Persistent genotypic differences in mouse activity under unusually varied circumstances¹

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Abstract

Twenty-one comparisons of activity differences among C57, DBA and C3H strains of mice have appeared over the past 11 yr. Despite wide variations in the use of substrains, experimental techniques and testing devices, strain rank order remains statistically stable. Such uniformity may indicate well-buffered physiological correlates.

Problem

The changeable nature of gene action is well known to behavior geneticists. Generally three modes of variation are recognized: (1) differential gene expression contingent on the prevailing genotypic background; (2) diverse canalization of gene action due to environmental pressures during development; and (3) varied responses depending on the level and kind of environmental stimulation. Such diversity of response demonstrates unequivocally gene-environment interaction, but at the same time provides an array of individual variation often difficult to work with experimentally and conceptually. This report summarizes data which are exceptional in that phenotypic differences in behavioral activity among three inbred strains of mice tend to persist under all three sources of variation noted above.

Method and Results

The increasing use of inbred strains of mice for behavioral work made it possible to compile and compare activity data from a variety of sources and conditions of measurement. Available data on spontaneous activity for the C57, DBA and C3H strains are shown in Table 1. For each of the 21 independent comparisons, the relative standings of the three strains are indicated. The strain showing the greatest amount of activity is arbitrarily assigned the score of 100 and the two other strains are adjusted in value to show their positions relative to the highest strain. In three cases, unequal numbers of substrains within major strain lines were tested (Bruell, 1964a,b; Thompson, 1953); consequently, substrain scores were averaged and used as single scores. Short latencies of response, where applicable, are considered equivalent to high activity.

Sources of animal, experiential and experimental variation are greater than most planned experiments possibly could be. Eight substrains of the C57 line were used, some separated from the original line for nearly 44 yr. Four substrains of the DBA line were tested, some which diverged from the parental stock 35 yr. ago. Six substrains of the C3H stock were observed, again

in some cases, with separate breeding histories extending over 35 yr. Experiential and experimental variations are just as great. Some investigators applied early noxious stimulation to their animals (Lindzey et al, 1960, 1963); others used alcohol fuming immediately prior to testing (Schlesinger et al, 1962); and one altered population density by 20-fold (Thiessen, 1964). Moreover, the investigators worked on the East and West coasts and the Midwest of the United States over a period of 11 yr. Both male and female mice were tested, ranging in age from 30 to 150 days and six different kinds of testing devices were used. Observations of activity varied in length from 3 to 200 min.

Despite wide variations in animal nomenclature and experimental design, relative strain differences tend to be maintained, with the order of activity from high to low, C57, DBA and C3H. For the 21 comparisons, Kendall's Coefficient of Concordance (W) is .59 ($p < .001$) for the three strains, .38 ($p < .001$) for the C57 and DBA lines, .18 ($p < .10$) for the DBA and C3H lines and 1.00 ($p < .001$) for the C57 and C3H strains. The reversals of the C57, DBA and C3H rank order are accounted for primarily by reversals between the DBA and C3H strains. In no instance does the C3H strain outscore the C57 strain. It would appear that the conditions of testing generally separate the strains in the same order. The obvious exceptions are the data by Lindzey et al (1960, 1963), where DBA's show the shortest latency to emerge from a stovepipe. It can be argued that emerging from one environment into another

Table 1. Relative Position of Three Strains of Mice on Various Tests of Spontaneous Activity

Activity Measure	Mouse Strain			Reference #
	C57	DBA	C3H	
Rotating Wheel	100	97	93	1
Multiple-Section Maze	100	93	71	2
Washtub	100	68	49	4
Washtub	100	81	53	4
Washtub	100	41	62	5
Washtub	100	58	73	5
Washtub	100	94	98	5
Washtub	100	56	72	5
Modified Open-Field	100	75	37	10
Modified Open-Field	100	89	28	6
Modified Open-Field	100	60	32	8
Modified Open-Field	100	53	58	8
Modified Open-Field	100	95	61	8
Hole-in-Wall	100	65	53	8
Hole-in-Wall	100	33	35	8
Hole-in-Wall	100	30	14	8
Hole-in-Wall	100	24	12	9
Stovepipe	34	100	23	4
Stovepipe	38	100	18	4
Stovepipe	51	100	49	5
Stovepipe	50	100	49	5

is a matter quite different from the other situations where the animal simply locomotes from one part of an apparatus to another. If these four studies are treated separately, concordance for the remaining conditions jumps to .77 ($p < .001$) for the three strains and 1.00 ($p < .001$) for the C57 and DBA strains. The data for stovepipe emergence remain internally consistent.

Discussion

With increasing frequency investigators point to the uniqueness of any behavior and to the complexity of gene-environment interactions. Coupled with this is the growing feeling that each unit of behavior must be studied separately and may only have relevance within the context in which it is studied (Hirsch, 1962). However, multiple instances of stable activity differences between strains of mice suggest that in some instances gene-environment interactions are minimal and that well-buffered physiological systems underlie different levels of behavior. The 21 independent comparisons of spontaneous activity between the C57, DBA and C3H strains involve at least 11 major differentiating characteristics. Yet rank order separation of strains remains fairly stable, despite breeding separation of the sublines known to affect other genetic differences (Staats, 1964) and despite a variety of experiential and testing differences. Separation is more uniform when emergence tests are considered separately. The latter tests may involve more than activity per se, since animals must move between highly distinctive environments. Differences in activity are also more uniform between the C57 strain and the other two strains than between the DBA and C3H strains. This may be accounted for by the fact that the C57 lines have an origin distinct from that of the other strains, whereas the C3H lines originated in 1920 from a cross between Bagb albino and DBA mice. Thus the C3H and DBA strains probably share genes in common relevant to activity.

The constancy of gene action under very general conditions may afford a behavioral model for the study of physiological correlates that influence activity independently of specific conditions of testing.

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Note

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