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Response to 30 Generations of Selection for Open-Field Activity in Laboratory Mice

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High and low lines resulting from 30 generations of bidirectional selection for open-field activity have nonoverlapping distributions and more than a thirtyfold difference in mean activity. Open-field defecation scores of low-active lines are approximately 7 times higher than those of high-active lines, substantiating earlier reports of a large, negative genetic correlation between these characters. Since the selection experiment is replicated, other variables which are found to be reliably different among the high, control, and low lines are likely to be causally related to open-field activity; thus these selected lines of mice may be of use to other investigators.

KEY WORDS: open-field behavior; selection; mice; activity; albinism.

INTRODUCTION

Although selection studies were undertaken early in the history of behavior genetics (see DeFries, 1967) and continue to serve as a powerful tool for the genetic analysis of behavioral characters (DeFries and Plomin, 1978), relatively few long-term selection experiments have been reported. The primary objective of the present communication is to describe the response to 30 generations of selection for open-field activity in laboratory mice (*Mus musculus*).

A large-scale genetic analysis of open-field behavior in mice was initiated by the senior author in 1964. As a major part of this study, bidirectional selection (with replication and controls) for open-field activity was

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undertaken. The rationale for the design of the experiment and the response to 20 generations of selection have been previously reported (DeFries *et al.*, 1974).

METHOD

Before the selection experiment was begun, open-field behavioral data were obtained on 2641 mice, including members of two highly inbred strains (BALB/cJ and C57LB/6J) and their derived F_1, backcross, F_2, and F_3 generations. Forty litters from the F_3 generation constituted the foundation population for the selection experiment. Ten F_3 litters were chosen at random, and the most active male and female and the least active male and female from each litter were selected to become progenitors of two selected lines (H_1 and L_1). Progenitors of two replicate lines (H_2 and L_2) were identified in the same manner from ten other F_3 litters. A male and a female from each of ten additional litters were selected at random to serve as progenitors for one control line (C_1), and those of the replicate control line (C_2) were chosen in the same manner from the remaining ten F_3 litters. High-active, low-active, and control mice were then mated at random within line to produce offspring representing the first selected generation (S_1).

In subsequent generations, the most active male and female were selected when available from each litter in lines H_1 and H_2, whereas the least active male and female were chosen in lines L_1 and L_2. In C_1 and C_2, one male and one female were randomly chosen from each litter by lots. These animals were retained for breeding and were mated at random within line. With ten mating pairs per generation in each of the six closed lines and within-litter selection, the expected increase in the coefficient of inbreeding is less than 1.5 per cent per generation.

The total number of mice composing generations S_1 through S_{30} (tested between June 1966 and November 1976) was 14,184. The numbers tested in individual lines each generation ranged from 44 to 108.

Behavioral Testing

Throughout the entire study, each animal was tested for 3 min on each of 2 consecutive days at 40 ± 5 days of age in the same automated open field. This field is square (91.44 by 91.44 cm) and constructed of plexiglas painted white. It is illuminated from above by two 20-W fluorescent tubes which provide incident light levels of 48 ft-c. Two sets of light sources are located on adjacent sides of the field and directed through five equally spaced holes and infrared filters to photoconductive cells on the opposite sides. This arrangement results in a grid of light beams which partitions the floor of the field into 36 squares, 15.24 by 15.24 cm each. Interruption of photobeams activates counters which record activity scores.

At the beginning of each test, the mouse was placed in a plexiglas cylinder in one corner of the field. The mouse was then released from the cylinder, and the counters were activated for a 3-min period. After the mouse was removed from the field at the conclusion of the test, the number of fecal boluses deposited in the field was recorded. The floor was then rinsed with tap water and wiped with a clean paper towel.

The total number of light beams interrupted during the two test periods and the total number of boluses are used as each animal's activity and defecation scores. In earlier reports (DeFries *et al.*, 1966; DeFries and Hegmann, 1970), square root transformations of these data were employed. However, various statistical analyses have been found to yield highly similar results when applied to either raw or transformed data. Because raw data are more readily interpreted, only untransformed data will be reported in the present communication.

