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Ether Resistance in *Drosophila melanogaster*

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Summary. Strains set up from single inseminated females of *D. melanogaster* from the wild differ in their resistance to the anaesthetics, ether and chloroform. The main differences between four selected extreme strains could be explained by additive genes, which in the case of ether resistance were located to regions of chromosomes 2 and 3. The lack of correspondence between ether and chloroform resistance between strains indicates that although the type of genetic architecture controlling the traits is similar, the actual genes differ, which is reasonable in view of their differing chemical structures. Quite high heritabilities were found for resistance to ether based on five inbred strains. No significant associations between resistance to ether and body weight, developmental rate or longevity were found.

It is clear that resistance to both anaesthetics would be amenable to more detailed genetic analyses. It is pointed out that the general conclusions reached from such studies will have implications with respect to the effect of chemicals such as insecticides, not naturally present in nature.

Introduction

Although ether has long been used as an anaesthetic agent, little is known about variations between organisms in their resistance to it. Where variations have been found, few genetic analyses have been carried out.

Stern, Schaeffer and Spencer (1944) found that *D. virilis* was substantially more resistant to ether than *D. americana*. It was shown that the difference was chromosomally controlled, and Crow (1957) reported the trait to be polygenic. Rasmuson (1955) found that a wild-type chaeta selection line of *D. melanogaster* was extremely sensitive to ether. The sensitivity depended on both cytoplasmic factors and chromosomal genes, the gene dependent sensitivity being polygenic. When the sensitive and normal strains were crossed, it was found that a stimulating agent was transmitted via the sperm of the sensitive strain which changed the reactive system present in the cytoplasm of the normal strain. The stimulating agent in the male was only produced if the genotype and cytoplasm were sensitive. On the other hand Ogaki, Nakashima-Tanaka and Murakami (1967) found no evidence for cytoplasmic factors in *D. melanogaster* but they developed an ether resistant strain in which the third chromosome was mainly responsible, with major genetic activity at 61, and minor activity on the X and fourth chromosomes.

In this paper, investigations into ether resistance in wild populations will be described, with some genetic analyses of ether resistant and sensitive strains. The possibility of correlations with certain other traits will be discussed.

Method

The strains used consisted of fifteen from Leslie Manor (LM) near Camperdown, Victoria collected in December 1965, and seventeen from Eltham (*E*) near Melbourne collected in January 1968. They were set up from single inseminated founder females from the wild populations. Five strains, inbred by sib-mating for at least 300 generations were also used in some of the experiments.

The method of etherization was similar to that developed by Ogaki, Nakashima-Tanaka and Murakami (1967). Etherizations were carried out in a corked 50 ml. vial at 25 °C. A flat headed screw was inserted into the cork and around the exposed end, lgm. of absorbent cotton wool was wrapped and then covered with a piece of gauze. In order to anaesthetize the flies, 2.8 ml. of diethyl ether was pipetted onto the cotton wool plug and the vial immediately stoppered. After leaving the vial for four minutes, 30 virgin male or female flies were rapidly introduced, after which the vial was again corked and left for a further two minutes (unless otherwise specified). At the conclusion of the two minutes, the flies were transferred to a fresh vial containing medium. Mortalities were assessed 24 hours later.

Flies were etherized at 24 hours of age, because the effect of ether was found to be age-dependent, in that percentage mortality was found to increase over the period 4—120 hours (Figure 1). In particular at four

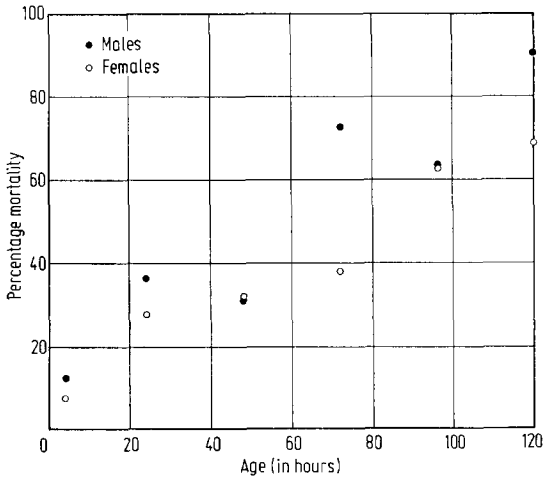

Fig. 1. Percentage mortality after etherization plotted against age, for males (•) and females (○)

