evidence of absence of genetic background was detected for arterial oxygen saturation at birth.

Key Words: Bayes Factor, Neonate Metabolism, Survival, Vitality


Introduction

Preweanling mortality represents a significant economic loss in pig production, although selection of this trait has not been considered because of its low heritability (Knol et al., 2002). Therefore, indirect genetic improvement through related traits such as birth weight or the within-litter homogeneity in birth weight has been proposed (Knol et al., 2002).

Early physiological or behavioral variables may also represent an alternative approach by predicting the survival ability of the piglets. After birth, newborn pigs must adapt to the new environment quickly because a delay could create a great disadvantage in terms of access to resources (Fraser and Thompson, 1991). In addition, Herpin et al. (1996, 1998) reported that the degree of asphyxiation suffered during delivery had a significant influence on piglet adaptation and posterior viability. This period of hypoxia also initiates drastic changes in various physiological variables that, in turn can influence piglet survivability (Herpin et al., 1996, 1998; Tuchscherer et al., 2000). Several authors have related preweaning piglet mortality with early metabolic variables such as body temperature or arterial oxygen saturation (Herpin and Le Dividich, 1998, Herpin et al., 2001; Casellas et al., 2004a), or initial suckling behavior (Herpin et al., 1996; Tuchscherer et al., 2000). Moreover, heart rate has been also included in the vitality score (Randall, 1971).

However, knowledge about the additive genetic variation of these traits is practically nonexistent. One important question is whether there is a genetic background in the observed phenotypic variation. Recently, a Bayes factor (BF) procedure for testing the genetic background of quantitative traits was developed (García-Cortés et al., 2001; Varona et al., 2001). In this

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context, this article is an attempt to examine the additive genetic background of several physiological and vitality variables closely related to the first minutes of life after birth.

Materials and Methods

Animals

One hundred eight litters from Iberian × Meishan F1 gilts mated with eight Iberian × Meishan F1 boars were recorded in Nova Genètica farm of Solsona (Lleida, Spain) between November 2001 and May 2002. These F1 individuals came from three unrelated Iberian boars and 18 Meishan sows, and they provided 1,039 piglets born alive, 34 stillbirths, and 27 mummified fetuses. Matings were designed to avoid possible inbreeding. These data were obtained in the scope of a F2 design for detection of QTL for reproductive traits (Grant AGL2000-1229-C03). Primiparous sows were housed in climate-controlled rooms (24°C) during farrowing and lactation, and penned in standard farrowing crates with heating plates for piglets (38°C). Feeding of sows was restricted during the gestation period (9.2 MJ of NE, 13.5% CP, and 0.48% lysine), and ad libitum during lactation (9.8 MJ of NE, 17.5% CP, and 0.82% lysine). During parturition, veterinary interventions were kept minimal; 20 I.U. of oxytocin was administered by i.m. injection when the interval between births exceeded 30 min. Furthermore, sows that did not deliver before d 113 of gestation received 175 g of cloprostenol to elicit farrowing (intravulvar injection).

Animal procedures followed ethical norms of IRTA.

Physiological and Vitality Trait Recording

Birth weight, time, and presentation (anterior or posterior) were recorded for each piglet, and the vitality score was determined following in part the procedures described by Randall (1971). Three variables were scored by subjective evaluation (see Casellas et al., 2004b): time to the onset of respiration, muscle tone, and attempts to stand. The sum of these three values defined vitality score. Piglets were monitored for heart rate (HRL), arterial oxygen saturation (OS1), and rectal temperature at birth (RT1) and 60 min later (HR2, OS2, RT2), using a Vet/Ox 4404 monitor pulsoxymeter (Heska Corp., Fort Collins, CO). Given that all the piglets had black skin, heart rate and arterial oxygen saturation measurements were taken by tongue, using an Exotic Reflectance Sensor (Heska Corp.). The time interval between birth and the measurement of OS was also recorded, which was used to adjust arterial oxygen saturation (OS) to 90 s after birth (OS1), applying the GLM procedure of SAS (SAS Inst., Inc., Cary, NC) because Herpin et al. (1998) observed a large increase in OS during the first seconds of life. All piglets were ear tagged for identification purposes, weighed, and placed near the posterior side of their mother. This allowed for recording the time that elapsed between birth and first teat contact, as well as the first suckle (TS).