RESULTS AND DISCUSSION

Preliminary Analysis

Quantitative genetic analyses of transformed data from the inbred parental strains and their derived F_1, backcross, F_2, and F_3 generations were previously reported by DeFries and Hegmann (1970). Group averages based on the raw data are presented for the first time in Fig. 1. Means were calculated separately for males and females within the various generations and reciprocal-cross mating classes and were then averaged to yield these unweighted means. It may be seen that there is about a tenfold difference in mean activity between the two highly inbred strains and that the means of the derived generations are intermediate. The mean of the F_1 generation exceeds that of the segregating F_2 and F_3 generations, indicating some directional dominance for activity. There is approximately an eightfold difference in mean defecation scores between the two inbred strains and a pronounced negative correlation with activity across generations.

Activity Response

Mean open-field activity scores of the six closed lines are presented in Fig. 2. It may be noted that the response to selection for open-field activity

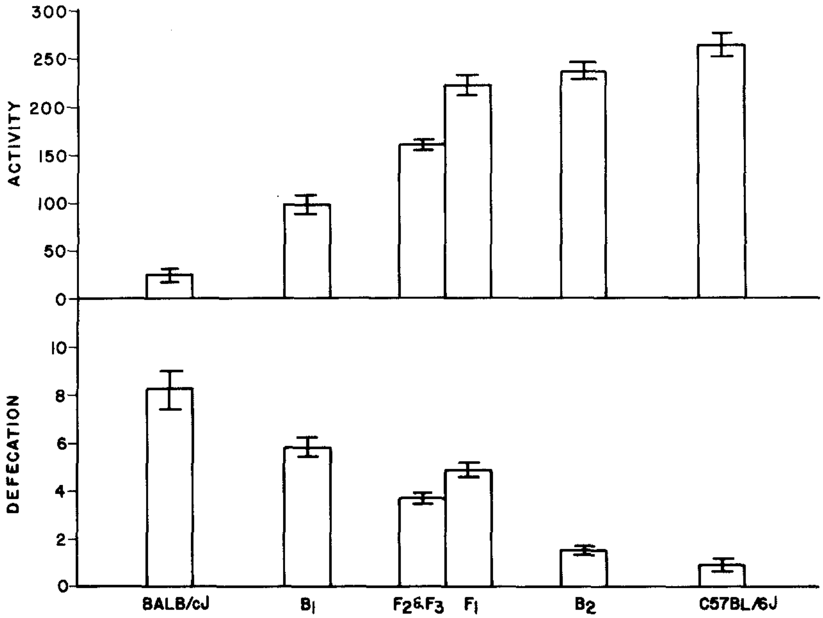

Fig. 1. Mean open-field activity and defecation scores (± twice the standard error) of BALB/cJ and C57BL/6J mice and their derived F_1, backcross (B_1 and B_2), F_2, and F_3 generations. Sample sizes were as follows: BALB, 64; B_1, 257; F_2 and F_3, 1478; F_1, 415; B_2, 315; and C57BL, 112.

has continued through generation S_{30}. After 30 generations of bidirectional selection, H_1 and H_2 have mean activity scores more than 30 times higher than those of L_1 and L_2. This difference is almost 3 times greater than that observed between the inbred parental strains (BALB/cJ and C57BL/6J), which are well known for their considerable difference in open-field behavior. Thus this character is almost certainly influenced by genes at many loci. The response to selection under the conditions of this study is highly reliable, as indicated by the remarkable similarity of the replicate selected and control lines after 30 generations of selection.

Although the response of the high and low lines was symmetrical through generation S_{20}, an asymmetrical response to selection occurred during the last ten generations. In S_{30}, the deviation of the mean activity of the high lines from controls is 352, whereas that of the low lines from controls is 237. This is apparently the result of a "floor effect," due to the impossibility of obtaining activity scores less than zero. The existence of this floor effect is obvious in Fig. 3, which summarizes the distributions of the high and low lines at five-generation intervals. Scores of individuals from replicate lines are grouped for this figure, and the unweighted mean of the two control lines is indicated by an arrow. It may be seen that there is a marked "piling up" of scores at the lower end of the distribution for the low line which becomes progressively more pronounced during the course of selection. The gradual separation of the distributions of the high- and low-active lines is also evident. By S_{30}, the distributions are nonoverlapping. In the case of the high lines, there is no evidence for an approach to a "selection limit" (Falconer, 1960).

