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Expression of genetic and environmental variation during ageing

1. Estimation of variance components for number of adult offspring in *Drosophila melanogaster*

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Summary. To test for different gene activity during ageing, an experiment was set up to determine whether or not genetic variation and genetic correlations between fitness traits at different ages change in a systematic way through time. Additive genetic and environmental variance components as well as genetic correlations between different age periods were calculated for the fitness trait "number of adult offspring" in a population of *Drosophila melanogaster*. Genetic correlations between age periods were all positive and, hence, did not support the theory postulating that genes with beneficial effects on early fitness have pleiotropic unfavourable effects on late fitness. The environmental variation as well as the additive genetic variance showed a clear increase with age. The increase of environmental variation is probably a result of the individuals' increasing difficulties in coping with environmental stress due to physiological deterioration with age. Increased additive genetic variation may be explained by more and more genes being "turned on" with age. Alternatively, it could be caused by accumulation of deleterious mutations with different effects and may reflect the individuals' capacity of DNA repair.

Key words: Age changes – Genetic and environmental factors

Introduction

Animal breeders have mainly concentrated their efforts on improving production capacity to obtain maximum genetic progress per unit of time. In the future, however, it might be of increasing importance to investigate total production capacity and to attempt to increase both lifespan and lifetime production.

The phenomenon of ageing is extremely difficult to define but may be operationally described as a process starting after sexual maturity and early adulthood, characterized by a constant functional decline and leading to increasing difficulties for the individual in coping with environmental stress. There are many theories on the primary causes of ageing, but two contrasting views of the phenomenon can be distinguished. The first is that ageing is a random process of accumulated cellular damage which results in increased vulnerability of the various organs, and the second is that it is a programmed and hence genetically controlled degeneration of the organism.

Medawar (1952), among others, suggested that ageing might be caused by an accumulation of late-acting deleterious mutations. These mutations would tend to accumulate because of their small effect on early fitness. This theory postulates that the environmetal as well as the genetic variation of fitness traits would increase with age. Another theory (Liljedahl et al. 1984) is that formerly inactive genes are turned on during ageing and offer a mechanism to counteract the negative effect of increased sensitivity to environmental stress. This theory also suggests increased environmental and genetic variation of fitness traits with age. The pleiotropy theory (Williams 1957) suggests that genes with beneficial effects on early fitness components have pleiotropic unfavourable effects on late fitness components but are, nevertheless, favoured by natural selection operating at different ages. This theory postulates negative genetic correlations between early and late fitness traits.

Most traits of interest in animal breeeding are continuous traits, which are assumed to be influenced by a large number of unknown genes, each having a small effect. Quantitative genetic methodology is a suitable tool to investigate the net effects of all loci influencing a trait.

Thus, to obtain evidence for different gene activity during ageing, one may ask whether or not genetic variance and genetic correlations of fitness change in a systematic way through time.

In a study on the genetic and the environmental variation relative to age in two populations of laying hens, Liljedahl et al. (1984) found an increase in both components of variance with increasing age for egg production, egg weight and egg quality traits. Rose and Charlesworth (1981 b), dealing with *Drosophila melanogaster*, found decreased fertility at early ages when selecting for increased reproductive output at late ages. The present study further investigates the effects of ageing on fitness variation in *Drosophila melanogaster*, by comparing additive and environmental variance components as well as genetic correlations of total progeny production from females of different ages.

Materials and methods

The investigation was performed using a population of *Drosophila melanogaster* which was obtained from a cross between four wild-type strains of different origin, each contributing equally to the four-way hybrid strain. After ten generations of random mating to allow decay of linkage disequilibrium, a sample of 25 sires and 89 virginal dams were taken at random, all collected within 7 h. Each sire was mated with three-four dams. The virginal duaghters from these matings (approximately six per dam) were collected within 12 h.

All daughters were kept in separate vials containing 2 cm of standard medium (10 g agar, 60 g syrup, 50 g bakers yeast, 40 g powdered mashed potatoes, 0.75 g ascorbic acid and 2 ml propionic acid per litre of water). The flies were kept in the same incubator at 25 °C and 45% relative humidity. All handling was performed at room temperature using carbon dioxide anaesthesia.

After eclosion, each daughter was placed in a vial with one unrelated randomly chosen male of the same age. These couples were kept together throughout the experimental period, except when the male died and was replaced by a randomly chosen one. This experimental design reflects the effects of ageing in both sexes. At approximately 1 week of age the couples were transferred to new vials, for 2 consecutive days of egg laying. Couples were than transferred to vials awaiting another egg laying period. The procedure was repeated throughout the experiment with the egg laying periods starting at 6, 14 and 20 days of age. In order to obtain an accurate account of progeny, the number of adult offspring was recorded and discarded on the 10th as well as on the 15th day after egg laying in each age period. The number of offspring at day 10 and at day 15 were combined and used as a single observation.

The statistical analysis is based on daughters surviving the whole experimental period to avoid selection bias caused by mortality. A second restriction imposed is that only daughters having adult offspring in each age period are included in the analysis (Table 1). Mean progeny number declined as the females aged, and in order to decouple the mean and the variance, data were transformed to a logarithmic scale with base ten. The method used to calculate variance components and genetic parameters for the different age periods was multivariate-restricted maximum likelihood, using a random model with daughter as the only factor together with a complete relationship matrix (Meyer 1986). The variance component between daughters estimates the additive genetic variation whereas the variance component within daughters estimates the environmental variation, assuming no dominance, epistasis, maternal or X-linked effects. Standard errors for variance components as well as genetic parameters were calculated according to Meyer (1985, 1986).

