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A method to detect large influences of specific sex chromosomes on quantitative traits

C. Hagger and G. Stranzinger

Department of Animal Science, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zurich, Switzerland

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Summary. It is shown that the heterogametic sex of crosses between two highly inbred lines of animals provides a simple means to detect large effects of specific sex chromosomes on quantitative traits. Linear combinations of adjusted trait averages of matching types of crosses between three inbred lines of chickens were used to investigate sex chromosome effects. Evidence for a large influence of the W chromosome of one line on body weight was found. Estimated effects were between 2.4 and 7.2% of the corresponding phenotypic means. The autosomal genetic background exhibited a strong influence on the effect, thus suggesting a sizable amount of epistasis (interaction between sex chromosomes and genetic background).

Key words: Inbred lines – QTL – Epistasis – Body weight

Introduction

Sex linkage for certain traits in fowl has been known for a long time. Hutt (1949) summarized studies of this phenomenon for feather color and body size. It was also found to be of relevance for liveability traits, e.g., resistance to avian leucosis (Harris et al. 1984). In the latter case, maternal effects are of importance too and may be confounded with sex linkage. However, maternal effects are not considered to be very important for quantitative traits in laying hens (Fairfull and Gowe 1986), although some influence of maternal egg weight on body weight of offspring is known. The list of genes with large effects (major genes) on qualitative traits located on the Z and W chromosomes of chicken is given by Somes (1984). In the simplest case, sex linkage may occur from one gene on either sex chromosome that contains an allele with large effect.

The demonstration and description of major genes are important for their possible future use in quantitative trait loci (QTL) (Geldermann 1975) selection procedures. Methods for detecting genes with large effects on quantitative traits were based until very recently on the assumption of many genes with small effects (infinitesimal model) and one major gene with large effect influencing a particular trait, and therefore causing a non-normal distribution of such a trait. Statistical measures of the deviation of such a distribution from normal were used by Mérat (1968) and by Hammond and James (1970), among others, in an animal breeding context. The lack of statistical power is a severe disadvantage of this approach. Elston and Stuart (1971) developed a method called segregation analysis to search for major genes in humans, and it is based on similar principles.

The heterogametic sex of crosses of highly inbred lines of chickens or mammals provides a means to identify specific effects of genes located on the sex chromosomes X or Z and Y or W (ZW = female, ZZ = male in birds). This is possible because reciprocal crosses between two lines are genetically identical except for the sex chromosomes. Only the heterogametic sex can easily be used unless the sex chromosomes can be identified by some marker. Linear combinations of adjusted trait averages of matching type of such crosses are, therefore, useful in investigating the presence of large additive effects of either sex chromosome on quantitative traits. However, if such effects are found, it cannot be determined whether they are due to a single QTL, to a haplotype (several closely linked loci) exerting a large cumulative effect, or to several independent loci on the relevant chromosomes. It is further assumed that the exchange of genetic material between the sex chromosomes (recombination) does not influence the estimation in cases where crossed animals with sex chromosomes from different lines are involved. Knowing the inbred line of origin of the sex chromosomes provides the same information as a segregating marker linked to such chromosomes, and therefore the approach is closely related to the methods used nowadays in molecular genetics.

The probability of detecting such effects is dependent on their size, the variance of the trait, and the number of informative observations (Soller and Genizi 1978). Hastings (1990) used the approach to look for large effects of the average X chromosomes of two lines of mice selected for large and small body weight. Briggs and Nordskog (1973) found effects of the average sex chromosome of two genetically fairly distant breeds of laying hens on quantitative traits.

There is a long history in the discussion of epistatic effects, their usability, and their importance in selection schemes. The approach outlined also makes it possible to investigate one type of epistatic effects, i.e., differences between particular sex chromosomes in various genetic backgrounds, and thus to investigate the presence of epistatic effects (interactions) between the genes on these two chromosomes and the autosomal genetic background.

The aim of this investigation was to look for large effects of either sex chromosome on quantitative traits in female offspring of a crossing system with three highly inbred lines of laying hens.