Bayes Factor Analysis

For each variable the significant effects previously analyzed in Casellas et al. (2004b) were considered (Table 1), with the exception of birth weight (BWT), which was analyzed following in part the fixed model proposed by Roehe (1999), with sex and litter size as systematic effects, and a random source of variation characterized by the litter. We estimated the BF between the models with and without genetic effects following Garcia-Cortés et al. (2001) and Varona et al. (2001). The first model (Model 1) includes the additive genetic effects:

\[ \mathbf{y} = \mathbf{X}\beta + \mathbf{Z}_1\mathbf{u} + \mathbf{Z}_2\mathbf{p} + \mathbf{e} \]

where \( \mathbf{y} \) contains phenotypic records; \( \mathbf{X}, \mathbf{Z}_1, \) and \( \mathbf{Z}_2 \) are the incidence matrices relating observations to systematic (\( \beta \)), additive genetic (\( \mathbf{u} \)), and random litter (\( \mathbf{p} \)) effects; and \( \mathbf{e} \) is the vector of residuals. The vectors \( \mathbf{u}, \mathbf{p}, \) and \( \mathbf{e} \) are assumed to be normally distributed.

\[ \mathbf{u} \sim N(0, \mathbf{A}\sigma_u^2) \]
\[ \mathbf{p} \sim N(0, \mathbf{I}\sigma_p^2) \]
\[ \mathbf{e} \sim N(0, \mathbf{I}\sigma_e^2) \]

where \( \sigma_u^2 \) is the additive genetic variance, \( \sigma_p^2 \) is the variance of the random litter effects, \( \sigma_e^2 \) is the residual variance, and \( \mathbf{A} \) is the numerator relationship matrix. Model 1 can be reparameterized as:

\[ \mathbf{y} = \mathbf{X}\beta + \mathbf{Z}_1\mathbf{u} + \mathbf{e}^* \]

where

\[ \mathbf{e}^* = \mathbf{Z}_2\mathbf{u} + \mathbf{e} \]

Consequently,

\[ \mathbf{e}^* \sim N(0, \mathbf{V}) \]

\[ \mathbf{V} = \mathbf{Z}_1\mathbf{A}\mathbf{Z}_1\sigma_u^2 + \mathbf{I}\sigma_e^2 = \sigma^2_1[\mathbf{Z}_1\mathbf{A}\mathbf{Z}_1\rho^2 + \mathbf{I}(1 - \rho^2)] \]

where \( \rho^2 = \sigma_u^2/\sigma_e^2 \) is the intraclass correlation, and \( \sigma^2_1 = (\sigma_u^2 + \sigma_e^2) \) is the variance of \( \mathbf{e}^* \). The joint distribution of all variables in Model 1 is:

\[ p_1(\mathbf{y}, \beta, \mathbf{p}, \sigma^2_1, \sigma^2_u, \sigma^2_p, \rho^2) = p_1(\mathbf{y}|\beta, \mathbf{p}, \sigma^2_1, \rho^2)p_1(\beta)p_1(\mathbf{p}|\sigma^2_p)p_1(\sigma^2_1)p_1(\rho^2)p_1(\sigma^2_u) \]

where
where we can assume that prior distributions \( p_2(\beta), p_2(p \mid \sigma_2^2), p_2(\sigma_2^2), \) and \( p_2(\sigma_1^2) \) are identical to the prior distributions of the previous model. And the likelihood of the model is

\[
p_2(y \mid p, \beta, \sigma_1^2, \sigma_2^2) \sim \text{N}(X\beta + Z_2p, V)
\]

