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SELECTION FOR AGONISTIC BEHAVIOR
IN WILD FEMALE MUS MUSCULUS

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ABSTRACT

Artificial selection was used to establish different levels of agonistic behavior in laboratory-reared wild female Mus musculus. Preliminary investigations indicated that female agonistic behavior could be easily induced and reliably measured in the laboratory.

The original population consisted of wild-trapped Mus musculus from two different rural locations near Bowling Green, Ohio. A within-family selection design with replicated high and low lines and two non-selected control lines was employed. Thus, a total of six lines, each containing ten breeding pairs were tested in each of four selected generations. Females only were tested at eight weeks of age on two consecutive days. Testing consisted of placing a C57BL/6 female mouse in the home cage of the wild mouse for seven minutes or until an attack occurred. The wild females were rated on a five-point scale for agonistic behavior. The sum of the scores over the two test days was the criterion for selection.

By the fourth Selected Generation, the responses of the high and low lines had diverged in the expected directions and appeared to be symmetrical with respect to the control lines. One way analyses of variance indicated reliable differences among high, low, and control lines in the Second, Third, and Fourth Generations. The realized heritability was .49 for the combined high lines, and .38 for the combined low lines. When analyzed separately, the realized heritabilities for H_1 and H_2 were .55 and .43 respectively. Separate low lines analyses yielded $H^2 = .32$ for L_1 and $H^2 = .35$ for L_2 . It was concluded that female agonistic behavior is influenced by genotype, and that within a closed population, the level of this behavior can be manipulated through the use of artificial selection.

The study was successful in establishing line differences in female agonistic behavior, and these differences were unrelated to variations in weight or maternal competence. It was proposed that female agonistic behavior might be related to maternal defensive behavior, thus indicating an adaptive function for female agonistic behavior in a population of wild mice. Additionally, it was suggested that the lines established in the present study could be used in future research investigating physiological correlates of agonistic behavior and possible relationships between male and female agonistic behavior.

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SELECTION FOR AGONISTIC BEHAVIOR IN WILD FEMALE MUS MUSCULUS

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The artificial selection study has been shown to be an effective tool for studying the inheritance of behavior. A review of the literature on the use of the artificial selection study in behavior genetics is found in Appendix A. In the present study, the artificial selection technique was used to establish different levels of agonistic behavior in a laboratory-reared population of wild female Mus musculus. Agonistic behavior in male mice has been extensively studied, and is known to be influenced by genotype. (See Appendix B for a review of the literature on the mechanisms controlling agonistic behavior in mice.) However, relatively little is known about agonistic behavior in female mice. Early investigators reported finding no agonistic behavior in females when tested under the same conditions as males. Fredericson (1952) reported that while females could be induced to fight in competition over food, they did not engage in what he referred to as "spontaneous aggression" or fighting which occurred with no apparent reason. However, the fighting involved in competition over food was qualitatively very different from the active biting and wrestling usually observed in male agonistic behavior.

White et al. (1969) found that female Swiss-Webster mice could be induced to fight if the opponent mouse was smaller than the tested mouse. Weltman et al. (1968, 1972) found that female albino mice (CFW's) would become highly aggressive toward other female mice in paired-encounter

situations after being isolated for prolonged periods of time.

Another line of research on agonistic behavior in female mice deals with the defense of the young by a lactating female. Gandelman (1972) stated that hormones associated with lactation (prolactin) are probably involved in this form of aggression. An intruder mouse is not attacked if the pups are 14-20 days of age, or if the pups are removed from the nest at least five hours prior to testing. A drop in prolactin has been found to correspond with those two conditions.

St. John and Corning (1973) tested four different inbred strains and a heterogenous stock of mice in a maternal defense test situation. Both parents of a litter were tested on the sixth and seventh day postpartum, either in the home cage with the mate and litter removed, or alone in a strange cage filled with fresh bedding. The first test consisted of placing a strange adult male of the heterogenous stock into the cage. The strange male was restrained by the tail. The animals were observed for two minutes or until an attack occurred. The largest differences in percentage of attacks was found among different strains rather than between sexes. That is, lactating females of highly aggressive strains were more likely to attack the intruder than lactating females of relatively unaggressive strains. The similarity of performance of males and females of the same strain possibly indicates that maternal defensive aggression and male agonistic behavior are not completely unrelated in terms of the central mechanisms involved.