Materials and methods

Three highly inbred lines of White Leghorn chickens, numbered 75, 77, and 87, developed and kept on the experimental farm 'Chamau' of the Swiss Federal Institute of Technology (ETH-Zurich), were used to produce F_1s, backcrosses, and F_2s in 3 or 4 successive years, starting in 1986. The history and description of the lines is given in detail by Hagger (1985) and by Fritschi and Stranzinger (1985). The lines were propagated through full-sib matings using artificial insemination. All lines had calculated inbreeding coefficients above 0.95, which is reached after more than 14 generations of full-sib mating. The flock was reproduced in four or five weekly hatches in early summer every year. All mating types were contemporaneous. Chicks were reared intermingled on deep litter and transferred into three-floor, single-cage batteries at 16 weeks of age. Twelve hours of light were provided from hatch to about 40 weeks and then increased gradually to 15 h. Individual egg production was recorded 7 days a week at the beginning of the laying period and for 6 days later on. Egg number was adjusted for missing test days using individual records of laying rate. Egg weight was recorded for all hens around the 40th week. Only hens from crossings were included in the analysis. Survivors to 55 weeks that produced more than nine eggs between 21 and 40 weeks and also between 41 and 55 weeks, which had more than two eggs weighed and which had weight differences above −150 g between 21 and 40 weeks and between 41 and 55 weeks, were included in the analysis. The additional constraints removed 4.5% of the surviving hens and left 1,162 birds in the data set.

With all lines, both types of F_1s, i.e., 75 × 77, 77 × 75 . . ., the F_2s, and the backcrosses to inbred males, i.e., 75 × (75 × 77), 75 × (77 × 75) . . ., where the first number always indicates the male line, were produced. With lines 77 and 87 the backcross to the F_1 male, (77 × 87) × 77 and (77 × 87) × 87, were also produced. The complete system was repeated for 3 years, crosses between lines 77 and 87 for 1 additional year. Between two and four matings were made for all combinations in every year. With the exception of inbred and F_1 males, only females were kept in the experiment.

According to the sex chromosomes the combinations for two lines A and B, given in Table 1, were available, where again the first letter(s) indicate(s) the line or line combination of the male. Offspring of the underlined mating types, i.e., F_2s and backcrosses to F_1 males, could not be separated for their combination of sex chromosomes. Therefore, it was assumed that both types were equally represented among female offspring. The differences between chromosomes in 3/4A and 1/4A are free of this assumption.

Recombination between the two different Z chromosomes in male crosses, to be supposed from observations of chiasmata in chicken spermatocites by Pollock and Fechheimer (1978), would affect mostly the estimates of Z_B-Z_A in the two genetic backgrounds of 3/4A and 1/4A. Within the genetic background of 1/2A, estimates of W_B-W_A and Z_B-Z_A would perhaps not be influenced heavily by recombination because a large part of it should be cancelled out. This assumption is based on inspection of the linear combinations given in Table 2.

The differences between these line combinations, given in Table 2, were used to look for large additive influences of the sex chromosomes on quantitative traits. The symbols \3/4A, \1/2A, or \1/4A indicate that the effect was observed in a genetic back-

Table 1. Combinations of sex chromosomes of two inbred lines, A and B, available in the experiment

Crossing type	Line combination	Sex chromosomes in female offspring
F_1	AB	Z_AW_B
	BA	Z_BW_A
Backcross	A (AB)	Z_AW_B
	A (BA)	Z_AW_A
	B (AB)	Z_BW_B
	B (BA)	Z_BW_A
	$\underline{\text{(AB) A}}$	$Z_AW_A + Z_BW_A$
	$\underline{\text{(BA) A}}$	$Z_AW_A + Z_BW_A$
	$\underline{\text{(AB) B}}$	$Z_AW_B + Z_BW_B$
	$\underline{\text{(BA) B}}$	$Z_AW_B + Z_BW_B$
F_2	$\underline{\text{(AB) (AB)}}$	$Z_AW_B + Z_BW_B$
	$\underline{\text{(AB) (BA)}}$	$Z_AW_A + Z_BW_A$

