corresponding increase in extent of branching until at a concentration of 5 percent (and to a somewhat lesser extent at 3 percent and 4 percent) the cultures were macroscopically indistinguishable from those grown in the presence of high concentrations of sorbose. Microscopically, the hyphae strongly resembled sorbose-grown hyphae (Figs. 1*c* and 1*d*), although marked variations in morphology and extent of branching were sometimes found in different parts of the same colony. The ability of snail digestive juice to induce colonial morphology declined with increasing age of the enzyme preparation. At a concentration of 10 percent snail digestive juice, growth did not occur. It is of special interest that all the typical features of colonial morphology as observed in sorbose-grown cultures can be induced by snail digestive juice, including initiation of branches at the hyphal tip, increase in branching, and some shortening of cell length. Growth was normal in the presence of autoclaved snail digestive juice, as well as serum albumin, N-Z-Case, and various proteolytic enzymes. Not enough is known about the mechanism by which branches are produced to explain these results, especially in view of the complex enzymatic content of snail digestive juice. In the absence of much sorely needed information, one can only speculate that a weakening of the cell wall by enzymatic digestion, in association with the high internal pressure known to exist in *Neurospora* hyphae (*12*), could lead to an increase in the number of branches initiated. The results described above suggest that sorbose may induce colonial growth in a similar manner, perhaps by inhibiting synthesis of the glucose polymer in the cell wall.

The results reported herein show that, in some cases at least, colonial morphology occurs in association with changes in cell wall structure. However, these observations cannot be placed in their proper perspective until further information is available on normal wall structure, cell wall metabolism in the presence of sorbose, and wall structure of some other colonial forms of *Neurospora,* notably the colonial mutants (*13*).

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9a. *Note added in proof*: In M. R. J. Salton's *Microbial Cell Walls* (Wiley, New York, 1960), reference is made on page 20 to unpublished results, apparently of M. R. J. Salton and M. P. Hatton, reporting the presence of glucose and glucosamine in *Neurospora* cell wall polysaccharides.

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## Measurement of the Relations between Chromosomes and Behavior


*Abstract.* The relations between the three major *Drosophila melanogaster* chromosomes and individual differences in geotaxis are assayed in populations selected for positive and negative geotaxis and in an unselected foundation population. The major changes which occur with selection and the differential roles in geotaxis of the three large chromosomes are described.


Experimental behavior genetics has usually been limited to selective-breeding and strain-comparison studies (*1*). In a few experiments the effects of known loci on behavior have been analyzed (*2*). Recently it has been found that it is feasible to study the relations between variations in sets of chromosomes and individual differences in behavior (*3*). Efficient, reliable, and objective methods developed for the observation of behavior in populations can now be combined in behavior genetic analysis with genetic techniques developed for assaying chromosomes. Such analysis can yield information about both the relative importance of particular chromosomes in producing individual differences in behavior and the nature of the relations between each chromosome and a behavior.

In the study reported here (*4*) the role in geotaxis of the three major *Drosophila melanogaster* chromosomes and their several interactions has been assayed with a multiple inversion tester stock (*5*) in a $2^8$ factorial breeding experiment, reported in detail elsewhere (*6*). The chromosome assay method described by Mather and Harrison (*7*) depends on comparison of the geotactic effect of the chromosomes from a population under study with that of their homologues from a common tester stock. The homologous chromosomes of different populations under study can then be compared with one another by means of this common standard of reference. Direct comparison of the chromosomes from different populations is impossible because the chromosomes cannot ordinarily be identified and followed in segregation. The chromosomes of the tester stock contain inversions, however, which reduce recombination in heterozygotes; they also contain dominant morphological marker genes, which make it possible to follow in a backcross the segregation of these chromosomes from their homologues.

The assay breeding procedure consists of crossing a multiple inversion tester stock to the population being tested and then backcrossing the resulting $F_1$ hybrid to the same population. It produces individuals having either of two chromosome combinations for each of the three major *D. melanogaster* chromosome pairs. A pair of chromosomes is thus structurally either heterozygous or homozygous—that is, either the inversion chromosome from the standard tester stock is paired with its homologue from the tested population or both homologues come from the tested population. From the difference in geotactic behavior between the structural heterozygotes and the structural homozygotes an estimate is obtained of the geotactic effect of a given chromosome from a tested population.

The observations in this study are distributions of geotactic scores in the mass screening maze (*8*) for the eight combinations of structural heterozygotes and structural homozygotes produced by each assay. The maze affords objective, automatic, and reliable mass screening measurements of individual differences in both positive and negative geotaxis in populations under constant stimulus conditions.