According to Varona et al. (2001), only the analysis with the complex model (Model 1) is required. Following García-Cortés et al. (2001) and Varona et al. (2001):

\[
\text{BF}_{12} = \frac{p_1(\rho^2 = 0)}{p_1(\rho^2 = 0 \mid y)} = \frac{1}{p_1(\rho^2 = 0 \mid y)}
\]

because \( p_1(\rho^2 = 0) = 1 \) or simultaneously:

\[
\text{BF}_{21} = \frac{p_1(\rho^2 = 0 \mid y)}{p_1(\rho^2 = 0)} = p_1(\rho^2 = 0 \mid y).
\]

A \( \text{BF}_{12} (\text{BF}_{21}) > 1 \) (<1) indicates that the model with additive variance components (heritable) is more suitable. On the contrary, a \( \text{BF}_{12} (\text{BF}_{21}) < 1 (> 1) \) indicates that the non heritable model is more probable. From now on, we will refer to \( \text{BF}_{12} \) as BF.

According to Jeffreys (1984), the BF can be classified according to the levels of evidence:

- \( \text{BF} < 1 \) Null hypothesis supported
- \( 1 < \text{BF} < 3.16 \) Not worth more than a bare mention
- \( 3.16 < \text{BF} < 10 \) Substantial evidence
- \( 10 < \text{BF} < 31.62 \) Strong evidence
- \( 31.62 < \text{BF} < 100 \) Very strong evidence
- \( \text{BF} > 100 \) Decisive

Table 1. Number of individuals studied, means (X), and standard errors of the mean (SEM) for the analyzed variables, as well as the fixed and significant random effects included in mixed models

<table>
<thead>
<tr>
<th>Trait</th>
<th>No.</th>
<th>X</th>
<th>SEM</th>
<th>DB</th>
<th>BWT</th>
<th>VS</th>
<th>LE</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT1, °C</td>
<td>415</td>
<td>38.8</td>
<td>0.03</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
</tr>
<tr>
<td>RT2, °C</td>
<td>395</td>
<td>37.2</td>
<td>0.1</td>
<td>NS</td>
<td>***</td>
<td>***</td>
<td>***</td>
</tr>
<tr>
<td>HR1, bpm</td>
<td>371</td>
<td>147.4</td>
<td>2.5</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>***</td>
</tr>
<tr>
<td>HR2, bpm</td>
<td>288</td>
<td>221.9</td>
<td>2.8</td>
<td>NS</td>
<td>NS</td>
<td>**</td>
<td>NS</td>
</tr>
<tr>
<td>OS1, %</td>
<td>349</td>
<td>76.2</td>
<td>1.0</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>*</td>
</tr>
<tr>
<td>OS2, %</td>
<td>309</td>
<td>95.0</td>
<td>0.3</td>
<td>NS</td>
<td>*</td>
<td>NS</td>
<td>**</td>
</tr>
<tr>
<td>TT, min</td>
<td>441</td>
<td>23.2</td>
<td>1.3</td>
<td>NS</td>
<td>*</td>
<td>**</td>
<td>***</td>
</tr>
<tr>
<td>TS, min</td>
<td>418</td>
<td>49.0</td>
<td>1.6</td>
<td>***</td>
<td>*</td>
<td>***</td>
<td>***</td>
</tr>
</tbody>
</table>

\* \( P < 0.05. \)
\** \( P < 0.01. \)
\*** \( P < 0.001. \)

\( ^a \) RT1 = rectal temperature at birth; RT2 = rectal temperature 60 min after birth; HR1 = heart rate at birth (bpm = beats per minute); HR2 = heart rate 60 min after birth; OS1 = arterial oxygen saturation at birth; OS2 = arterial oxygen saturation 60 min after birth; TT = time to reach the teats; TS = time to the first suckle; and NP = number of piglets.