Ebert (1972) found that 25 percent of a population of laboratory-reared female offspring of wild mice would fight in a paired encounter situation. In a second population of wild-trapped mice which served

as the parental generation for the present study, it was found that over 21 percent of the females would attack a 657BL/6 female mouse placed in the home cages of the wild mice. These findings suggest that the domestication process may have reduced, if not eliminated, agonistic behavior in female mice.

Wild Mus musculus have not been used to any great extent in behavior-genetics research. Dawson (1932) analyzed the inheritance of wildness and tameness in mice. He defined wildness as having a fast time in running to the end of a 22-foot runway. During the course of his lengthy analysis, he systematically selected the fastest mice from his wild-trapped population, and the slowest mice from his domestic population. The wild mice did not respond to the selection process--presumably because they had already reached an asymptote. The domestic mice responded in the expected direction. This is an early and crude selection experiment, and he did not do bidirectional selection in both lines.

Smith (1972) attempted a more thorough behavior-genetic analysis comparing scores of wild and inbred mice on a test battery of several tasks commonly used in psychological research. The test battery consisted of an open field test, an activity wheel, an emergence test, an avoidance task, and an underwater escape task. In general, Smith found that the wild mice were characterized by poor avoidance learning, high activity, long emergence latencies, and extensive freezing behavior.

In the Ebert (1972) study mentioned above, offspring of wild-trapped mice and two inbred strains of mice were compared for agonistic behavior in a paired encounter situation. It was found that the wild

mice fought more than domestic mice under these conditions. The results were the same for both sexes. None of the domestic females fought. Hence it appears that there may be considerable behavioral differences between wild and domestic mice.

In the present study, agonistic behavior in wild female mice served as the basis for artificial selection. Preliminary investigation and the 1972 study indicated that this behavior could be easily induced and reliably measured in the laboratory. It was also observed that this behavior was variable within the laboratory population of wild females. It was further assumed that there would be much genetic variability in a wild population, and that this variability would make a wild mouse population especially suitable for the selection technique.

Since reports of agonistic behavior not involving maternal defense are rare for mammalian females, this study is unique in that it involves a systematic investigation of a phenomenon that was previously supposed to occur infrequently if ever. Also, examining the inheritance of agonistic behavior in females may lead to a better understanding of the adaptive function of this behavior for the species and the physiological correlates of this behavior (Appendix B). This study is also unique in that it represents the only attempt (Besides Dawson's 1932 crude attempt) to apply the behavior-genetic technique of artificial selection to a laboratory-reared population of wild Mus musculus. Single sex selection studies of males are fairly common (Appendix A), but this is the first time that females only have served as the selected sex.

METHOD

Subjects

The original population consisted of wild-trapped Mus musculus from two different rural locations near Bowling Green, Ohio. Mice were trapped during the months of September, October, and November, 1972. The two locations were far enough apart to insure sampling from at least two demes. This was done to increase the genetic variability of the original population. Offspring of some of the wild-trapped mice (usually those of females who were pregnant when trapped) were added to this population. This procedure was necessary in order to obtain a sufficient number of mice. More females than males were added in this manner, since females were more difficult to trap. Thus, out of the 60 mice making up the original population, 14 females and 23 males were wild-trapped, and 16 females and seven males were born in the laboratory. The 23 mice born in the laboratory represented eight different litters. Four of the mothers of these litters produced subsequent litters which were tested in the parental generation.

All mice were housed in standard laboratory cages (Carworth's Isosystem). These cages were made of clear plastic with wire tops and measured 15.2 x 25.4 x 12.7 cm. They were placed side-by-side on racks; and visual, auditory, and olfactory cues could be transmitted between cages. The temperature ranged from 74 to 80 degrees Fahrenheit with approximately 32 percent humidity. All mice had an ad lib supply of laboratory chow and water. The cage floors were covered with Bed-O-Cobs bedding. Cages were changed when litters were toe-clipped at seven days of age for identification, and when the litters were