hours, the percentage mortality was low and by 120 hours very high. Twenty-four hours was chosen rather than 120 hours, because at 120 hours it would have been necessary to reduce the time of exposure quite considerably, and it was thought that this might decrease the accuracy of the testing time. It will also be noted from Figure 1 that males are in general more sensitive than females, in agreement with Ogaki, Nakashima-Tanaka and Murakami (1967).

All analyses of variance based on percentage mortalities were carried out after applying the angular transformation to avoid a dependence of the variance on the mean.

Ether resistance in natural populations

The LM strains were tested four times over a period of eight generations; two replicates per sex being tested each time; and the mean percentage mortalities are given for the 15 strains in Table 1 together with an analysis of variance. The main effects were all highly significant. The sexes effect reflects greater male susceptibility, and the counts effect minor environmental differences between generations. Of particular interest is the highly significant strains effect. This shows genetic effects presumably arising from differences between the founder females. Thus the Leslie Manor population from which the founder females were derived is polymorphic for genes controlling resistance and sensitivity to ether. This agrees with work on a number of other physiological stresses such as high temperatures (Hosgood and Parsons, 1968; Parsons, 1969), Co^{60}-γ rays (Parsons, MacBean and Lee, 1969) and desiccation (Parsons, 1970). The *E* strains were tested twice, six generations apart, two replicates per sex being tested each time. Analogous data to those in Table 1 are given in Table 2 with an analysis of variance which indicates similar conclusions, except that the counts effect was insignificant.

In order to investigate the situation further, a diallel cross between two resistant *LM* strains 25 and 32, and two sensitives 26 and 30, was set up giving percentage mortalities as in Table 3. The data were analyzed according to the model of Griffing (1956) in Table 3b, and give large significant general combining abilities in both sexes, indicating additive differences between strains. Specific combining abilities were much smaller although significant for females. It is clear that for any crosses in which either of the ether resistant strains were involved i. e. 32 or 25, percentage mortalities were considerably lower than in those crosses between purely sensitive strains. This indicates that the ether resistant strains show some dominance over the sensitives, which is in partial agreement with Ogaki, Nakashima-Tanaka and Murakami (1967) who found resistance to be completely dominant. Table 3 also gives data for a 4×4 diallel cross between two resistant *E* strains 7 and 15, and two sensitives 3 and 5 with essentially

Table 1. a. *Mean percentage mortalities of 30 flies 24 hours after etherization for the 15 LM strains (Note: each entry represents the mean of two replicates for each of the four generations tested)*

Strain	Females	Males
20	26.27	53.85
21	26.30	53.96
22	55.63	72.18
23	24.99	76.19
24	18.84	53.48
25	11.45	43.70
26	53.50	86.32
27	19.87	54.48
28	36.91	52.96
29	18.59	54.79
30	53.64	86.82
31	32.65	40.91
32	12.03	51.89
33	31.52	52.69
34	18.38	46.41

b. *Analysis of variance*

Sources of variation	d.f.	M.S.	F
Strains	14	639.62	6.72***
Sexes	1	10962.83	115.19***
Counts	3	1492.53	15.68***
Strains × sexes	14	96.14	1.01
Strains × counts	42	99.07	1.04
Sexes × counts	3	53.26	0.56
Error	42	95.18	

*** $P < 0.001$

Table 2. a. *Mean percentage mortalities of 30 flies 24 hours after etherization for the 17 E strains (Note: each entry represents the mean of two replicates for each of the two generations tested)*