Table 2. Linear combinations of matching types of adjusted line means to estimate effects of sex chromosomes in different genetic backgrounds

Combination	Estimated effect
A (AB) − A (BA)	W_B-W_A\3/4 A
$\underline{\text{(AB) (AB)}} - \underline{\text{(AB) (BA)}}$	W_B-W_A\1/2 A
B (AB) − B (BA)	W_B-W_A\1/4 A
2 (AB $\underline{\text{(A) + (B}}$A) A − A (BA))	Z_B-Z_A\3/4 A
BA − AB + $\underline{\text{(AB) (AB)}} - \underline{\text{(AB) (BA)}}$	Z_B-Z_A\1/2 A
2 (B (AB) − (AB) $\underline{\text{B − (B}}$A) B)	Z_B-Z_A\1/4 A

ground that contained 3/4, 1/2, or 1/4 of the diploid autosomal genome of line A. The differences were estimated by linear combinations of the fixed group effects (e.g., Searle 1971, p. 180ff.) of the following linear statistical model:

$$Y_{ijkl} = \mu + \text{Year*Hatch}_i + \text{Room}_j + \text{Group}_k + b\text{*EWD} + e_{ijkl}.$$

The model contains a constant μ common to all observations, fixed year*hatch, room of laying house and genetic group effects, a linear regression (b) on egg weight of the dam (EWD), and a random residual. Egg weight of the dam was included in the model to eliminate a possible linear effect of this trait, especially on body weight of offspring. Estimation was by ordinary least squares. The estimated differences were tested for a deviation from zero. Effects of the following traits were investigated: body weights at 20, 40, and 55 weeks (BW20, BW40, BW55), egg number between 41 and 55 weeks (EN55), egg weight at 40 weeks (EW40), and age at first egg (AFE).

Table 3. Number of hens available in different genetic groups derived from inbred lines 75, 77, and 87

Genetic group of dam	75	77	87	Genetic group of sire (75 × 77)	(75 × 87)	(77 × 87)
75	57	32	37	–	–	–
77	57	128	75	–	–	67
87	57	69	136	–	–	70
(75 × 77)	28	19	–	24	–	–
(77 × 75)	28	28	–	47	–	–
(75 × 87)	27	28	–	–	40	–
(87 × 75)	30	28	–	–	44	–
(77 × 87)	–	36	40	–	–	81
(87 × 77)	–	32	41	–	–	69

Table 4. Means of traits for inbred lines 75, 77, and 87, and for the different types of crosses between two of them

Genetic group	BW20 kg	BW40 kg	BW55 kg	EN55	EW40 g	AFE d
75	1.45	2.04	2.09	53.1	56.4	211.5
77	1.22	1.49	1.54	68.4	47.8	223.8
87	1.30	1.51	1.57	79.3	49.9	180.4
77 × 87	1.44	1.61	1.74	86.6	51.5	159.7
87 × 77	1.50	1.67	1.79	85.2	51.5	165.4
77 × (77 × 87)	1.36	1.58	1.65	76.1	50.4	188.0
87 × (77 × 87)	1.49	1.78	1.88	77.4	52.3	176.6
(77 × 87) × (77 × 87)	1.40	1.64	1.74	76.9	50.6	180.7

Results

The numbers of hens in the different genetic groups that were included in the analysis are given in Table 3. Inbred hens would not have contributed to the differences between chromosomal effects, but could have increased the variance and thus were not taken into account. It is obvious from the numbers of pure line hens in this table and from the number of eggs produced (Table 4) that line 75 was the least fertile, which seems to be a consequence of the selection history of the relevant base populations (Hagger 1985). Egg size of these hens was large for members of a highly inbred line (Abplanalp 1986) and might have had a detrimental effect on hatchability. A distinct difference between the two reciprocal F_1 crosses given could be observed for AFE, a small one for body weight (Table 4). The larger number of hens from crossings between lines 77 and 87 was due to 4 years of data compared to only 3 for the other line combinations.