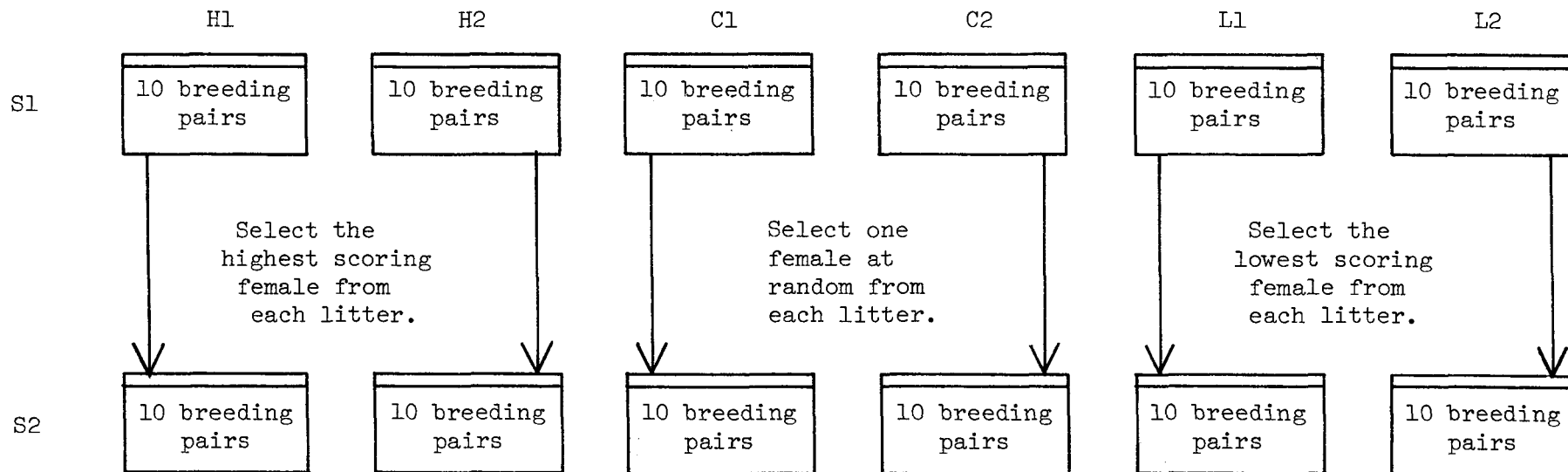
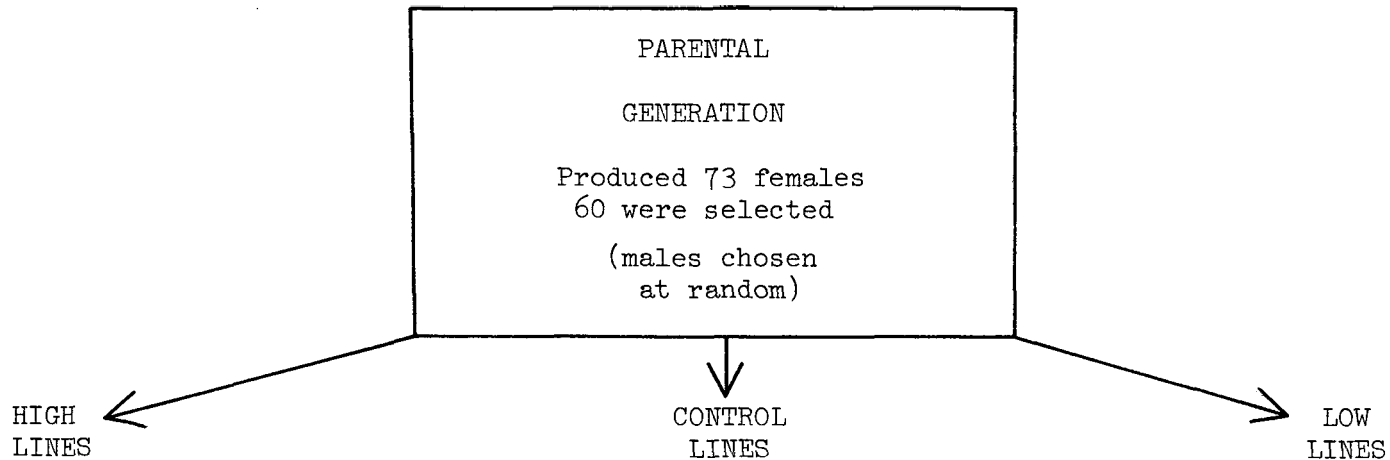
weaned. Litters were housed with both parents until weaning which occurred at 28 days of age. Female offspring were caged singly at this time. Males from each litter were housed together.

