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Reproductive fitness and artificial selection in animal breeding: culling on fitness prevents a decline in reproductive fitness in lines of *Drosophila melanogaster* selected for increased inebriation time

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Summary. The maintenance of reproductive fitness in lines subjected to artificial selection is one of the major problems in animal breeding. The decline in reproductive performance has neither been predictable from heritabilities and genetic correlations, nor have conventional selection indices been adequate to avoid the problem. Gowe (1983) has suggested that the heritabilities of reproductive traits are non-linear, with heritabilities being higher on the lower fitness side. Consequently, he has predicted that culling on reproductive fitness in artificial selection lines will be effective in preventing the usual declines in fitness. An experimental evaluation of Gowe's prediction has been carried out by comparing fitnesses of replicated lines of three treatments: selection for increased inebriation time without culling on fitness (HO), selection for inebriation time with culling of 20% (4/20) of selected females on reproductive fitness (HS), and unselected controls (C). Response to selection for inebriation time in the two selection treatments was similar. After 25 generations, the competitive index, a measure of reproductive fitness, was significantly lower in the HO treatment than the HS treatment, while the HS treatment did not differ from the control lines or the base population. These results demonstrate for the first time that culling on reproductive fitness in selection lines can be used to prevent the usual decline in reproductive performance.

Key words: Reproductive fitness – Artificial selection – Ethanol tolerance – Quantitative character – *Drosophila melanogaster*

Introduction

Reproductive fitness traits represent the most difficult and least understood traits in quantitative genetics and animal breeding, yet they are among the most important in animal production (Frankham 1982).

The maintenance of reproductive performance in lines subjected to artificial selection is one of the major problems in animal breeding. However, it has been a largely intractable problem. Reproductive performance normally declines in populations selected in either direction (Latter and Robertson 1962) so its behaviour has not been predictable from heritabilities and genetic correlations. Further, conventional selection indices have not been adequate to cope with the problem. Selection indices that are built containing reproductive traits and other traits suffer from the problem that the heritability of reproductive traits is usually very low (Falconer 1981; Mousseau and Roff 1987; Roff and Mousseau 1987) so that the weightings for reproductive traits in indices are low. The broiler chicken industry provides a classic case of the difficulties involved in dealing with reproductive traits. The published estimates of genetic correlations between broiler growth rates and reproduction were low and positive (Kinney 1969), yet selection for broiler growth rate led to drastic declines in reproductive fitness.

Gowe (1983 and personal communication) predicted that heritabilities of reproductive fitness traits were non-linear, being close to zero in the upper 80%–90% of the range, and moderate in the lower 10%–20% of the range (due to the segregation of deleterious recessive genes in mutation-selection balance). Consequently, he predicted that culling on reproductive traits in artificial selection lines would be effective in preventing the usual declines in fitness. Gowe (1983) applied such culling against low fertility and hatchability in lines of chickens selected for increased egg production, and prevented fertility and hatchability declining. However, there has been no systematic evaluation of this approach involving selection for a trait with and without culling on reproductive fitness.

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Non-linear parent-offspring regressions have been found for various traits by Nishida (1972), Meyer and Enfield (1975), Robertson (1977) and Mäki-Tanila (1982) and discussed by them and by Curnow (1960), Kempthorne (1960), Abplanalp (1961), Nishida and Abe (1974), Bulmer (1980) and Gimelfarb (1986). Notable among the factors expected to lead to non-linear heritabilities are directional dominance for alleles affecting a trait, and directional allele frequencies.

The above theoretical considerations lead one to expect non-linear heritabilities for reproductive fitness traits (of the type proposed by Gowe), as such traits typically show directional dominance and directional gene frequencies. There is substantial evidence for directional dominance for higher reproductive fitness from the inbreeding depression and heterosis shown by such traits (see Falconer 1981). Further, deleterious mutations are predominantly recessive, or very nearly so, and are found at low frequencies in approximate mutation-selection balance. Non-linear heritabilities would be expected to cause asymmetrical response to selection. Richardson and Kojima (1965) and Richardson et al. (1968) have reported asymmetrical responses to selection for fecundity in *Drosophila*.