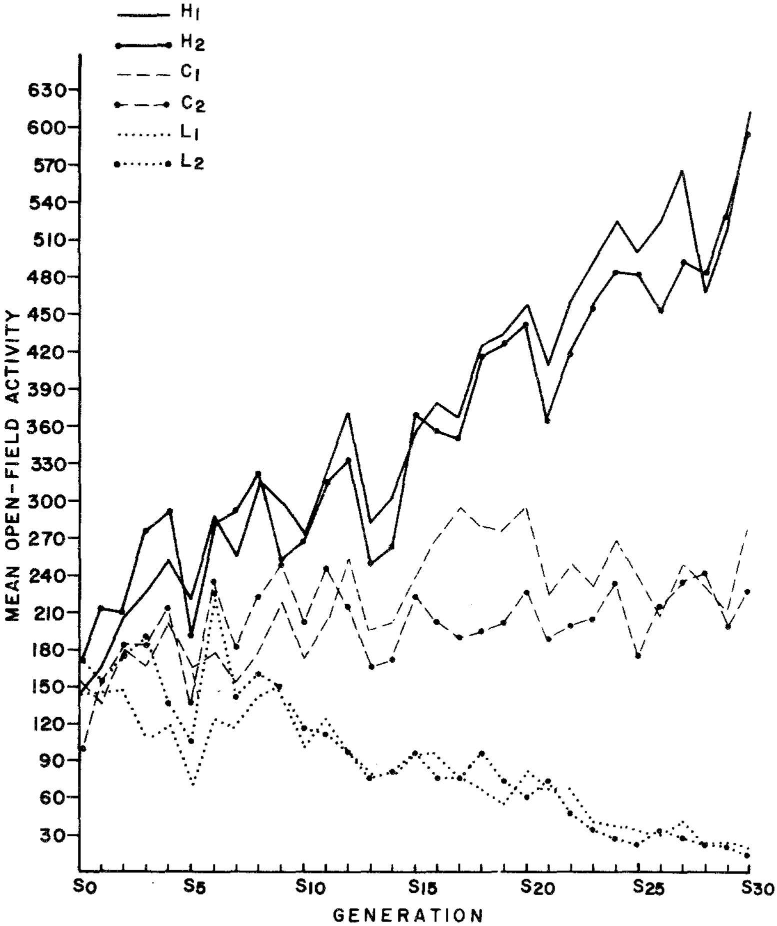

Fig. 2. Mean open-field activity scores of six lines of mice, two selected for high open-field activity (H_1 and H_2), two selected for low open-field activity (L_1 and L_2), and two randomly mated within line to serve as controls (C_1 and C_2).