Design

A within-family selection design with replicated high and low lines was employed. There were also two non-selected control lines, giving a total of six lines, each of which contained 10 breeding pairs in all generations. DeFries (1967) recommended this type of design for several reasons. The use of replicated lines enables one to compare variation between lines selected in the same direction. Also, when correlated characters are examined, the presence of the same relationships in replicated lines increases one's confidence that these relationships are not fortuitous. The use of non-selected control lines enables one to detect any unusual environmental fluctuation within a particular generation. The within-family design serves both to decrease the amount of inbreeding and to control for maternal effects. According to McClearn and DeFries (1973), this design should result in an increase in the inbreeding coefficient of only approximately 2.5 per cent per generation ($\Delta F \approx \frac{1}{8N_{\text{males}}} + \frac{1}{8N_{\text{females}}}$, and $N = 10$ for both males and females).

The Parental Generation (P) consisted of the tested female offspring produced by the original population. A total of 73 female offspring were tested. Of these mice, 60 were selected to become the mothers of the First Selected Generation (S_1). These mice were assigned to high (H_1 or H_2) lines or to low (L_1 or L_2) lines depending on their aggression scores. Remaining mice were assigned to control (C_1 or C_2) lines.

Figure 1. Schematic of selection procedure.



Males are chosen at random within each group, with the exception that no brother-sister matings are made.

This method of assignment meant that the values for females in the control groups were intermediate between the high and low lines (Figure 1). The restriction was made that only one female in a particular litter could be assigned to a particular line. These females were then mated to male offspring from the parental generation. These matings were done at random with the restriction that no brother-sister matings were made.

The subsequent selected generations for the high lines consisted of the highest scoring female from each litter paired with a male offspring from the same line, but from a different litter. In a similar manner, the lowest scoring females were assigned to the subsequent selected generations for the low lines. For the control lines, a female was chosen at random (a random numbers table was used) from each litter. Males in the low and control lines were assigned in the same manner as for the high lines. Extra males and females from some of the larger litters in all groups were saved and mated so that the lines could be expanded to 10 families if any of the originally assigned pairs failed to reproduce.

Procedure

Females were tested on two consecutive days at eight weeks of age. On a test day the females' cages were moved into the testing room. Lights in the testing room were dimmed, and a small lamp was used to illuminate the sink in order to minimize disturbance from movements of the experimenter. As each mouse was tested, her cage was placed in a 35.6 x 38.1 x 27.9 cm. sink, the cage top removed, and a plexiglas cover placed over the cage. A divider, also made of plexiglas, was

inserted through the slit in the cover, restricting the mouse to one-half of the cage area.

A C57BL/6 female mouse of approximately five weeks of age was then selected, marked on the tail with a felt tipped pen, and weighed. Preliminary work had shown that these mice could elicit fighting from wild females, but that they would never initiate an attack themselves. The use of these mice insured that any fighting behavior would be instigated by the wild females. The C57BL/6 was lowered into the unoccupied side of the cage of the wild mouse. Then, the experimenter raised the divider and began timing. If an attack was made by the wild mouse within seven minutes, the latency was recorded and the test was terminated. An attack was defined as biting including shaking or wrestling. Each mouse was rated on a modified five point version of Lagerspetz's (1964) scale for aggression. (See Figure 2) If no attack occurred by the end of seven minutes, the test was terminated and the C57BL/6 was removed. The wild mouse was weighed at the end of the trial, returned to her cage, and the wire top replaced. The rating scale scores summed over the two consecutive testing days, was the criterion for selection. Therefore, the range of possible scores for each mouse was from two to ten.

RESULTS

Because a within-family selection design was employed, the number of females tested in each group for all generations depended on the number of female offspring born (Table I). The means for all six lines on the aggression rating scale scores are plotted over all tested

Figure 2. Sample of aggression rating scale.

Selection Study

Mouse No. _____

Sex _____

Parents' Mating Designation _____

Birthdate _____

Testing Dates _____

	Day 1	Day 2
Latency to attach		
Occasional nosing (1.)		
Frequent nosing (2.)		
Frequent, vigorous nosing (3.)		
Tail rattling, following (4.)		
Slight wrestling, tail rattling (5.)		
Wt. of tested mouse		
Wt. of C57 Bl		

TABLE I

Number of females tested in all generations for each line.