\( ^b \) DB = covariate effect of the interval between the start of parturition and birth; BWT = covariate effect of birth weight; VS = categorical fixed effect of vitality score; and LE = random litter effect.

\( ^c \) Not significant.
Bayes factor for newborn pig vitality traits

Table 2. Mode, mean, and 2.5 and 97.5 percentiles for posterior distributions of heritability estimates and average Bayes factor value for the analyzed variables

<table>
<thead>
<tr>
<th>Trait</th>
<th>Bayes factor</th>
<th>Mode</th>
<th>Mean</th>
<th>2.5</th>
<th>97.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>BWT, kg</td>
<td>2.27</td>
<td>0.13</td>
<td>0.22</td>
<td>0.01</td>
<td>0.68</td>
</tr>
<tr>
<td>RT1, °C</td>
<td>13.82</td>
<td>0.40</td>
<td>0.39</td>
<td>0.10</td>
<td>0.55</td>
</tr>
<tr>
<td>RT2, °C</td>
<td>0.42</td>
<td>0.11</td>
<td>0.23</td>
<td>0.02</td>
<td>0.58</td>
</tr>
<tr>
<td>HR1, bpm</td>
<td>1.22</td>
<td>0.21</td>
<td>0.38</td>
<td>0.04</td>
<td>0.71</td>
</tr>
<tr>
<td>HR2, bpm</td>
<td>48.90</td>
<td>0.29</td>
<td>0.32</td>
<td>0.07</td>
<td>0.62</td>
</tr>
<tr>
<td>OS1, %</td>
<td>0.29</td>
<td>0.11</td>
<td>0.22</td>
<td>0.02</td>
<td>0.55</td>
</tr>
<tr>
<td>OS2, %</td>
<td>0.42</td>
<td>0.12</td>
<td>0.19</td>
<td>0.02</td>
<td>0.46</td>
</tr>
<tr>
<td>TT, min</td>
<td>1.03</td>
<td>0.17</td>
<td>0.38</td>
<td>0.04</td>
<td>0.79</td>
</tr>
<tr>
<td>TS, min</td>
<td>0.56</td>
<td>0.10</td>
<td>0.18</td>
<td>0.01</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*aBWT = birth weight; RT1 = rectal temperature at birth; RT2 = rectal temperature 60 min after birth; HR1 = heart rate at birth (bpm = beats per minute); HR2 = heart rate 60 min after birth; OS1 = arterial oxygen saturation at birth; OS2 = arterial oxygen saturation 60 min after birth; TT = time to reach the teats; and TS = time to the first suckle.*

Sampling from the conditional distribution of $\rho^2$ was performed using a Gibbs sampler (Gelfand and Smith, 1990), with a Metropolis-Hastings step (Hastings, 1970). To calculate the posterior distribution of the heritability ($h^2$), the following formula was used every iteration:

$$h^2 = \frac{\rho^2 \sigma_t^2}{\sigma_p^2 + \sigma_t^2}$$

A total of 12,500 iterations were performed, and 10,000 iterations were used after discarding the first 2,500. All correlated samples were used to calculate the posterior distributions using the ergodic property of the chain (Gilks et al., 1996). Convergence was checked using the algorithm of Raftery and Lewis (1996).

Results

A variable number of records was analyzed for each variable, ranging from 288 (HR2) and 869 (BWT) newborn pigs. The average BWT was 1.14 kg, with a SD of 0.24 kg. Sex and the number of piglets and random litter effects were included in the assumed model for BWT. In addition, Table 1 shows average values, standard errors, and the assumed model for each vitality and physiological variable. The assumed model for each variable was determined by the results obtained by Casellas et al. (2004b) with the same data set. A detailed discussion of these results was presented in that study.