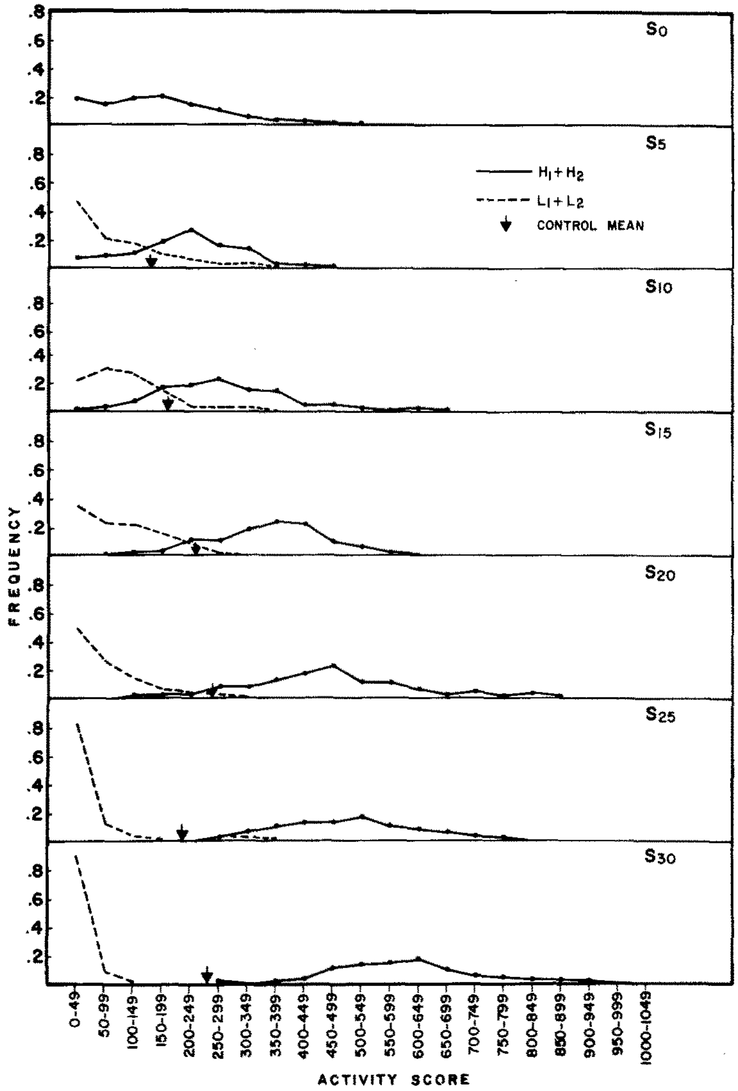

Fig. 3. Distributions of activity scores of lines selected for high and low open-field activity. Average activity of controls each generation is indicated by an arrow.

Defecation Response

From the unweighted mean defecation scores presented in Fig. 4, it may be seen that a sustained, correlated response to selection has also occurred. After 30 generations of selection, average defecation scores of L_1 and L_2 are approximately 7 times higher than those of H_1 and H_2. As may be noted, this correlated response is highly asymmetrical. The existence of a floor effect for this character is clearly evident in Fig. 5. In spite of this effect, the distributions of defecation scores for the high- and low-active lines have progressively diverged so that very little overlap remains by generation S_{30}. This correlated response to selection substantiates previous

