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JUVENILE IGF-I RESPONSE IN INRA RFI SELECTION LINES PARTLY REFLECTS CHANGES IN POST-WEANING ATTRIBUTES

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SUMMARY

Performance data were recorded at INRA in two lines divergently selected for residual feed intake (RFI) for eight generations (G0 to G7). A subsample of piglets were bled shortly after weaning to establish concentrations of juvenile IGF-I. The line effect was clearly detected for juvenile IGF-I, confirming previous studies which found that juvenile IGF-I is an indirect early predictor of efficiency. The line difference in juvenile IGF-I was partly explained by differences between the RFI lines in their growth immediately after weaning, but remained significant after post-weaning growth was accounted for. Selection for efficiency has implications for post-weaning management to limit feed deprivation and growth delays during the post-weaning period.

INTRODUCTION

Selection for feed efficiency is important, but phenotyping is costly. Previous studies have demonstrated that juvenile IGF-I recorded shortly after weaning is genetically correlated with feed intake, efficiency and fatness traits in pigs (Bunter *et al.* 2005), as well as piglet birth weight (Hermesch *et al*. 2001), and that selection for lower RFI is accompanied by reduced juvenile IGF-I (Iowa State lines) (Bunter *et al.* 2010). Therefore, juvenile IGF-I is an early predictor of efficiency during growing-finishing growth stages. Postnatal IGF-I is related to growth and development (Le Roith *et al.* 2001) but literature on its role in the early post-weaning stage is scarce. In this study, an independent validation of the results reported from the Iowa State lines was investigated, and the impact of post-weaning growth for the measured levels of juvenile IGF-I were explored, using the INRA lines - divergently selected for RFI over 8 generations.

MATERIALS AND METHODS

Animals and records. Performance data were recorded at INRA in two lines divergently selected for residual feed intake (RFI) for eight generations (G0 to G7). A total of 419 pigs from lines divergently selected for low (LRFI) or high (HRFI) residual feed intake were tested in 8 batches. Male and female piglets born in generation G7 (after 7 generations of selection: 117 LRFI and 123 HRFI) and entire males from generation G8 (106 LRFI and 73 HRFI) were recorded. The difference between lines for RFI in G8 was 137 g/day ($P < 0.001$). Details of the selection of the RFI lines have been given in Gilbert *et al.* (2017a). In a given batch, pigs were born the same week, weaned on the same day at 28.3 ± 1.7 days and followed exactly the same protocol for performance testing. At weaning, pigs were penned per line in groups of 24. During the growing-finishing period (10 weeks of age (START) until slaughter weight of 115 kg), 12 pigs of the same line and sex were allotted per pen equipped with a single-place electronic feeder to record feed intake (ACEMA 64).

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Pigs were weighed at birth (BIRTH_WT), at weaning (WEAN_WT), and the week after

weaning at the time of blood sampling for IGF-I measurements (35.3 ± 1.7 days) (IGF-I_WT). Average daily gain (ADG) traits between time points were calculated. The summary statistics of the traits are given in Table 1, together with the trait abbreviations.

Table 1. Summary statistics for weight (WT), growth (ADG) and log IGF-I traits after outlier elimination

Traits	unit	N	Mean	SD	Min	Max
BIRTH_WT	kg	416	1.50	0.31	0.50	2.45
WEAN_WT	kg	417	9.0	1.5	3.6	12.9
IGF-I_WT	kg	415	10.0	1.6	5.1	14.8
ADG_BIRTH_WEAN	g/day	416	265	48	99	397
ADG_BIRTH_IGF-I	g/day	415	242	40	121	365
ADG_BIRTH_START	g/day	412	353	57	194	507
ADG_WEAN_IGF-I	g/day	415	149	102	-186	570
ADG_WEAN_START	g/day	412	416	83	181	634
lIGF-I (RIA)	log(ng/mL)	178	3.99	0.39	3.00	4.98
lIGF-Ij (ELISA)	log(ng/mL)	417	4.50	0.49	3.18	5.65

IGF-I data. Animals were bled post-weaning to measure concentrations of juvenile IGF-I using radioimmunoassay (RIA) (IGF_I) or ELISA (IGF-Ij) methodology. Blood samples were obtained from the jugular using a vacutainer and deposited on the Primegro IGF-I bloodspot cards (for IGF-Ij). For 178 G7 pigs, 5 mL of blood was also collected into heparin tubes, centrifuged and plasma was aliquoted and stored at -20°C for RIA measurements. Samples extracted from Primegro bloodspot cards were assayed using an IGF-I Quantikine ELISA Kit (R&D systems). As per manufacturer's instruction, the raw values were standardized to NIBSC/WHO 02/254 values by applying a multiplication factor of 1.54. For the RIA methodology, concentrations of plasma IGF-I were determined using a double antibody RIA after an acid-ethanol extraction (Louveau and Bonneau, 1996) with recombinant human radiolabelled IGF-I (PerkinElmer).