Line	Generations			
	S ₁	S ₂	S ₃	S ₄
H ₁	28	24	26	25
H ₂	30	29	26	31
C ₁	14	20	15	24
C ₂	20	20	24	22
L ₁	24	22	27	40
L ₂	22	23	21	24
Total	138	138	139	166

generations (Figure 3). The high and low lines have diverged in the expected directions. By the Fourth Selected Generation, the response appears to be symmetrical with respect to the control lines. In the Second and Third Generations there is some overlap of the high and control lines. By combining the replicated high, low, and control lines, the picture is somewhat simplified (Figure 4). Again, the response of the high and low lines appears to be symmetrical with reference to the control groups by the Fourth Selected Generation.

One way analyses of variance were performed on each generation (Table II). Significant F ratios, indicating significant differences among high, low, and control lines, were obtained in the Second, Third and Fourth Generations. Within these generations, the Scheffé Test was used to compare all possible group mean differences (Table III). With only one exception, the low groups were significantly different from the high groups. With only one other exception, the low groups were significantly different from the control groups in the Second and Third Generations. In the Fourth Generation, the combined groups analysis shows all three groups to differ significantly from each other.

The variances of the six groups over the four selected generations were examined (Figure 5). There seems to be a trend toward decreasing variances in the two high lines, but not in any of the other lines.

The distributions of the rating scale scores for the Parental Generation, the combined high groups, the combined low groups, and the combined control groups of the Fourth Generation illustrates how the selection procedure has resulted in differential shifts in the distributions of scores for the high and low groups (Figure 6). Since

Figure 3. Mean aggression rating scale scores for all six lines, plotted over the four selected generations.