Strain	Females	Males
1	21.96	47.46
2	15.45	69.46
3	25.40	76.43
4	13.29	40.73
5	37.12	58.43
6	20.46	45.64
7	2.50	17.24
8	15.83	41.71
9	18.41	20.24
10	11.92	42.89
11	3.12	13.80
12	17.59	31.33
13	16.04	42.46
14	6.83	25.90
15	6.71	20.26
16	7.51	26.84
17	30.13	40.37

b. *Analysis of variance*

Source of variation	d.f.	M.S.	F
Strains	16	310.25	11.71***
Sexes	1	4371.54	165.03***
Counts	1	2.92	0.11
Strains × sexes	16	62.09	2.34
Strains × counts	16	69.53	2.62*
Sexes × counts	1	26.09	0.99
Error	16	26.49	

* $P < 0.05$, *** $P < 0.001$

Table 3. *a. Mean percentage mortalities of 30 flies 24 hours after etherization in the 4 × 4 diallel cross between 4 LM strains, and 4 E strains (based on two replicates)*

LM strains	Strain of male parent	Mortality in females				Mortality in males			
		32	25	30	26	32	25	30	26
Strain of	32	7.74	12.90	11.29	20.81	28.79	43.52	49.84	61.71
♀ parent	25	10.89	27.95	16.15	23.33	29.24	59.63	28.59	37.10
	30	10.00	14.79	65.63	47.58	54.37	69.64	78.34	84.28
	26	11.29	23.01	76.37	70.49	58.07	54.20	76.67	79.31
E strains		15	7	5	3	15	7	5	3
Strain of	15	33.31	6.46	21.61	30.84	66.96	57.63	76.59	88.10
♀ parent	7	26.04	22.29	31.70	51.15	43.59	47.26	83.73	98.94
	5	28.98	30.09	39.12	76.57	51.67	77.41	76.16	98.34
	3	19.73	26.92	43.79	75.94	76.86	96.66	89.85	100.00

b. *Analyses of variance (F values)*

Source of variation	d.f.	F values			
		LM Strains		E Strains	
		Females	Males	Females	Males
General combining ability	3	50.80***	13.89***	30.67***	48.89***
Specific combining ability	6	9.68***	2.05	4.72**	4.42**
Reciprocal effect	6	2.12	2.33	5.84**	2.67
Error	16				

** $P < 0.01$, *** $P < 0.001$

the same results. Therefore, in conclusion ether resistance in natural populations is mainly controlled by additive genes, but the resistant genes show some dominance.

The next step was an attempt to locate genetic activity to chromosomes, and two extreme strains, LM25 (resistant, designated A) and LM26 (sensitive, designated B), were taken. The chromosome assay technique of Kearsey and Kojima (1967) was adopted. This enables the production of eight true breeding substitution lines AAA, AAB, ABA, ABB, BAA, BAB, BBA and BBB, where the sequence of letters corresponds to the source of the X, 2 and 3 chromosomes. These eight lines were then crossed to obtain all the possible 27 female and 18 male homozygous and heterozygous chromosome combinations (see also Parsons, MacBean and Lee, 1969). For each combination, 30 flies of each sex were etherized. Analyses of variance are given in Table 4. The sum of squares was partitioned into individual components to test the additive and dominance effects of each of the three main chromosomes and interaction effects between them, the error component being obtained from the pooled triple interaction components. The additive effects were more important than the dominance effects, in agreement with the diallel crosses. Major effects were associated with chromosome 3, and to a lesser extent chromosome 2 (although the importance of the chromosome 2 effect was enhanced by an additional analysis not presented here).

Some attempts were then made to localize genetic activity more precisely. Considering firstly chromosome 2, a marker stock *al cn bw*, the genes being at 0, 57.5 and 104.5 respectively, was taken and crossed to LM25 and LM26, and the F_1's backcrossed to the marker stocks. For each backcross there were eight progeny phenotypes which were tested in five replicates of 30 flies per sex. Etherization was carried

Table 4. *Analyses of variance (F values) of the percentage mortalities after etherization for strains LM25 and LM26 using the chromosome assay technique of Kearsey and Kojima* (1967)