In spite of the above information, there is no general appreciation that heritabilities of reproductive traits might be non-linear. Further, the implications of this possibility have received scant attention in spite of their potential practical applications.

The above considerations lead to three predictions, namely: (i) that the parent-offspring regression for reproductive fitness traits will be non-linear (or becomes so in selection lines and other lines subjected to mild inbreeding); (ii) that there will be asymmetrical responses to selection for reproductive fitness traits; (iii) that culling on low reproductive fitness in lines selected for another trait will be effective in preventing the usual declines in reproductive performance.

The aim of this work was to evaluate the third prediction. The reproductive fitnesses of lines of *Drosophila melanogaster* selected for increased inebriation time with and without culling on reproductive fitness were compared to those in controls and in the outbred base population. Reproductive fitness was significantly lower in the lines selected without culling on fitness, while the fitness of the selection lines culled on fitness was not different from the controls or the base population.

Materials and methods

The outbred Armidale strain of *Drosophila melanogaster* was used as the base population for this study. This strain was founded from a large number of wild inseminated females caught at Armidale, N.S.W., Australia in March 1986. It was obtained from J.S.F. Barker in September 1986 and maintained in about 20 bottles (approximately 25 pairs of parents/bottle) on PS medium (see below) from that time.

(i) Selection experiment

Three treatments were used, namely: (a) HO: these lines were selected for increased inebriation time (no culling on reproductive fitness); (b) HS: these lines were selected for increased inebriation time with culling on reproductive fitness; (c) C: these lines were unselected random mating controls.

Three replicate lines (a–c) of each treatment were maintained. In the selection lines, the selection intensities for inebriation time were approximately 20% in females for the first generation and 4%–5% (standardized selection differentials of 2.154–2.063) in females only (overall selection differential of 1.077–1.032: equivalent to 34%–36% for equal intensities in both sexes) (Becker 1967) for the remaining generations. Twenty inseminated females (plus five spares) were selected from 800–1000 flies (females plus males) run each generation after the founding generation. Males were not selected. Spares were used at random to replace vials containing abolutely no progeny. Most such vials had females (dead) stuck in the medium, so this state was considered to be primarily due to human error.

In the HS lines, 4/20 selected females were culled for reproductive fitness. The reproductive fitness measure was the number of pupae produced by single inseminated females as Osario (1981) found it to be a simply measured character closely related to productivity of single mated pairs. Vials within a line were ranked visually on pupae numbers. We have established that such visual ranking of vials on pupae numbers closely predicts rankings in progeny numbers, particularly at the low end of the range.

The control lines were maintained with 20 randomly chosen single pair matings per generation. Line Ca was discarded at generation 8 due to potential contamination (flies were found to be escaping through a hole in the lid) and refounded at that point from the base population.

The selected character was inebriation time as measured in the inebriometer (Cohan and Graf 1985; Weber 1986). In brief, the inebriometer consists of a vertical tube (with a series of baffles) through which a controlled flow of ethanol vapour is passed. Ethanol vapour is generated by bubbling air through ethanol, the vapour concentration being modulated by controlling the air flow and the temperature of the ethanol. Flies are introduced into the top of the tube and collected automatically as they fall out of the apparatus into polyflouroethylene (fluon)-coated test tubes in a fraction collector. The tubes of the fraction collector are advanced once per minute. The fluon in the tubes prevents flies from crawling out, and the diameter of the tubes is too narrow to allow flies to fly out. In addition, there is a cover over the tubes after the flies are collected.

It is necessary to increase the ethanol vapour concentration as the selection lines respond to selection in order to avoid problems from increasing phenotypic variation and ragged phenotypic distributions. The temperature of the ethanol was 18.9 °C initially and was progressively increased to 22 °C over generations as the selection lines responded to selection.

Progeny flies to be run in the inebriometer were collected 10 days after setting up the parents, exposed to ethanol vapour (for 2 min initially and for 5 min from generation 3) and stored in 284-ml bottles on yeasted ordinary medium at densities of approximately 200 until run on day 14. The prior exposure to ethanol vapour was imposed in an attempt to ensure uniform induction of ethanol metabolizing enzymes.