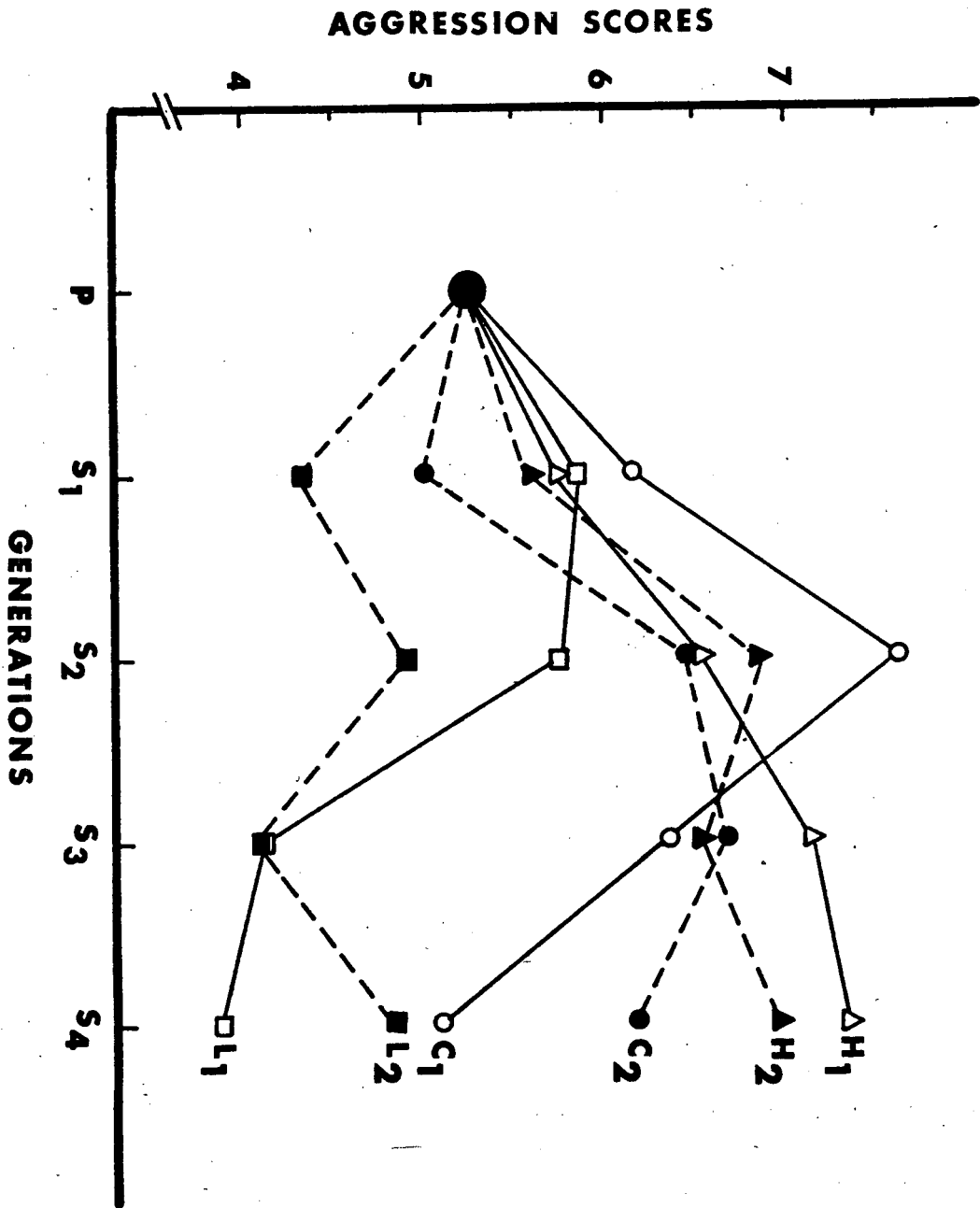


Figure 4. Mean aggression rating scale scores for combined replicated lines, plotted over the four selected generations.

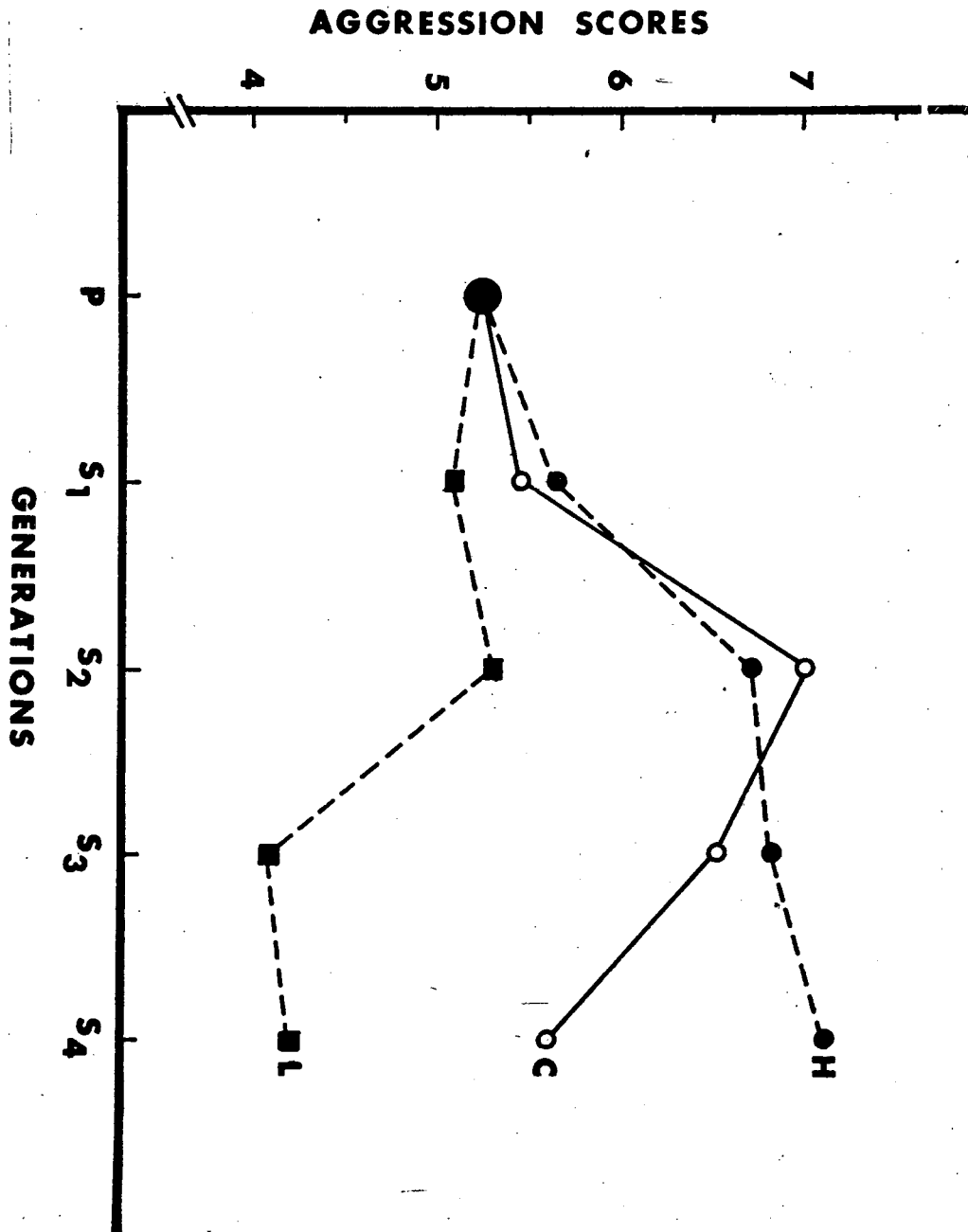


TABLE II

F-values obtained by one way analyses of variance of the rating scale scores for the high, low and control lines, calculated for the First through Fourth Selected Generations.