Source of variation	Chromosome	Females		Males	
		d.f.	F	d.f.	F
Additive (a)	X	1	<1	1	6.08
	2	1	<1	1	8.10*
	3	1	17.69**	1	15.72*
Dominance (d)	X	1	<1	.	...
	2	1	<1	1	3.34
	3	1	4.66	1	<1
a × a	X × 2	1	12.67**	1	4.93
	X × 3	1	5.88*	1	2.58
	2 × 3	1	<1	1	<1
d × d	X × 2	1	2.42	.	...
	X × 3	1	<1	.	...
	2 × 3	1	4.50	1	1.70
a × d	X × 2	1	3.55	1	<1
	2 × X	1	3.42	.	...
	X × 3	1	1.25	1	<1
	3 × X	1	3.70	.	...
	2 × 3	1	<1	1	<1
	3 × 2	1	1.03	1	<1
Error		8		4	

* $P < 0.05$, ** $P < 0.01$

Table 5. a. *Analyses of variance (F values) to determine the regional effects of chromosome 2 for LM25 and LM26*

Source of variation	d.f.	LM25		LM26	
		Females	Males	Females	Males
Region A	1	3.31	4.37*	7.68**	20.95***
Region B	1	0.27	0.44	0.07	0.37
Region C	1	7.10*	10.95**	0	0.01
A × B	1	3.34	0.03	3.78	1.78
A × C	1	0.17	0	1.97	0.05
B × C	1	0.25	0.21	6.05*	1.12
A × B × C	1	0.01	0.22	1.25	1.09
Replicates	4	2.85*	4.25**	1.51	6.17**
Error	28				

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

b. Effects of the three regions given as percentages compared with the marker chromosomes

Chromosomal region	A	B	C	A	B	C
♀	+3.9	−1.4	−6.4	+10.0	+0.5	+0.2
♂	+7.8	+3.6	−14.8	+20.7	+2.6	+0.2

\+ indicates region of sensitivity
− indicates region of resistance

Table 6. a. *Analyses of variance (F values) to determine the regional effects of chromosome 3 for LM25 and LM26*

Source of variation	d.f.	LM25		LM26	
		Females	Males	Females	Males
+/*se*	1		3.16	13.96***	106.42***
+/*e*	1		7.48*	0.52	1.45
se × *e*	1		1.59	1.44	0.81
Phenotypes	3	1.84	4.08*	5.31*	36.23***
Replicates	5	1.22	5.13**	4.67*	55.16***
Error	15				

Note: 1 d.f. components for LM25 for female data were not obtained as the phenotypes effect was insignificant.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

b. *Effects of the two regions given as percentages compared with the marker chromosomes*

Chromosomal region	*se*	*e*	*se*	*e*
♀			+11.96	+2.41
♂	−9.98	+15.96	+21.77	+2.34

\+ indicates region of sensitivity
− indicates region of resistance

out for 2 minutes 15 seconds for females and 2 minutes for males, because of the greater male sensitivity. Analyses of variance which split the strain effects into seven 1 d. f. components are given in Table 5. These analyses test the effects of each of the three regions and interaction effects between them. In the analyses A represents the region marked by *al*, B by *cn*, and C by *bw*. For LM25 the major effect was associated with the C region, and so indicates a gene or gene complex for resistance at the distal end of chromosome 2, and in the males there was a suggestion of sensitivity at the proximal end of chromosome 2 (Table 5b). For LM26 there was a major effect associated with the *A* region indicating a gene or gene complex for sensitivity at the proximal end of chromosome 2.

For the chromosome 3 analysis for the same strains (Table 6), the marker stock *se e* (*se* and *e* are at 26.0 and 70.7 respectively) was used which marks a substantial segment of the chromosome. Six replicates were used and the etherization times were 2 minutes in females and 1 minute 45 seconds in males because of a new batch of ether, which was stronger than that used in previous experiments. LM25 showed no significant effects in females and in males there was an effect significant at the 5% level for the +/*e* comparison, which indicates some sensitivity in this region even though LM25 is a resistant strain, and so may indicate a weak sensitivity gene close to the region, or a stronger sensitivity gene further away. The apparent resistance associated with *se* was not significant. However, LM26 showed extremely significant sensitivity associated with the *se* region, indicating a gene or gene complex on the left arm of chromosome 3 possibly quite close to *se*.