Mean inebriation times were based on the mass of flies in the fractions. We have established that mass of flies in the fractions provides an accurate measure of means.

All flies were raised at 25 °C on PS medium. The PS medium consists of Edgell's Instant Mashed Potato (main constituents potato, plus skim milk powder) with added castor sugar and methyl-4-hydroxy benzoate (2.75 kg potato, 500 g sugar and 21.7 g benzoate).

Single female vial (10 cm × 2.5 cm) cultures from the lines were raised individually until day 8. At that time, the stoppers were removed, and the vials placed in cylindrical tins so that progeny from different cultures within a line could emerge together and mate at random. The cylindrical tins (15.5 cm height × 18 cm diameter) had plastic clip-on tops containing a transparent plastic window and a 25 mm diameter opening into which an estafoam stopper was placed.

(ii) Reproductive fitness determinations

Relative fitnesses based on the competitive index (Knight and Robertson 1957) were determined by competition with a compound chromosome strain (Jungen and Hartl 1979; Haymer and Hartl 1982, 1983) for flies sampled from all selection and control lines and the Armidale base population at generation 25. The *C(2L), b; C(2R), cn bw* compound chromosome strain was used. Its constitution was confirmed by mating it to a chromosomally normal *vg* mutant strain. As expected, the crosses yielded eggs that did not hatch into larvae.

Each competitive index test was commenced with a ratio of 50% compound: 50% line. Parents used in the tests were raised under standardized conditions with 15 pairs of parents used per 284 ml bottle of PS media for the lines and 80 females plus 10 males per bottle for the compound strain. These densities gave healthy cultures that were not overcrowded. Virgins of the line and the compound were collected, and 20 pairs of compound and 20 pairs of line flies put in each 284-ml bottle after mixing the collected flies to ensure an even contribution of parents of different ages and from different bottles. Parents were all collected on the one day. Any effects of position in the fly room were controlled by placing one HS, one HO and one C line per tray. Parents were transferred to fresh bottles after 3 days, and removed from these latter bottles after a further 3 days.

Six replicate bottles were set up for each line to be tested (one bottle was lost in HSc). All emerging progeny to day 17 were scored from the original and transfer bottles, and the counts pooled for analyses. The competitive index was the ratio of wild-type progeny to compound chromosome progeny, as used by Jungen and Hartl (1979).

Statistical analyses were performed on the proportion of wild-type flies as recommended by Jungen and Hartl (1979), rather than on competitive index, as the latter is a ratio for which reliable statistical tests are not available.

The proportion of wild-type flies was subjected to the arcsin square root transformation prior to performing an analysis of variance. The missing value of one replicate bottle for the HSc treatment was replaced with the treatment mean value and one degree of freedom subtracted from the replicates-within-lines term.

Results

Responses to selection for increased inebriation time are shown in Fig. 1. Responses are expressed as a percentage of the mean of the control lines as Weber (personal communication) has found this to be an appropriate scale for the situation where the control performance declines over generations due to the increases in ethanol vapour concentration imposed. Rankings of a range of genotypes remains the same with different ethanol concentrations (Frankham unpublished) so genotype × environment interactions are most unlikely to be of importance under these circumstances. Five generation averages (four in the case of the last points) are plotted. The lines averaged approximately double the controls at the end of the experiment. The realized heritabilities for inebriation time in the HO and HS treatments were 10.4% and 14.3% based on regressions of deviations from the controls on cumulative selection differentials up to generation 10.

The notable feature of the response to selection for this study is that responses were similar in the HO and HS treatments.

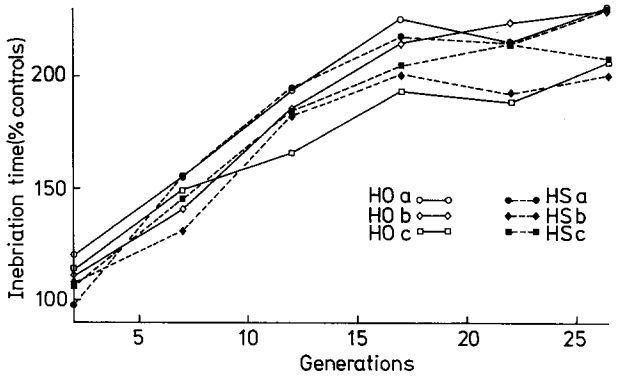

Fig. 1. Response to selection for inebriation time in the lines selected for increased inebriation time with (HS) and without (HO) culling on reproductive fitness, expressed as percentages of the control means