All three differences between the additive effects of the W chromosome combinations could be estimated in three genetic backgrounds, as shown in Table 5. In many cases, no significant difference between the W chromo-

Table 5. Estimated differences between effects of chicken sex chromosomes in different genetic backgrounds on quantitative traits

Estimated effect	BW20, g	BW40, g	BW55, g	EN55	EW40, g	AFE, d
$W_{77}-W_{75}\backslash 3/4\ 75$	−3	15	12	−3.7	−0.6	−0.1
$W_{77}-W_{75}\backslash 1/2\ 75$	−2	−25	−38	0.5	−0.8	4.8
$W_{77}-W_{75}\backslash 1/4\ 75$	8	5	−13	0.7	0.3	1.2
$W_{87}-W_{75}\backslash 3/4\ 75$	30	32	63	−1.2	−0.5	0.5
$W_{87}-W_{75}\backslash 1/2\ 75$	−15	−23	−12	3.6*	−0.2	0.5
$W_{87}-W_{75}\backslash 1/4\ 75$	−47	−64	−83	0.6	−1.6*	3.7
$W_{87}-W_{77}\backslash 3/4\ 77$	−57*	−72*	−105**	−1.6	−1.0	−4.2
$W_{87}-W_{77}\backslash 1/2\ 77$	−36*	−39	−50	−0.1	−1.1**	−1.3
$W_{87}-W_{77}\backslash 1/4\ 77$	−40	3	−3	1.5	0.2	1.7
$Z_{87}-Z_{77}\backslash 3/4\ 77$	−38	47	−28	−1.1	−0.8	−7.7
$Z_{87}-Z_{77}\backslash 1/2\ 77$	34	35	13	−1.6	−1.0	4.3
$Z_{87}-Z_{77}\backslash 1/4\ 77$	59	95	57	1.1	−0.1	8.4
$Z_{75}-Z_{77}\backslash 1/2\ 75$	−4	24	20	−2.9	1.2	−3.5
$Z_{75}-Z_{87}\backslash 1/2\ 75$	−116***	−25	7	0.5	1.4	2.1

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

somes of different lines was observed. However, for body weight the differences $W_{87}-W_{77}$ in hens with 3/4 of the genome of line 77 were highly significant, where W_{87} caused a reduction in body weight. In hens with 1/2 of the genome from each line, the differences decreased and remained significant for BW20 only. No significant difference was detected in hens with 1/4 of the genome of line 77. A similar, but reversed, trend according to the genetic background was observed for the differences $W_{87}-W_{75}$ in body weight also. There, positive differences in hens with 3/4 of the genome of line 75 changed to clearly negative ones in hens with 1/4 of the 75 genome, with intermediate differences in hens with 1/2 the genome of each line. One significant effect of the W chromosomes was observed for EN55 and two for EW40. In all three of these cases, line 87 again was involved. For $W_{87}-W_{77}$ the trend from the change in genetic background could also be observed for EN55 and AFE. Briggs and Nordskog (1973) observed an influence of the average W chromosome of one breed of laying hens on age at first egg in a cross with one other breed.

The Z chromosomes of the three inbred lines used seemed not to cause as large a genetic difference as the W chromosomes. One highly significant difference, $Z_{75}-Z_{87}$, in hens with 1/2 of the genome of each line was found in body weight of pullets (BW20). The difference $Z_{87}-Z_{77}$ showed a similar increasing trend with a decreasing amount of the 77 genome, as with the corresponding W chromosomes. The same trend was also found for AFE. For all other traits investigated, no large effect of one particular Z chromosome was detected. It must be remembered that all differences between particular Z chromosomes may be influenced by an uneven distribution of the two indistinguishable classes of sex chromosomes among offspring of certain crosses (Table 2) and two of the differences by the recombination effect between the Z chromosomes in male crosses. For the average Z chromosome of one breed of laying hens, Briggs and Nordskog (1973) found an influence on age at first egg and, thus, also on egg production in a cross with one other breed.