Generation	Combined Groups Analysis H, C, L	Separate Groups H ₁ , C ₁ , L ₁	Analysis H ₂ , C ₂ , L ₂
S ₁	.62 N.S.	.17 N.S.	1.59 N.S.
S ₂	7.60**	3.63**	5.78**
S ₃	22.66**	14.66**	9.59**
S ₄	23.85**	17.31**	6.22*

* $\underline{p} < .05$

** $\underline{p} < .01$

N.S. = not significant

TABLE III

Group mean differences analysed by the Scheffé test for all possible comparisons in the generations in which a significant F-ratio was obtained.

Comparison	S ₂	S ₃	S ₄
Combined Groups			
H - L	1.41*	2.75*	2.89*
H - C	-.30 N.S.	.36 N.S.	1.51*
C - L	1.71*	2.39*	1.38*

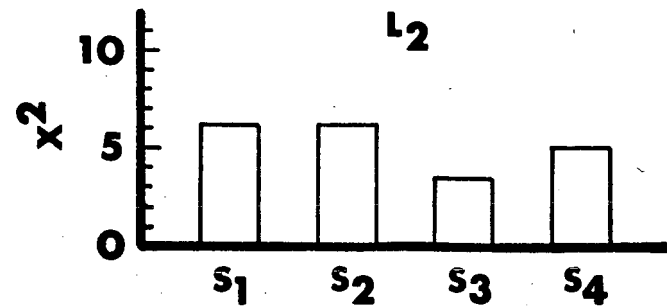
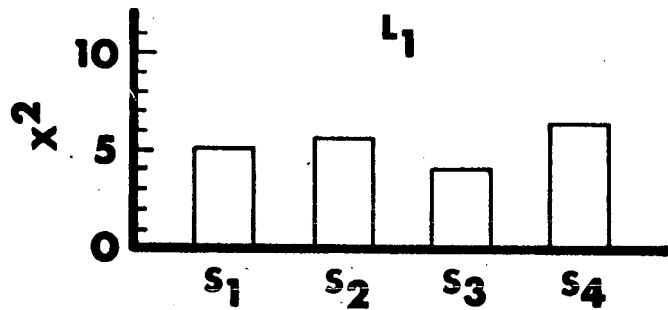
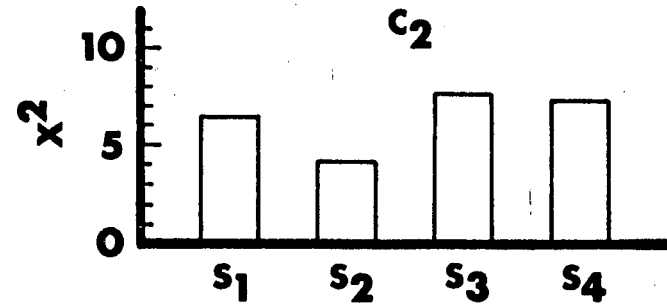
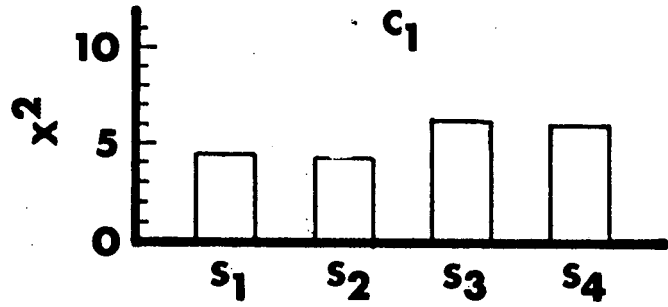
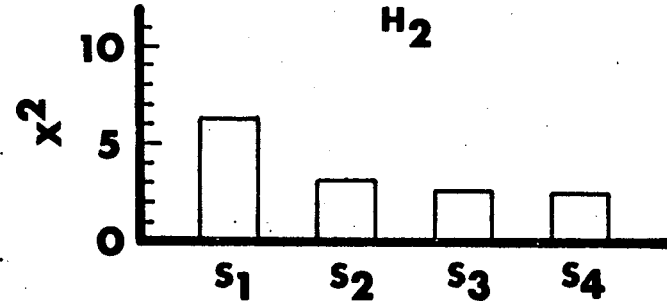
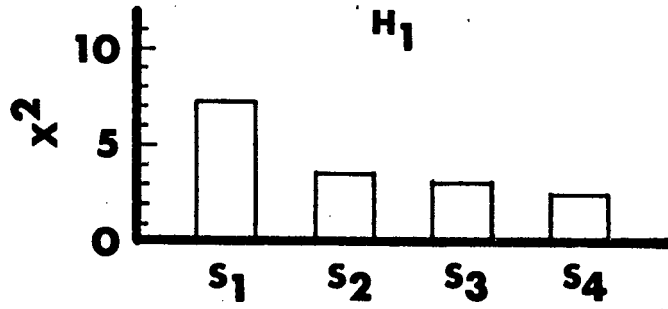
Separate Groups			
H ₁ - L ₁	.81 N.S.	3.04*	3.48*
H ₁ - C ₁	-1.06 N.S.	.82 N.S.	2.28*
C ₁ - L ₁	1.87*	2.22*	1.20 N.S.