Table 1. Reproductive fitness for the lines and the base population

Line	Relative fitness[a]	Competitive index[b]	Arcsin $\sqrt{p}$[c]
HOa	0.47	19.92	1.355±0.019[d]
HOb	0.37	15.49	1.324±0.012
HOc	0.69	29.06	1.389±0.011
Mean HO	0.51	21.49	1.356
HSa	0.63	26.66	1.384±0.018
HSb	1.11	47.07	1.445±0.029
HSc	0.91	38.52	1.416±0.013
Mean HS	0.89	37.42	1.415
Ca	0.97	40.87	1.421±0.015
Cb	0.99	41.71	1.423±0.020
Cc	0.69	28.96	1.389±0.013
Mean C	0.88	37.18	1.411
Armidale	1.00	42.23	1.419±0.008

[a] Ratio of competitive index in the line to the competitive index in the Armidale base population
[b] The competitive index is the ratio of line flies to compound chromosome flies amongst emergences
[c] Arcsin square root (in radians) of the proportion of line flies emerging in competition with the compound chromosome strain
[d] Standard errors of the means based on variation among the 5–6 replicates

Table 2. Analysis of variance of the reproductive fitness data (arcsin $\sqrt{p}$)

Source of variation	*df*	Mean squares $\times 10^2$
Treatments		
HO vs other treatments	1	4.2114*
HS vs C vs Armidale	2	0.0151
Lines/treatments	6	0.4705*
Replicates/lines	49	0.1728
Total	58	

* $P < 0.05$

The most notable results are those for the competitive index measures of reproductive fitness (Table 1). As statistical analyses have to be performed on the transformed proportions of wild-type flies emerging in competition with the compound chromosome strain (in radians) (Jungen and Hartl 1979), results are presented in this form and in two forms that are more readily comprehended, namely as the competitive indices relative to the compound chromosome strain and as the ratio of the line competitive index to the competitive index of the Armidale base population (relative fitnesses). Reproductive fitness was lower in the HO lines than in the HS lines and controls. The extent of the decline in relative fitness in the HO treatment was 49% compared to the base population and 42% compared to the control treatment. In contrast, the HS treatment had a fitness 11% less than the base population and 1% greater than the controls.

The analysis of variance of the results (Table 2) showed that the HO treatment had a significantly lower fitness than the other treatments, while the HS treatment did not differ in fitness from the controls or the base population. There was a significant difference among replicate lines within treatments. The tests of significance for the treatment effects used the lines-within-treatments mean square as the error term.

Discussion

The results of these experiments provide the first controlled demonstration that culling on reproductive fitness is effective in preventing the decline in reproductive fitness normally exhibited in lines subjected to artificial selection for another trait. These results confirm the indirect evidence from chicken data (Gowe 1983) that culling on fitness in selection lines is effective. They also supply evidence to justify the practice of many commercial poultry breeders of culling on reproductive fitness traits in lines selected for other traits.

It is appropriate to point out that inebriation time behaves as a typical quantitative character (Cohan and Graf 1985; Cohan and Hoffman 1986; Weber 1986; Hoffman and Cohan 1987; Frankham unpublished). It exhibits a unimodal distribution that is essentially normal and is affected by a range of loci (Frankham unpublished). The relationship of this character to genotypes at the alcohol dehydrogenase locus is tenuous at best and inconsistent across different populations (Cohan and Hoffman 1986).

The competitive index measure of reproductive fitness (Knight and Robertson 1957) used in this experiment is recognised as perhaps the best single measure of fitness in *Drosophila melanogaster* (Haymer and Hartl 1982, 1983) and was used by Latter and Robertson (1962) in their classic study of the effects of inbreeding and artificial selection on reproductive fitness. It is a measure of fitness that includes all components of fitness.