Therefore, based on these two strains alone, there are indications of genes controlling variations in resistance and sensitivity in various parts of chromosomes 2 and 3. If other strains were taken no doubt different regions of activity would emerge, since they were shown to be different based on the comparisons between strains (Tables 1 and 2). Therefore the genetic architecture of ether resistance (and sensitivity) can be assumed to be quite complex, and it would be of considerable interest to study it further.

An estimate of the heritability of the trait was obtained based on five inbred strains which had been inbred for over 300 generations in the laboratory by sib-mating, which were crossed to form a 5×5 complete diallel cross (Table 7a) based on etherization for 1 minute 30 seconds in females and 1 minute 15 seconds in males. Combining ability analyses are given in Table 7b omitting the inbred strains. The general combining abilities were highly significant indicating additive differences between strains, and the specific combining abilities although significant were less so, indicating some dominance effects. The general combining abilities in Table 7c show that Y2 and OR were resistant and Y4 extremely sensitive, the remaining two strains being intermediate. Table 7a shows Y2 and OR in particular to be dominant to Y1, N4 and Y4, which agrees with previous findings that ether resistance tends to be dominant to sensitivity, and explains the significant specific combining abilities found in the analyses of variance. From the combining ability analyses,

Table 7.
a. *Mean percentage mortalities of 30 flies 24 hours after etherization for a 5×5 diallel cross between 5 inbred strains (based on two replicates)*

Strain of ♂ parent		Mortality in females					Mortality in males				
		Y2	OR	Y1	N4	Y4	Y2	OR	Y1	N4	Y4
Strain of ♀ parent	Y2	1.62	0	1.62	9.79	0	0	7.17	5.24	19.59	5.00
	OR	0	0	5.17	1.79	3.23	0	3.79	4.17	10.35	12.02
	Y1	0	6.56	45.97	0	8.74	0	13.25	50.23	9.62	17.31
	N4	3.23	0	0	45.00	22.41	3.23	5.56	20.00	41.55	52.52
	Y4	6.56	18.57	17.86	10.71	35.49	3.34	29.49	38.01	75.86	20.58

b. *Analyses of variance (F values)*

Source of variation	d.f.	Female data F	Male data F
General combining ability	4	8.72***	23.90***
Specific combining ability	5	4.07**	6.41***
Reciprocal effect	10	1.87	2.78*
Replicates	1	6.19*	5.17*
Error	29		

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

c. *General combining abilities (Percentages)*

Y2	−11.52	−27.40
OR	− 5.23	−10.58
Y1	− 2.47	− 4.35
N4	+ 1.85	+26.13
Y4	+17.37	+26.20

estimates of heritabilities in the broad and narrow sense came to 0.755 and 0.379 in females, and 0.895 and 0.612 in males respectively. This analysis of the inbred strains, showing a high degree of additivity and quite high heritabilities shows that the trait is amenable to further detailed genetic analysis as is clear from the earlier data presented.

Possible Correlated Traits

Chloroform

Crow (1957) found some correlation between chloroform and ether resistance, since *D. virilis* was more resistant to both ether and chloroform than *D. americana*. In order to see if this applies within *D. melanogaster* the LM strains were tested for chloroform resistance. The method of administering chloroform was basically the same as used for ether, but since chloroform was found to be considerably more potent, only 1.0 ml of chloroform was pipetted onto the cotton wool plug and flies were exposed for one minute only. Scoring was carried out at four hours compared with 24 hours for ether. This was because at 24 hours after exposure to chloroform, almost all flies were dead, and death occurred progressively over the 24 hour period. In comparison, etherized flies died rapidly usually under the anaesthetic, there being little difference in the number dead at one hour or 24 hours after etherization. Thus the mortality curves imply different modes of action of the two anaesthetics in *Drosophila*, presumably by interacting with different metabolic systems. This is not surprising since the anaesthetics are quite different chemically, ether being C_2H_5-0-C_2H_5 and chloroform contains C1 atoms, its formula being $CHCl_3$. In man the effects of the anaesthetics differ, since chloroform has two or three times the potency of ether and leads to degenerative changes in the liver and kidney, and depression of the heart and blood vessels.