Five variables reached average BF larger than 1: heart rate 60 min after birth (48.90), rectal temperature at birth (13.82), birth weight (2.27), heart rate at birth (1.22), and the interval between birth and first teat contact (1.03). Following the classification of the BF by Jeffreys (1984), there was very strong evidence for the presence of genetic background of HR2, and strong evidence in RT1. The posterior modes (means in parentheses) of their heritability were 0.13 (0.22), 0.21 (0.38), 0.29 (0.32), 0.40 (0.39), and 0.17 (0.38) for BWT, heart rate at birth and 60 min later, RT1, and time between birth and first teat contact, respectively (Table 2). The rest of the variables attained BF <1, varying between 0.56 for elapsed time between birth and first suckle and 0.29 for OS1, all with posterior modes for heritability smaller than 0.13 (Table 2). The distributions of the heritability estimates were clearly asymmetrical, revealing great differences between the posterior mode and the posterior mean for the heritability, with the exception of the HR2 and RT1 variables.

Discussion

The BF is the basic tool for comparing models in the Bayesian framework (Kass and Raftery, 1995). In contrast with likelihood-based approaches for testing significance, it does not require one to define any null or alternative hypothesis model, providing a probability of both candidate models and avoiding the calculation of levels of significance. However, some authors (Jeffreys, 1984; Kass and Raftery, 1995) have defined levels of evidence in favor of any of the alternative models from BF, allowing for its use as a test between the null and alternative hypotheses. Another important property of the BF is that it does not need to invoke asymptotic assumptions, and it provides exact results, even with small samples. Moreover, whereas the likelihood-based approaches make use of the likelihood on the maximum likelihood estimates in both models, the BF includes the information provided by data after integrating out along the parametric space, using all available information on the data, not only conditioned by the maximum likelihood estimates.

The application of the BF for testing the genetic background described by García-Cortés et al. (2001) requires the reparameterization of the model in terms of phenotypic variance and intraclass correlation because the BF can only be computed between nested models that differ in a bounded variable using this approach. In this
case, the bounded variable is the intraclass correlation, and the comparison between models is calculated between a model with zero intraclass correlation (nonheritable) against a model with intraclass correlation between 0 and 1 (heritable).

The main disadvantage of the application of the BF is its strong dependence on the assumed prior distributions. However, in this case, the prior distributions for all parameters, with the only exception of the intraclass correlation, are cancelled because they are assumed to be the same in both candidate models (Varona et al., 2001). In addition, the final formula only includes the marginal prior and posterior distribution for the intraclass correlation ($\rho^2$), and, as a consequence, the BF results are robust for modifications of this prior distribution. When the prior distribution of $\rho^2$ is modified, the posterior distribution changes in the same direction and, as a consequence, the BF remains stable.

Physiological variables and initial feeding behavior may play an important role during adaptation to the external environment and subsequent survivability in newborn pigs (Fraser and Thompson, 1991; Herpin et al., 1998; Casellas et al., 2004a). Variables like heart rate, rectal temperature, or OS characterize the metabolic situation of piglets after birth, the degree of asphyxiation suffered during delivery, and the ability to recover physiological levels (Herpin et al., 1996, 1998; Casellas et al., 2004b). Notwithstanding, our knowledge of these variables is limited, especially concerning their genetic component. To our knowledge, this is the first study that analyzed the genetic background of heart rate, arterial oxygen saturation, or rectal temperature in neonates. Thus, our results open a new research field related to neonate physiology in general and the genetic aspects of newborn pig metabolism in particular.