Culling was applied on one measure of reproductive fitness (productivity of females) in the selection lines and the fitnesses of the lines assessed using another (competitive index). For the culling to be causally implicated in preventing the decline in fitness as assessed using the competitive index, these non-competitive and competitive measures of fitness must be related. Based on data presented by Haymer and Hartl (1983), the correlation between female productivity (fecundity × egg-to-adult viability in their data) and competitive index is 0.63. Consequently, culling on female productivity can be causally implicated in preventing the decline in fitness of the HS lines.

Are the declines in competitive index that we have observed in our lines comparable to those found by other authors? Latter and Robertson (1962) assessed the competitive indices of a series of control and selection lines that were all maintained with 10 pairs of parents per generation. Their control lines declined to 61% of the base population level at generation 25, compared to the figure of 88% in our larger (20 pairs of parents) controls. Their sternopleural bristle selection lines had a mean competitive index of 41% of their base population at generation 25, while their abdominal bristle selection lines had a mean 22% that of their base population at generation 20. Latter (1966) observed a competitive index only 27% that in his base population after only 10 generations of selection for increased scutellar bristle number (harmonic mean of 20 pairs of parents per generation). The 49% decline in competitive index in our HO treatment (20 pairs of parents per generation) at generation 25 does not appear excessive in comparison to the above-mentioned studies.

Our results do not specifically establish that there are non-linear heritabilities for reproductive fitness traits, even though they were predicted from such considerations. How else could the results be explained? Firstly, the heritability of reproductive fitness could be much higher in the population used than in other populations

(see Falconer 1981; Mousseau and Roff 1987; Roff and Mousseau 1987). This explanation is unlikely, as we have obtained an average estimate of 12% for the heritability of productivity per pair (for a single days laying in one vial) in this population based on twice the daughter-dam regression. A second possible artifact is that reproductive fitness in this population could be affected by a maternally transmissible pathogen in a similar fashion to the effects of the lymphoid leukosis virus in chickens (Spencer et al. 1979; Gavora et al. 1980). This would elevate the daughter-dam regression estimate of heritability and so appears unlikely. The results cannot be accounted for by a positive genetic correlation between inebriation time and reproductive fitness as the HO treatment declined in reproductive fitness. Consequently, the most probable reason for our results is a non-linear heritability for reproductive fitness. Experiments are underway to test directly for non-linear heritabilities for reproductive fitness in the base population and in selection lines.

Our results do not necessarily imply that the heritability is non-linear in the base population. The frequencies of deleterious recessives in mutation-selection balance in the base population may be so low that they do not have sufficient effects on the genetic variation to be detectable. However, genetic drift due to the finite population size in selection lines will eliminate many such deleterious recessives, but will cause the frequency of others to drift to higher frequencies, where they are more likely to result in detectable non-linearities in the heritability. The increases in heritabilities due to population size bottlenecks reported by Bryant et al. (1986) may be a reflection of such effects of genetic drift.

Reproductive fitness may decline in selection lines due to four causes, namely (i) genetic drift causing the frequencies of some deleterious alleles to increase, (ii) deleterious pleiotropic effects of the alleles causing the response for the selected character, (iii) increases in the frequencies of deleterious alleles due to hitch-hiking with linked alleles causing response for the selected trait and (iv) genetic drift moving the frequencies of overdominant loci away from their equilibrium frequencies.

In the second and third cases, culling on fitness would be expected to cause a reduction in response in the selected trait. As we obtained a similar response to selection in the HO and HS treatments, the second and third classes of genes do not appear to be important.

As the population sizes in the selection lines and the controls were the same, it can be argued that the declines in fitness should be similar in the HO and C treatments. However, the effective population sizes in the selection lines will be approximately 20% lower than in the controls, due to the inbreeding effects of selection (based on substituting our parameter values in the equation of Robertson 1961). Thus, the effects of genetic drift are expected to be greater in the selection lines than the controls.

Consequently, it appears that the declines in fitness in our HO selection lines are due mainly to drifting in frequencies of rare deleterious alleles or alleles at loci exhibiting overdominance.

In conclusion, we have demonstrated that it is possible to prevent the usual decline in reproductive performance in selection lines by culling on reproductive fitness. Our results have important implications in animal breeding and in the breeding of outbred plant species.

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