Meta-analysis of the halothane gene effect on seven parameters of pig meat quality

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Introduction

What is meta-analysis?
A set of statistical procedures designed to accumulate experimental, quasi-experimental, and correlational results across independent studies that address a set of related research questions.
(Glass GV Primary, secondary, and meta-analysis of research. Educ Res 1976;5:3-8).

Objectives:
- Increase the power of statistical tests.
- Provide a more precise estimate of the overall treatment effects.
- Avoid doubt in cases of discordant results.

Difficulty: Synthesis is more difficult because of the heterogeneity between studies.
Objective

Using meta-analysis to study the effect of halothane gene on pHu, pH45, colour attributes (L*,a*,b*), DL and lean%.

Why these seven attributes?

- Seven of the most relevant attributes of the technological pig meat quality, which are influenced by the halothane gene.
- The position of the heterozygous animals "Nn" is subject to controversy.
- Existing inconsistencies in the literature about the significant effect of the halothane gene on some attributes (e.g. pHu).
Selection of articles and the conception of the database

The selection criteria of publications:

- Published between 1990 and 2007.
- Comparison of the 3 genotypes: NN, Nn and nn.
- Sample sizes for each treatment.
- Standard deviation (SD) or Standard error of the mean (SEM for models).
- Age and slaughter weight.
- Fasting duration.
- Breed & sex.
- Type of muscle.

30 selected studies were entered into the database (www.qpc6.dk)

23 references, the most homogeneous (≈ 3530 animals)
Statistical analyses

The method of «Effect-size» (Whitehead and al., 2002)

« Effect-size »: measurement of the size of the treatment effect $\theta$ for each trial.

$$\hat{\theta} = \bar{Y}_{NN} - \bar{Y}_{nn}$$

Principle of the statistical analysis

- **Homogeneous data**: Common effect to all the trials
  $$\hat{\theta}_i = \theta + \varepsilon_i$$
  Error terms explaining the variability between-studies.

- **Heterogeneous data**: A random effects meta-analysis model to estimate the common effect
  $$\hat{\theta}_i = \theta + \nu_i + \varepsilon_i$$
  Random effect of «Study» factor $\sim N(0, \tau^2)$

- **Regression**: Consideration of covariates that could explain the «between-study» variance.
Statistical analyses

The regression method (St Pierre, 2001)

Y (pHu,pH45,L*) = μ + Genotype (fixed factor) + covariates (breed, sex, slaughter weight) + Study (random factor) + ε

- Only significant factors are retained in the models (P < 0.05);
- The interactions were not included in the models (few data);
- Weighting by the inverse of the variance of each study (St Pierre, 2001).
Results: Halothane gene effect on pHu

- 2 studies among the 11 combined studies concluded that pHu (nn) is higher than pHu (NN).
- 5 studies among the 11 combined studies found a non-significant effect of the halothane gene on the pHu.

Effect-size = pHu(NN) - pHu(nn)
### Results: Halothane gene effect on pHu

<table>
<thead>
<tr>
<th>The « Effect-size » method</th>
<th>The RE regression method</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant differences between Nn and nn.</td>
<td>Comparison of genotype lsmeans: no significant differences between Nn and nn.</td>
</tr>
<tr>
<td>Reduction of the proportion of the total study variance that was due to the «between-study» variation (≈60%).</td>
<td>The «between-study» variance represents a very important proportion of the total variance (≈95%).</td>
</tr>
<tr>
<td>Heterogeneity was partially explained by the effect of «Slaughter weight » in the comparison between the NN and nn genotypes.</td>
<td>All the tested covariates were not significant.</td>
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</table>
Results: Halothane gene effect on pH$_{45}$

- Significant effect of the halothane gene on the pH$_{45}$ attribute in all the selected studies.
- A very important heterogeneity between the 11 combined studies.

Regression

Sex explain 69% of the «between-study» variance.
Results: Halothane gene effect on L*, a* and b*

The « Effect-size » method

Significant effect of Hal gene on genotype differences, compared two by two for the 3 attributes, except on NN-Nn and Nn-nn comparisons of a*.

Breed explains 79% of the between-study variance of b* attribute between Nn-nn.

Heterogeneity between the combined effect-sizes of L* and a* was not significant (lower than 25%).

The RE regression method

Significant effect of halothane genotype on colour attributes, except on a*.

Significant effect of breed on the three colour attributes (L*, a* and b*).

The between-study variance was higher than 95% for the 3 attributes.
Results: Halothane gene effect on DL

Comparison of DL between the 3 halothane genotypes

- $\theta_{NN-Nn} = -0.34 \pm 0.37$
- $\theta_{Nn-nn} = -1.04 \pm 0.18$

- NN vs nn et Nn vs nn: Significant differences + between-study variance explained by Breed.
- NN vs Nn: Differences between genotypes are not significant???

Bayesian estimation of this difference was significant.
Results: Halothane gene effect on lean%

Comparison of lean% between NN and Nn halothane genotypes

- $\theta_{NN-Nn} = -0.975 \pm 0.139$

The « Effect-size » method

Standardized effect-size are homogeneous (Only 29% of the total variability is due to the between-study variance)

The RE regression method

High heterogeneity between the combined data in the RE regression method ($\approx 98\%$).
Conclusion and perspectives

 Persistent heterogeneity in all the selected models, especially in the RE regression method.

 Comparison between the two meta-analytic methods:

 - The «Effect-size» method allows to reduce the «between-study» variance.
 - The standardized effect-size allows to combine data of attributes differentially measured (DL, lean);
 - The «Effect-size» method shows the significant effect of slaughter weight on the differences of pHu between homogeneous genotypes NN and nn.

 Except that…

 This method allows to compare only two levels of the studied factor …

 Perspectives:

 - Increasing the number of included studies.
 - Conducting meta-analyses on raw data (to study the interactions).
 - Conduct meta-analyses on another factors affecting pig meat quality (lairage, transport, fasting,…)


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