Table 1. Descriptive statistics, additive genetic (V_A) and environmental (V_E) variance components together with their standard errors ($\pm$SE) and the cumulative percentage of daughters excluded at different ages

Age (days)	*N*	Mean	Standard deviation	Excluded (%)	$V_A \pm SE^a$ ($\times 10^{-4}$)	$V_E \pm SE^a$ ($\times 10^{-4}$)
6– 8	422	73.4	18.2	4	7± 7	311±17
14–16	422	59.6	17.1	12	35±18	151±17
20–22	422	26.8	14.2	25	231±97	692±84

[a] V_A and V_E are calculated from data transformed to a logarithmic scale with base ten

Table 2. Descriptive statistics in the last recorded age period, for daughters excluded between different ages

Time of exclusion (days)	*N*	Mean	Standard deviation
6– 8; 14–16	45	60.0	26.5
14–16; 20–22	73	48.1	20.5

Results

Descriptive statistics for the daughthers on which the analysis is based are presented in Table 1. The mean progeny number decreases throughout the experimental periods while the phenotypic standard deviation decreases with the mean. Table 2 shows descriptive statistics for daughters excluded from the analysis at different ages. The values are based on recordings from the latest time of measurement, that is values for daughters excluded between 6–8 days and 14–16 days of age are based on the recordings during day 6–8. The figures in Table 2 show almost the same pattern as those in Table 1. Estimates of the additive genetic and the environmental variation generally increase with age as can be seen from Table 1. Genetic and phenotypic correlations as well as heritabilities are presented in Table 3. The correlations are positive and highest between age periods close to each other. The heritability for the first age period is lower than that for the two other periods.

Table 3. Heritabilities (diagonal), genetic correlations (lower triangle) and phenotypic correlations (upper triangle) with their standard errors for the different age periods (data transformed to a logarithmic scale with base ten)

Age (days)	Age 6–8 (days)	Age 14–16 (days)	Age 20–22 (days)
6– 8	0.02±0.02	0.52±0.02	0.17±0.03
14–16	0.94±0.10	0.19±0.09	0.40±0.04
20–22	0.71±0.49	0.91±0.18	0.25±0.10

Discussion

This study covers a comparatively long period of the animal's life in contrast to most previous investigations. The results may describe a systematic change of genetic and environmental variation in productivity throughout life, and not only temporary changes in early life. The descriptive statistics for the daughters excluded show a very similar pattern as compared with those included in the analysis. The mean is slightly lower and the variance generally larger for excluded daugthers. The excluded animals do not form a deviating group and their exclusion thus cannot be the cause of the observed changes with increasing age.

The results presented here do not support the pleiotropy theory which states that genetic correlations between early and late fecundity are expected to be negative. No negative correlations were found for the age periods dealt with in this investigation. The estimates of the additive genetic variance and the environmetal variance show a clear increase with age, with the exception of the environmental variance in age period two.

The increased additive genetic variation could be explained by X-linked effects, epistasis and dominance contributing more to the total genetic variation at a late age than at an early age. This investigation does not consider, however, variation caused by these factors. In a similar investigation, Rose and Charlesworth (1981 a) found no evidence of X-linked, epistatic and/or dominance effects for fecundity.

Increasing phenotypic or environmental variation has been observed in several studies (Clayton and Robertson 1966; Flock 1977; Liljedahl et al. 1984; Rose and Charlesworth 1981 a; Burla and Taylor 1982) where the animal's reaction to stressful environments or different ages has been investigated. The most plausible explanation to this phenomenon related to ageing is that the animals experience increasing difficulties coping with environmental stress. It has been postulated that this is due to physiological deterioration with age.

One explanation of the increased additive genetic variation with age is accumulation of late-acting deleterious mutations (Medawar 1952; Edney and Gill 1968). Alternatively, more and more genes may become active during ageing. Differentiated gene action is well known during the developmental process in several species (Kolata 1982, among others), but has not been demonstrated during the post-developmental period. Genome reorganization during cellular senescense has also been described (Macieira-Coelho 1984). Furthermore, activation of different genes under different stressful environments has been shown by Hammond et al. (1982). One probable mechanism for gene activation during the ageing process could be alterations in the internal cellular environment, as suggested for gene activation during stress (Hammond et al. 1982).

Mutation rates certainly vary between species depending on protective mechanisms such as the repair capacity of DNA damages. A shift in the pattern of DNA repair with age has been observed, and from this it can be concluded that genetic expression is altered as well (Niedermüller et al. 1985). Moreover, differences between individuals of the same age with regard to DNA repair have been detected (Kempf et al. 1984). The action of these protective mechanisms are presumably under genetic control, and hence may also contribute to the increased additive genetic variation with age.

In a later study a selection experiment will be set up to test several hypotheses. First, is it possible to increase lifespan through selection for fitness at a late age? Second, is there a genetic background for the rate of change of variation with age?

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