Statistical analyses. The IGF-I and IGF-Ij measurements were log-transformed (lIGF-I and lIGF-Ij, respectively) for analysis. Outlier values for raw and log data exceeded 1.5 times the inter-quartile range based on the log transformed distribution and excluded from the analyses (2 pigs excluded). The relationships between IGF-Ij measurements, divergent selection for RFI and early growth were evaluated using a series of model comparisons. The simplest models accounted for the batch effect (production traits, Model M0) or a combination of batch and assay (BA, accounting for sampling date and generation) (lIGF-Ij, M1), along with sex within generation and line effects. For all samples but 11, effects of batch, sampling date and assay were confounded. Age at sampling was not significant for IGF-Ij traits and not included. A second level of models applied to lIGF-Ij fitted additional linear covariates across lines: early body weights until blood sampling (M2 to M4) or early ADG traits (M5 to M7, Table 2).

RESULTS AND DISCUSSION

Correlations between assay procedures for IGF-I. The correlation between the ELISA values, corrected for batch of birth and assay effects, and RIA measurements of IGF-I, corrected for batch, was 0.72. Thus, only results on IGF-Ij will be reported on the following to maximise the number of available measurements.

Line effect on IHG-Ij and early growth. The line effect was significant for weaning body weight (9.2 kg in LRFI vs 8.7 kg in HRFI, $P<0.001$), ADG from birth to weaning (270 vs 260 g/d, $P=0.04$) and ADG from weaning to blood sampling (120 vs 177 g/d, $P<0.001$) (Table 2). Piglets

from both lines were born with similar birth weights, but LRFI piglets were 0.5 kg heavier at weaning. This is consistent with differences between these lines reported by Gilbert et al. (2017a). Due to reduced growth in the LRFI line immediately after weaning the line difference in body weight was no longer significant at one week post-weaning. Subsequently, overall growth until the end of the post-weaning period was similar in the two lines. In a study on the G9 pigs of the same selection lines, a larger line difference (-66 g/d) in ADG the week after weaning was observed in piglets having no creep feeding before weaning. This was accompanied by a 25% reduction in feed intake in the LRFI piglets (Gilbert et al. 2017b).

A very significant difference in IGF-Ij levels was found between the lines, regardless of adjustments for growth or weight measured at different time periods, with lower (untransformed) values in the LRFI line compared to the HRFI line (-35.4 ng/mL, $P < 0.001$). A larger line difference in IGF-Ij (47 ng/mL) measured in G5 of the Iowa State lines was reported by Bunter *et al.* (2010). This study confirms the association between selection for low RFI and reduced IGF-Ij.

Table 2. Model R^2 and the significance of the line effect (P(line)) on weight (WT), growth (ADG) and juvenile IGF-I (lIGF-Ij) traits, including models fitting body weight or average daily gain as linear covariates for lIGF-Ij

Model*	Trait	R^2	P(line)	P(WT)	P(ADG)
M0 Y = batch + sex + line	BIRTH_WT	0.08	0.26	-	-
M0 Y = batch + sex + line	WEAN_WT	0.07	<0.001	-	-
M0 Y = batch + sex + line	IGF-I_WT	0.04	0.54	-	-
M0 Y = batch + sex + line	START_WT	0.07	0.73	-	-
M0 Y = batch + sex + line	ADG_BIRTH_WEAN	0.06	0.04	-	-
M0 Y = batch + sex + line	ADG_BIRTH_IGF-I	0.05	0.32	-	-
M0 Y = batch + sex + line	ADG_BIRTH_START	0.07	0.60	-	-
M0 Y = batch + sex + line	ADG_WEAN_IGF-I	0.22	<0.001	-	-
M0 Y = batch + sex + line	ADG_WEAN_START	0.11	0.16	-	-
M1 Y = BA + sex + line	lIGF-Ij	0.41	<0.001	-	-
M2 Y = BA + sex + line + BIRTH_WT	lIGF-Ij	0.42	<0.001	0.04	-
M3 Y = BA + sex + line + WEAN_WT	lIGF-Ij	0.42	<0.001	0.11	-
M4 Y = BA + sex + line + IGF-I_WT	lIGF-Ij	0.49	<0.001	<0.001	-
M5 Y = BA + sex + line + ADG_BIRTH_WEAN	lIGF-Ij	0.42	<0.001	-	0.22
M6 Y = BA + sex + line + ADG_BIRTH_IGF-I	lIGF-Ij	0.49	<0.001	-	<0.001
M7 Y = BA + sex + line + ADG_WEAN_IGF-I	lIGF-Ij	0.65	<0.001	-	<0.001

