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Detection of Major Genes for Cortisol in Pigs Divergently Selected for Stress Responses

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BACKGROUND and OBJECTIVES

Background:

• CORTISOL is the product of the hypothalamo-pituitary-adrenal (HPA) axis;
- •affects fat, carbohydrate and protein metabolism and hence meat quality, weight gain and growth rate.
- •indicator of stress and behavior in animals and other mammals.
- •Stress in animals has high economic, health and welfare implications.
- •Stress is difficult to record and to select against - cortisol is the alternative measurement of stress, recordable and heritable.

•No study has so far investigated heritabilities and mode of inheritance of cortisol (polygenic or a mixture of polygenes and a major gene?) in pigs.

•The knowledge of genetic properties of cortisol is essential to develop breeding programs or QTL experiments for selection against stress in pigs.

Main objectives:

• Estimate genetic and phenotypic parameters of cortisol using records from controlled cortisol experiments in ETHZ Zürich.

•Apply Bayesian segregation analysis (BSA) methods using Monte carlo Markov Chain (MCMC) techniques.

MATERIALS

•CORTISOL EXPERIMENT in ETH started in 1995's to study differences of the HPA axis in two lines of Swiss Landrace pigs with striking differences in response to various stressors such as Corticotropic Releasing Factor or Vasopressin administration.

• Animals were housed individually in the metabolic cages for 48 h.

•Urine samples taken at the second day (after acclimatization) for 24 h.

•Cortisol was measured using Cortisol kit (catalog Nr. TKCO1 DPC, USA).

•Measured also urinary creatinine levels to adjust for water intake .

• Total of 299 informative records on urinary cortisol levels and 489 pedigrees (small full-sib groups nested within half-sib sire families).

• Polygenic heritability (h^2) for cortisol from REML analysis was high (0.40 to 0.70) – motivation for major gene analysis.

METHODS

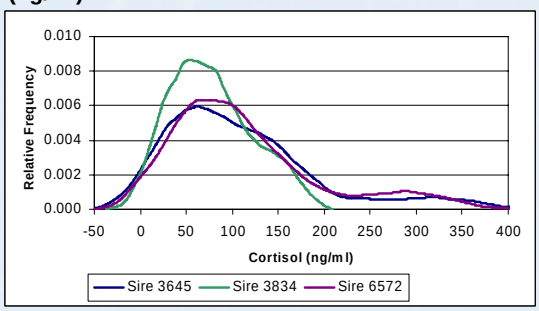
•Segregation Analysis was based on the method of *Kadarmideen and Janss (2005)* which shows detection of major gene for binary traits using MCMC methods and estimation of Mendelian transmission probabilities to distinguish environmental and genetic transmission.

• Additionally we used Bartlett's test to show variance heterogeneity between families in exploratory analysis, prior to full BSA.

•These routines are available in a software called ***iBay*** (*Janss* 2006).

RESULTS

Figure 1. Variance of heterogeneity among 3 largest sire families and bi-modal distribution of progeny groups of two sire families showing evidence for major gene for cortisol levels (ng/ml)[1]



[1]Bartlett's test for homogeneity of variance was strongly rejected (P<0.0001)

Table 1. Posterior mean and SD of parameters of segregation analysis of urinary cortisol (ng/ml), with left and right bounds of Highest Posterior Density Regions ($HPDR_{95}$)

Parameter of BSA model	Post. mean	Post. SD.	$HPDR_{95}$ -left	$HPDR_{95}$-right
Error variance	1122	253.0	628.4	1622
Polygenic variance	1257	379.5	551.1	2013
Major gene variance	2045	961.9	421.6	3992
Freq. recessive allele	0.256	0.067	0.131	0.388
Additive effect (a)	85.30	7.204	70.86	99.17
Dominant effect (d)	-96.90	12.85	-123.2	-72.87
a-|d|	-11.60	15.10	-42.78	16.72

Table 2. Confirmation of Mendelian segregation by estimation of transmission probabilities[1]

Transmission prob.	$HPDR_{95}$-left	$HPDR_{95}$-right
Pr(A|AA)	0.703	0.978
Pr(A|AB)	0.436	0.726
Pr(A|BB)	0	0.600

[1] Results indicate that these probabilities are close to those expected by Mendelian segregation

DISCUSSION

Barlett's Test

• since sire groups are well distributed over environmental factors then heterogeneity is of genetic origin - most plausible explanation is the segregation of a large genetic factor

• Data shows two groups of "normal" and "high" variance - consistent with a recessive cortisol-increasing major gene

Bayesian segregation analysis

•Polygenic and major gene h^2 is 0.29 and 0.44, respectively.

• Evidence of major gene with a recessive allele that increases cortisol. It has a frequency of 0.26 and an additive effect of 86 ng/ml (major gene variance was highly significant).

Estimation of Mendelian Transmission Probabilities

• Mendelian segregation was confirmed by estimation of transmission prob. by setting variances, allele effect and frequency at the fitted BSA model.

REFERENCE

Kadarmideen & Janss (2005). *Genetics* 171:1195-1206
Janss (2006). iBay Reference. http://www.lucjanss.com/