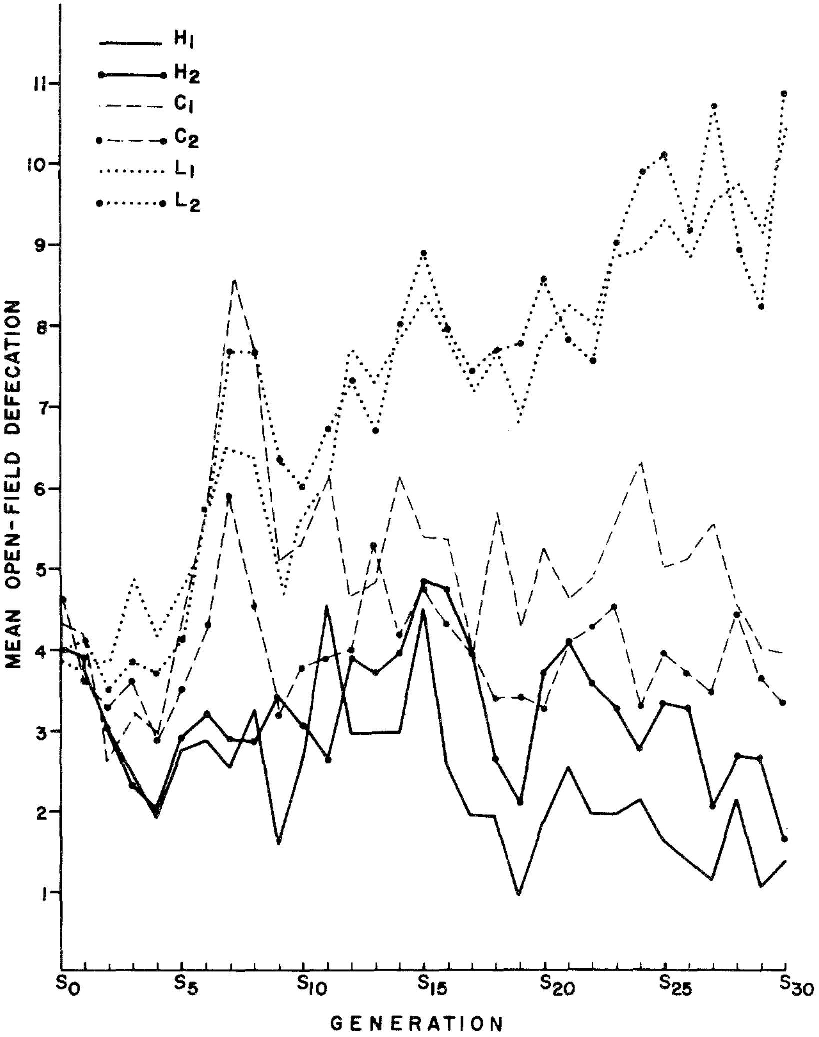

Fig. 4. Mean open-field defecation scores of six lines of mice, two selected for high open-field activity (H_1 and H_2), two selected for low open-field activity (L_1 and L_2), and two randomly mated within line to serve as controls (C_1 and C_2).

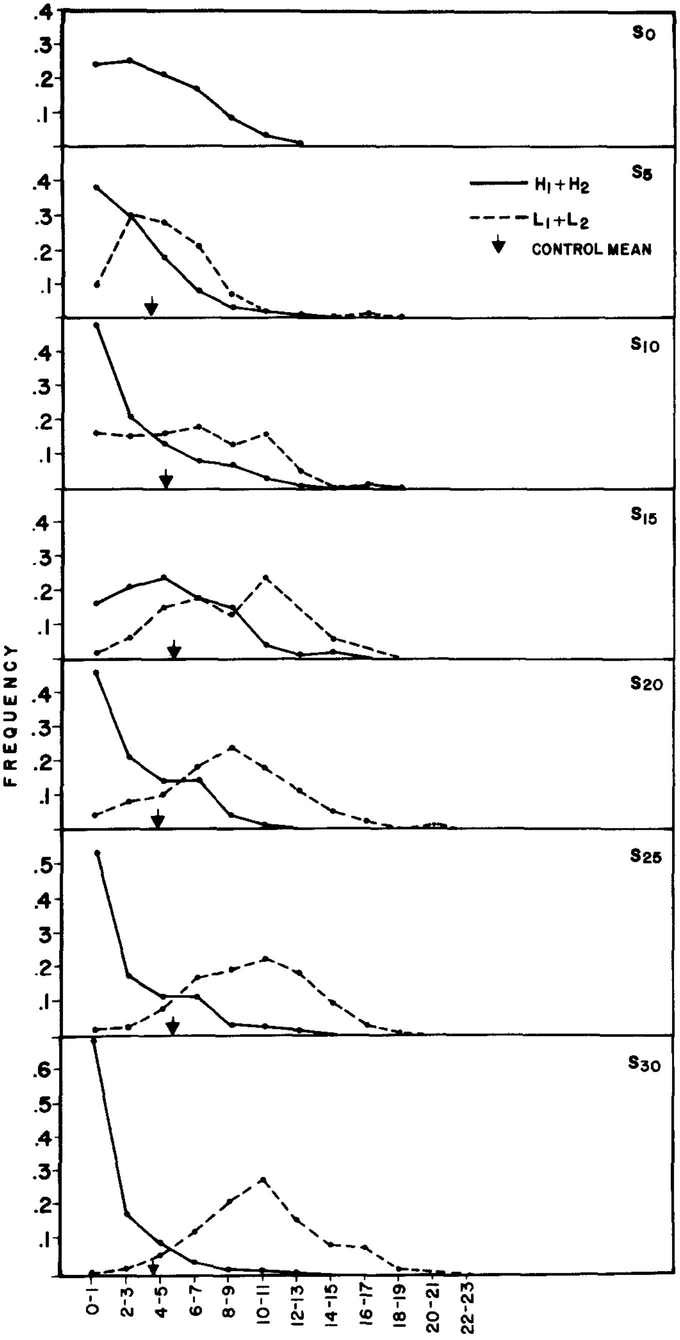

Fig. 5. Distributions of defecation scores of lines selected for high and low open-field activity. Average defecation score of controls each generation is indicated by an arrow.

evidence that a large, negative genetic correlation exists between open-field activity and defecation (DeFries and Hegmann, 1970) and indicates that these two characters are influenced by many of the same genes.