Selective-breeding analysis (*6, 8*) has previously shown that the variance in individual differences in geotaxis contains a large genetic component and that the sign of this taxis is a property of the individual genotype. Geopositive and geonegative populations have been developed by selection from a heterogenic foundation population (*6, 8*) which has itself remained geotactically polymorphic while being maintained as

Table 1. Estimates, averaged over assay replications, of the differences in geotactic score between the structurally heterozygous and the structurally homozygous forms of the chromosome pair of a column for the population of a row. Rows (roman type): estimates and standard errors for geotactic effects of chromosomes; (*italic type*): differences between homologues from selected and unselected populations, with standard errors.

| Chromosome | | |
|---|---|---|
| X | II | III |
| *Geopositive population* | | |
| 1.39* ± 0.13 | 1.81* ± 0.14 | 0.12 ± 0.12 |
| *0.36 ± 0.24* | *0.07 ± 0.19* | *0.41† ± 0.20* |
| *Unselected population* | | |
| 1.03* ± 0.21 | 1.74* ± 0.12 | −0.29 ± 0.17 |
| *−0.56‡ ± 0.26* | *−1.41§ ± 0.23* | *−0.78‡ ± 0.23* |
| *Geonegative population* | | |
| 0.47‖ ± 0.17 | 0.33 ± 0.20 | −1.08‖ ± 0.16 |

Degrees of freedom: *17; †34; ‡35; §31; ‖18.

a free-mating population during selection of the two derived populations. For each population, ten replications were made of the assay. From most replications behavioral measurements were made on two samples of approximately 200 females each.

Table 1 presents (i) estimates and standard errors for the effects on geotaxis of the three chromosomes in the three populations; (ii) differences between estimates in the selected and unselected populations, with standard errors; and (iii) degrees of freedom from Student's $t$ distribution for both the estimates and the differences which are significant ($P < .05$). Interactions among chromosomes were all negligible and are therefore omitted. The estimates are averages over assay replications of the differences in geotactic score between the structurally heterozygous and the structurally homozygous forms of the chromosome pair of a column for the population of a row.

The results of these experiments reveal the polygenic nature of individual differences in geotaxis. Genes on two chromosomes respond to selection for positive and for negative geotaxis; genes on another respond to selection for negative geotaxis only.

Selection studies have shown how large a part of the range of individual differences in geotaxis can be accounted for by differences in genotype. For the genetic background provided by the cross to the tester stock, the assay now shows (i) the extent of the difference between the selected populations attributable to differences in each of the three chromosomes; (ii) the different roles that the three chromosomes play in geotaxis; and (iii) how each chromosome in the two selected populations has changed in comparison with its unselected homologue in the foundation population. In the foundation population, chromosomes X and II contain factors which produce positive geotaxis, while chromosome III is slightly negative. All three chromosomes respond to selection for negative geotaxis: the positive effect of chromosomes X and II is markedly diminished, while the negative effect of chromosome III is considerably enhanced. In response to selection for positive geotaxis, chromosome III changes from negative to positive, chromosome II remains unchanged, and chromosome X has probably become slightly more positive. Clearly there are genes distributed over most of the genome which influence the response to gravity.

Analysis of the role of the chromosomes in behavioral variation suggests that it is now possible to specify with greater precision than ever before the structural basis of behavior. In organisms whose chromosomes are well mapped against their morphology, the chromosome map will suggest what structures intervene between a given chromosome and the behaviors with which it correlates. Furthermore, the chromosome-behavior correlations should contribute to the chromosome map, since each behavior will, in turn, suggest the structures that are involved in its execution.

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## Reversal of Phenylalkylamine Tachyphylaxis by Norepinephrine

*Abstract.* Since the responses to "neurosympathomimetic amines" are reduced in the reserpinized animal and restored by norepinephrine administration, it was postulated that norepinephrine might also affect the development of their tachyphylaxis. We found that norepinephrine infusion restored, at least partially, certain tachyphylactic responses to amphetamine or ephedrine and fully prevented the development of tachyphylaxis to tyramine.

The class of drugs known as neurosympathomimetic amines (*1*) exhibit tachyphylaxis. These amines, for example ephedrine, amphetamine, or tyramine, which produce greatly reduced effects or no effects in chronically reserpinized animals, have been shown to release norepinephrine; the administration of norepinephrine in such animals may restore the responses to these amines (*2*). We showed that the pressor response to ephedrine, abolished by large amounts of cocaine, could be restored by the infusion of norepinephrine itself or by agents which act as norepinephrine-sparing compounds (*3*). Therefore, it was postulated that the loss of norepinephrine from critical sites might be the etiological factor in the development of neurosympathomimetic amine tachyphylaxis. Experiments discussed below were devised to test this hypothesis.

Four parameters were measured in male cats, weighing from 2 to 4 kg, anesthetized with $\alpha$-chloralose (80.0 mg/kg, intraperitoneally) and pretreated with atropine sulfate (2.0 mg/kg, intravenously) and with polygalacturonic acid glycoside (Mepesulfate, 10.0 mg, total dose): (i) mean arterial blood pressure, (ii) heart rate, (iii) tonus, and (iv) contractions of the nictitating membrane. Blood pressure from the carotid artery was recorded with a Sanborn transducer (No. 267B), and the nictitating membrane responses with Grass transducer (No. FT03) on a Sanborn four-channel polygraph. One femoral vein was canulated for the injections of the neurosympathomimetic amines, and the other for norepinephrine infusions. The nictitating membrane was set up for recording after removal of the lens.

To ascertain the rate and extent of tachyphylaxis development, control experiments were performed in six cats for each neurosympathomimetic amine studied (*4*). Hourly intravenous injections of *dl*-ephedrine sulfate (1.5 mg/kg) or *dl*-amphetamine sulfate (0.35