Rectal temperature at birth or during the first day of life is historically the best-studied variable among those treated in this investigation (see Herpin and Le Dividich, 1998), perhaps with the exception of birth weight, but our knowledge about the possible heritability of body temperature is restricted to adult individuals. In this context, the evidence of heritable variation for body temperature has been the object of an important discussion in recent decades. Silcock and Parsons (1973) observed an additive genetic component for body temperature in mice, but subsequent studies were unable to find significantheritabilities (Lacy and Lynch, 1978; Lynch et al., 1988). Recently, a response of rectal temperature to selection was demonstrated in laboratory rats (Gordon and Rezvani, 2001) but, on the other hand, the heritability estimates for rectal temperature in leaf-eared mice (Phyllotis darwini) did not reach the statistical threshold, although other variables closely related to animal thermoregulation, such as thermal conductance, showed significantheritabilities (Nespolo et al., 2003). Unfortunately, our results did not allow us to clarify this controversy. Although rectal temperature at birth showed a large BF (13.82), with a moderate to high posterior mode for the heritability (0.40), rectal temperature 60 min after birth reached a lower posterior mode (0.11) and BF (0.42). This implies a great change in heritability over a short temporal space, although Casellas et al. (2004b) found a significantphenotypic correlation between both measures in the same data set. This results are perhaps comparable with the ones obtained in leaf-eared mice, where diurnal temperature was clearly nonheritable, whereas the genetic component of nocturnal temperature was almost significant ($P < 0.10$; Nespolo et al., 2003).

Moderateheritabilities were estimated for heart rate variables, with a BF >1, especially for heart rate 60 min after birth (48.90). In this context, an analysis carried out in adult humans also described a moderate heritability for heart rate (Singh et al., 1999), and Barry (1992) reported a high heritability for the maximum heart rate in adult human athletes (0.72). These results indicate the presence of a genetic component for these variables, compatible with the description of a QTL associated with heart rate in an F2 experiment involving CBA/CaJ and BALB/cJ mice strains (Sugiyama et al., 2002). However, both heart rate variables we measured have to be considered as different traits because Casellas et al. (2004b) did not find a significant genetic correlation.

Bayes factors for arterial oxygen saturations did not reach values greater than 1, so there is no evidence for the existence of an additive genetic component for these variables in neonates. It is also remarkable that the BF for OS1 was 0.29, or 3.45 in the opposite sense; thus, there is substantial evidence in favor of the model without genetic determinism. Notwithstanding, a major gene for OS has been described in Tibetan highlanders, obtaining a heritability of 0.41 ± 0.14 (Beall et al., 1994). Unfortunately, the effect of this major gene has never been evaluated in neonates or in swine. Similar values were obtained for the interval between birth and the first teats contact, as well as the interval between birth and the first colostrum intake. Only the interval between birth and the first teat contact reached a BF >1, but very close to 1. This result implies that the time spent searching for teats may be influenced by an additive component, but further studies are necessary to confirm this hypothesis.

Birth weight reached a moderate heritability (0.13) with a BF of 2.27. It did not provide us with substantial evidence regarding the genetic background of this trait; the posterior mode for heritability was similar to the value reported by Kerr and Cameron (1995), and slightly greater than the one described by Rohe (1999). However, the results of this study are limited by the structure of the data set, given that the experiment was designed for QTL detection in reproductive traits. The F2 design is not an appropriate design for detecting genetic background because in the F2 generation, genetic components related to dominance and linkage disequilibrium between loci usually appear. The additive genetic variance that we were able to detect in this
study was composed of half the genetic variance of the parental populations plus the segregation variance. This latter variance is the one that we shall be able to exploit in QTL analysis to detect specific loci related to the differences in these behavioral and physiological variables. Unfortunately, data from F₀ and F₁ generations were not available to allow for the discrimination between additive variances from the parental populations and the segregation variance (Birchmeier et al., 2002). In addition, it is expected that half the heterosis is still present in this F₂ generation and, in our opinion, its effect will be absorbed into the systematic effects.

**Implications**

Strong evidence of genetic determinism of rectal temperature at birth and heart rate 60 min after birth was found in F₂ Iberian × Meishan newborn pigs. The genetic determinism of these traits suggests the possibility of using indirect selection to improve the surviv-ability of piglets during the first days of life. The measurement of these traits is difficult, and as a consequence, their use in current breeding schemes in not feasible. Nevertheless, the genetic determinism of some of these traits involves the possibility of quantitative trait loci detection, which could be used in marker-assisted selection or introgression.

**Literature Cited**