Albinism

The frequency of albinism in the six lines as a function of selection is shown in Fig. 6. As expected, the frequency of this autosomal recessive con-

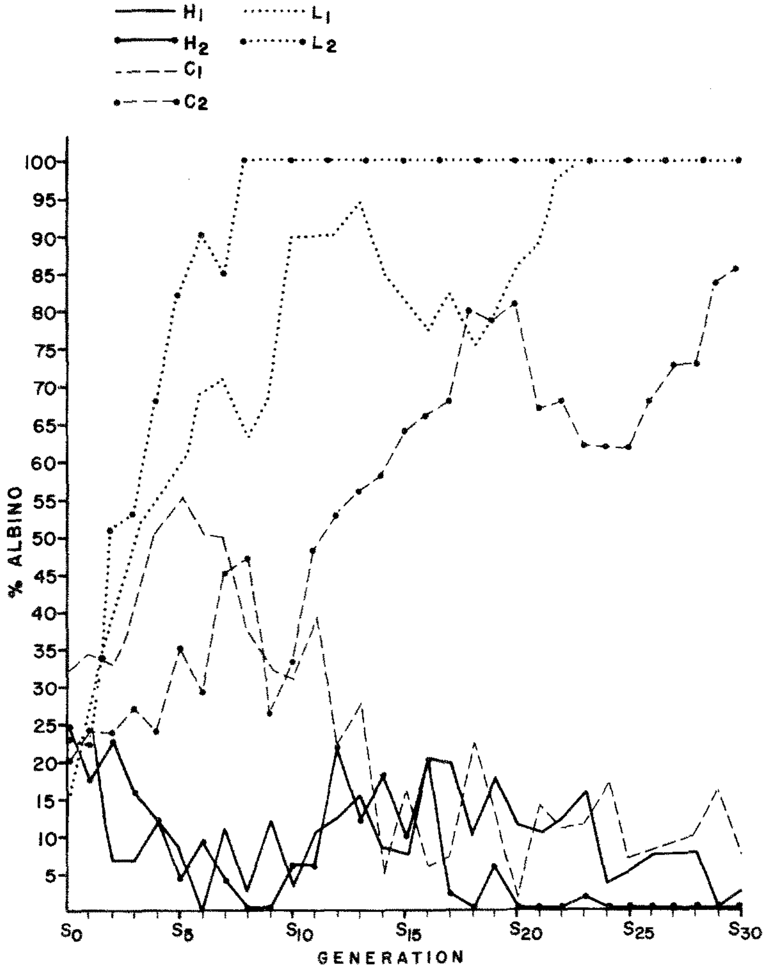

Fig. 6. Frequency of albinism in six lines of mice, two selected for high open-field activity (H_1 and H_2), two selected for low open-field activity (L_1 and L_2), and two randomly mated within line to serve as controls (C_1 and C_2).

dition is approximately 0.25 for all lines in S_0; however, a rapid divergence occurred as selective breeding progressed. Fixation for albinism occurred in L_2 during generation S_8 and in L_1 during generation S_{23}. Selection has apparently eliminated the albino allele from H_2 and has greatly decreased its frequency in H_1. Albinism results in lower open-field activity scores (DeFries *et al.*, 1966); thus selection within H_1 and H_2 during the latter part of this study was being exerted against a rare recessive. Since such selection is relatively impotent, it is possible that H_1 could continue to segregate for albinism for some time.

Quite unexpectedly, a marked divergence in the frequency of albinism between C_1 and C_2 also occurred. Since no selection for open-field activity was applied in these lines, these changes are likely due to stochastic processes (DeFries *et al.*, 1974).

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Although a continuing response to selection for open-field activity occurred across a time span of 30 generations, selection has been suspended and the lines are currently being maintained by random matings within lines. The high-active, control, and low-active animals are markedly different in psychologically relevant behaviors (Archer, 1975; Broadhurst, 1975, 1976). Thus these replicated lines may be of interest to other behavior geneticists. If any investigator wishes to obtain samples of these mice, please address inquiries to the senior author.

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