Mean percentage mortalities of flies based on two replicates two generations apart are given in Table 8a, and an analysis of variance in Table 8b. The analysis

Table 8. a. *Mean percentage mortalities of 30 flies of 15 LM strains 4hours after exposure to chloroform (Note: each entry represents the mean of two replicates for the two generations tested)*

Strain	Females	Males
20	1.11	1.38
21	23.98	43.09
22	4.85	22.15
23	9.87	25.37
24	20.34	41.50
25	22.68	43.52
26	16.54	44.63
27	25.23	37.23
28	8.02	26.57
29	15.42	35.61
30	21.50	47.85
31	32.82	34.77
32	10.82	36.67
33	38.77	79.85
34	13.41	28.90

b. *Analysis of variance (F values)*

Source of variation	d.f.	M.S.	F
Strains	14	443.93	9.49***
Sexes	1	2525.91	53.38***
Counts	1	103.91	2.20
Strains × sexes	14	43.89	0.93
Strains × counts	14	93.57	1.98
Sexes × counts	1	145.32	3.07
Error	13+	47.32	

*** $P < 0.001$

+ The error d.f. is reduced by one because of the need to estimate a missing plot.

shows males to be more susceptible than females as for ether, and also shows a strains effect as for ether, hence there are genetic differences between the strains for chloroform. Correlation coefficients for 14 d.f. were calculated on the percentage mortalities in Tables 1 and 8 and came to −0.063 and 0.079 for females and males respectively, neither of which differ significantly from 0. (Note: $r > |0.497|$ for significance at $P < 0.05$.) Hence the genetic control of the two anaesthetics differs at least partly in natural populations.

Table 9. a. *Mean percentage mortalities of 30 flies 4 hours after exposure to chloroform in a 4×4 diallel cross between 4 LM strains (based on two replicates)*

Strain of male parent		Mortality in females				Mortality in males			
		20	22	21	33	20	22	21	33
Strain of female parent	20	6.37	9.53	66.43	25.81	27.91	55.00	27.01	50.15
	22	8.03	10.62	19.11	21.70	39.55	17.82	44.10	66.64
	21	11.25	19.59	33.92	52.27	42.19	35.37	91.61	93.76
	33	25.32	40.86	67.30	71.98	55.18	81.21	76.69	92.19

b. *Analysis of variance (F values)*

Source of variation	d.f.	F values	
		Females	Males
General combining ability	3	38.01***	68.51***
Specific combining ability	6	2.48	11.54***
Reciprocal effect	6	5.99**	2.85*
Error	16		

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

The investigation of the genetic basis of chloroform resistance was taken one step further by setting up a 4×4 diallel cross between two chloroform resistant strains (LM20, LM22) and two sensitives (LM21, LM33), and percentage mortalities based on two replicates are given in Table 9a with combining ability analyses in Table 9b. The general combining abilities were highly significant indicating additive differences between strains. Some degree of non-additivity was indicated by the significant specific combining ability in males. Reciprocal effects were significant mainly due to the large difference between 21♀ × 20♂ and 20♀ × 21♂, but further work is needed to explain this. Thus like ether, there are large additive differences between strains for chloroform, but the genes controlling the two anaesthetics differ partly or wholly.

Body weight, developmental rate and longevity

It is possible that there may be an association between ether resistance and body weight. To test this, three ether-resistant (LM25, E7 and E12) and three sensitive (LM26, LM30 and E3) strains were taken, and percentage mortalities in both sexes assessed as well as mean body weights based on 25 flies per sex. Significant differences between strains for body weight were found ($P < 0.001$) but the correlation coefficients based on 5 d. f. between mean body weights and mortalities, after applying the angular transformation came to −0.061 and −0.514 in females and males respectively, which do not differ significantly from 0.