*BA= combination of batch of birth and assay accounting for sampling date and generation

Line effect on lIGF-Ij when early growth measurements are accounted for. Accounting for pre-weaning WT or ADG covariates in the analysis did not change the significance of line differences for lIGF-Ij or increase coefficient of determination (R^2) of the model: 0.41 (M1) vs 0.42 (M2, M3 and M5) (Table 2). There was no evidence in these data that weaning weight significantly affected post-weaning gain within or across lines, supporting results from M1 vs M3. In contrast, including body weight at blood sampling (M4) or ADG from birth to sampling (M6) increased the model R^2 to 0.49, but with limited impact on the estimated line difference for lIGF-Ij measurements. Finally, accounting for ADG_WEAN_IGF-I decreased the line difference by 49%, as showed in Figure 1. This suggests that the line difference in lIGF-Ij is partly due to line differences in weight gain after weaning. These results are consistent with the literature on the role of IGF-I as a growth factor involved in growth and protein metabolism (Le Roith *et al.* 2001) that depends on the feed intake and nutritional status of the animal (Caroll *et al.* 1998).

The LRFI piglets had a higher growth rate before weaning compared to HRFI piglets, and all were suckled only by LRFI sows, ie no cross-fostering was allowed across lines. Therefore, line

differences in piglet performance are potentially confounded with line differences in maternal effects. Weaning is a stressful event for piglets, with separation from the dam, a change of feed and mixing of litters. It generates a transient reduction of feed intake that can lead to digestive disorders. The greater difficulty of the LRFI piglets to adjust to weaning needs further examination to decipher the role of pre-weaning conditions from individual sensitivity to stress on these results. However, the absence of body weight difference between lines when growing-finishing starts also suggests a good resilience of these piglets, which return to a higher growth rate after the stress of weaning (Gilbert *et al.* 2017b).

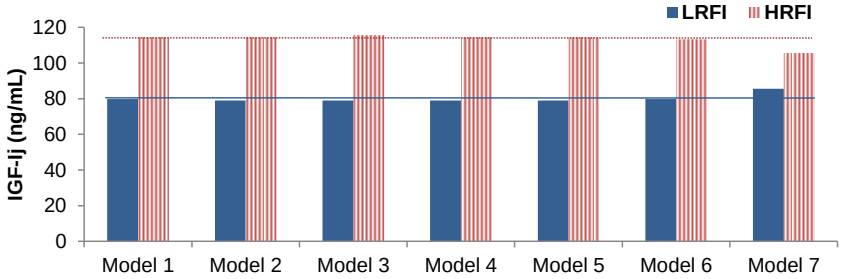

Figure 1. LSM of the line effects for back-transformed lIGF-Ij depending on the covariate included in the model – see Table 2 for details on the models.

CONCLUSION

Our study confirms that juvenile IGF-I is an indirect indicator of growing-finishing feed efficiency of the pigs. The immediate growth after weaning affected IGF-Ij, which could be considered for a better prediction of genetic merit for feed efficiency. The biological mechanisms underlying these phenomena remain to be studied for a better understanding of the relationships between post-weaning growth, juvenile IGF-I and subsequent feed efficiency. Our study confirmed that weaning creates a greater growth check in pigs selected for low RFI, not explained by variation in weaning weight, but also that LRFI pigs show good resilience to the challenge, as indicated by their overall post-weaning growth rate. Altogether, our results show that selection for reduced RFI should be combined with optimized management of the young weaned pig.

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