The significant differences observed in body weight were from 2.4 to 7.2% or on average 4.9% of the corresponding means (Tables 3 and 4). Therefore, relatively small differences could be detected in this trait.

Discussion

Maternal effects on the traits investigated were considered to be unimportant. The possible influence of maternal egg weight has been taken into account through including this trait as a covariate in the model used to estimate the group effects. The investigation has shown that loci containing alleles with relatively large effects on quantitative traits are located on the chicken W chromosome. Of the three highly inbred lines available in this study, the W chromosome of line 87 contained at least one locus with a specific allele exerting a large effect on body weight not present in lines 75 and 77. This conclusion is based on the small and not significant differences between W_{75} and W_{77} compared to the differences between the effects of these two chromosomes and W_{87} (Table 5). This result is of great interest, because the W chromosome has been thought to be almost entirely genetically inactive (heterochromatic). It seems logical that there is a higher probability of detecting loci on this chromosome that affect traits showing sexual dimorphisme, e.g., body weight, than other traits. In the linkage map of Somes (1984), so far only the locus for a histoantigen has been placed on the W chromosome. Hastings (1990) found evidence for a difference between the effects of the average X chromosomes from two selected lines of mice on body weight.

The results in Table 5 further indicate that the genetic background seems to be important for the expression of this genetic effect on body weight. In all cases where the differences $W_{87}-W_{75}$, $W_{87}-W_{77}$, and $Z_{87}-Z_{77}$ could be estimated, there was a distinct trend depending on the composition of the genetic background, i.e., 1/4, 1/2, or 3/4 of the autosomes from line 87. The first and the third of these genotypes are 50% inbred, whereas the second one is not inbred at all. Hartmann et al. (1986) also found an influence of the genetic background on the expression of particular genes. They observed a different pattern of mortality from Marek's disease for carrier hens of the B21 blood group allele in two different line crosses. The *B* locus in hens is located on a microchromosome, therefore, the behavior of a specific allele without a high probability of linkage with other major gene effects can be assumed. In the mouse, the effect of the recessive dwarfing gene was found to be strongly influenced by epistasis (Fowler and Edwards 1961).

Chromosomes W_{75} and W_{77} seem to contain different alleles on relevant loci influencing body weight, in spite of the fact that the estimated differences for their influence on this trait are very small. This becomes evident from the reversed trends of $W_{87}-W_{75}$ and $W_{87}-W_{77}$, respectively (Table 5). The first one changes from positive to negative, whereas the second one changes from negative to zero with an increasing proportion of the line 87 genome. Combining all these observations, it seems likely that the differences between the effects of the W_{87} and the other two W chromosomes are caused by one allele only.

The combined influence of background genome and W or Z chromosome on quantitative traits may be explained by epistatic effects between genes located on these two chromosomes and genes in the other part of the diploid genome. The epistatic relationships between alleles of two loci on different chromosomes also explains the observed trend in the series of genotypes containing 3/4, 1/2, and 1/4 of the genes of one line. If 3/4 of the genome are not from the sam line as the W or the Z chromosomes, more of these epistatic effects are expressed than if the background genomes contains only 1/2 or 1/4 of this genome. This must especially be true if highly inbred lines, which are close to homozygosity, are involved. Roberts and Smith (1982) proposed screening of extreme animals to detect major genes. The results of this study suggest that the genetic background in conjunction with a major gene (QTL of large effect) may be the important reason for the extreme status of a particular animal, as anticipated by the authors cited. Such at QTL should, therefore, be investigated in other genetic backgrounds too. As a consequence for practical animal breeding, it can be deduced that the effects of QTLs should be estimated from representative samples of the genome of a population and not only on individuals of a few families, before recommendations for selection on particular QTLs are given. However, a few families from an outbred population represent of course of much larger part of the genome of a population than two or three highly inbred lines, and thus should give more reliable information on the general influence of a QTL with large effect.

The inbred lines maintained an the crosses between them were used for several research projects. The data available did not originate from an experiment specially set up for this investigation and therefore, were suboptimal for this purpose.

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