Developmental rates of the six strains were assessed by setting up four replicates of 25 newly hatched larvae per vial, and two replicates of 200 newly hatched larvae per vial. Significant differences between strains were only found in the former case ($P < 0.05$), and correlation coefficients between percentage mortality to ether (sexes combined) and developmental rate came to 0.362 and 0.335 for the 25 and 200 larvae per vial data respectively, which did not differ significantly from 0.

Longevity was assessed by setting up four replicates per sex of 25 flies per vial, the flies being transferred to fresh food twice a week and the number of dead flies scored. Significant differences between strains were found ($P < 0.05$), based on the mean number of days at which 80% of the flies had died. Correlation coefficients for the female and male means and percentage mortalities to ether came to −0.180 and −0.070 respectively, which did not differ significantly from 0.

There is therefore no indication of significant correlations between resistance to ether and any of these traits, so providing little so far as interpreting the reasons why variations in ether resistance occur. The data are limited, so that small correlations if they exist, would not have been detected. Additional investigations would be of interest.

Discussion

The amount of variability in natural populations for ether resistance is high, and involves a number of loci, as yet not located, on chromosomes 2 and 3 in the strains analyzed in detail. No doubt analyses of other strains would reveal genetic activity in other regions and chromosomes (see introduction for a report of genetic activity on the X and 4th chromosomes). Most of the variability is additive which is convenient from the point of view of future genetic analysis. There have been several papers (Breese and Mather, 1960; Mather, 1966) arguing for a correspondence between the genetic architecture of a quantitative trait and the type of selection to which it has been exposed in the past. Thus directional selection will lead to a quantitative trait showing directional dominance and a duplicate-type gene interaction, as found for traits selected for uniformly high fitness such as viability (Breese and Mather, 1960) and hatchability (Kearsey and Kojima, 1967).

On the other hand, stabilizing selection leads to little dominance and weak interactions, and such dominance and interactions that do occur tend to be ambidirectional. The genetic architecture of ether resistance corresponds more to this latter situation, indicating the likelihood of an intermediate optimal level of ether resistance in a population. However, it is difficult to explain this without knowing more of the physiological and biochemical differences between strains having high or low levels of resistance, and such other traits as were tested did not provide any conclusive results. The same comments on genetic architecture apply to chloroform, so far as that analysis went, although the actual genes involved differed from those for ether resistance, which is reasonable because of the differing chemical structures of the two anaesthetics.

The approach to studying quantitative physiological traits used in this paper, seems to be useful in providing a first overall view of the genetic architecture of a trait, from which more detailed studies such as locating and studying actual genetic loci could proceed. It is of interest that resistance to ether, chloroform and Co^{60}-γ rays all show similar basic genetic architectures of additive genes, probably of reasonably large effect, as judged by the magnitude of the differences between strains. This means that extreme strains for these traits could be produced quite quickly by using the technique elaborated by Hosgood and Parsons (1967) and Lee and Parsons (1968) for selecting for quantitative traits, which involves choosing extreme strains, crossing them together, and then carrying out directional selection. Such a procedure lead to extremely rapid responses for selection for scutellar chaeta number. From such extreme strains, loci controlling the traits under study could be rapidly located and studied from various points of view e. g. physiologically, or the randomness of the distribution of the loci in the genome. Both of these points would be of considerable interest in the study of ether and chloroform resistance and would assist in explaining the high level of variability found for these traits. Presumably these explanations may be simplest for traits where there is an interaction directly with one or a few metabolic pathways rather than many as would be the case for resistance to extreme temperatures, desiccation or Co^{60}-γ rays.

The results have implications for the effect of environmental factors of a man-made type, which will probably increase in importance with time. Most examples of evolutionary change due to man-made changes in the environment have come from species of more economic significance than *Drosophila*, however the study of *Drosophila* is instructive. Thus the rapid build up of resistance to DDT in *D. melanogaster* is a good example, where the basic genetic architecture is additive (Crow, 1957). Presumably in nature before DDT appeared, flies were not subjected to directional selection for resistance as has no doubt occurred after its appearance. Therefore, responses to selection will be expected to be rapid as in fact seems to be the case. Thus, the study of the genetic effects of chemicals, not known to exist in nature such as anaesthetics, has implications of some economic and ecological significance.

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