H ₂ - L ₂	1.95*	2.44*	2.11*
H ₂ - C ₂	.41 N.S.	-.13 N.S.	.76 N.S.
C ₂ - L ₂	1.54 N.S.	2.57*	1.35 N.S.

* $\underline{p} < .05$

N.S. = not significant

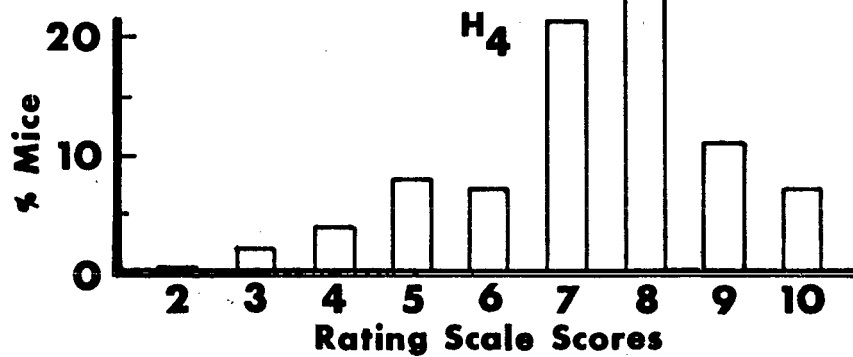
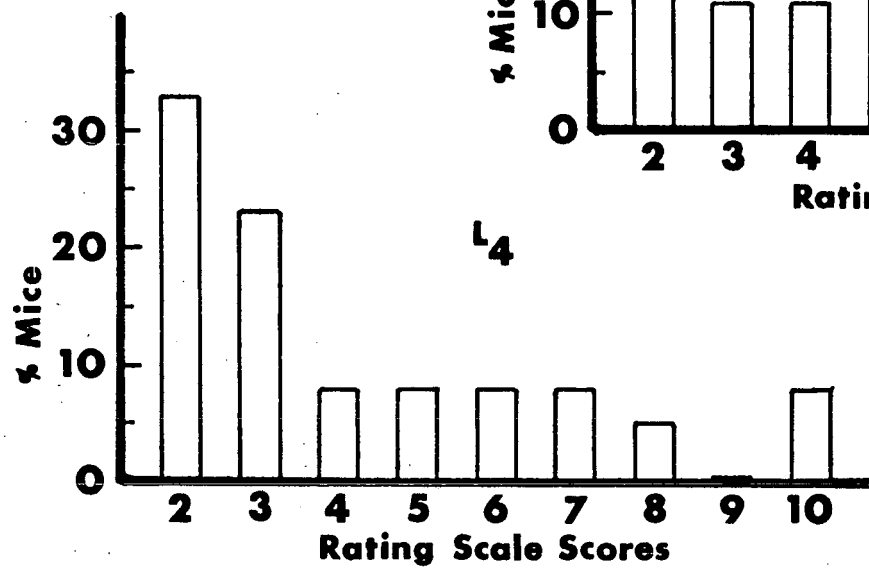
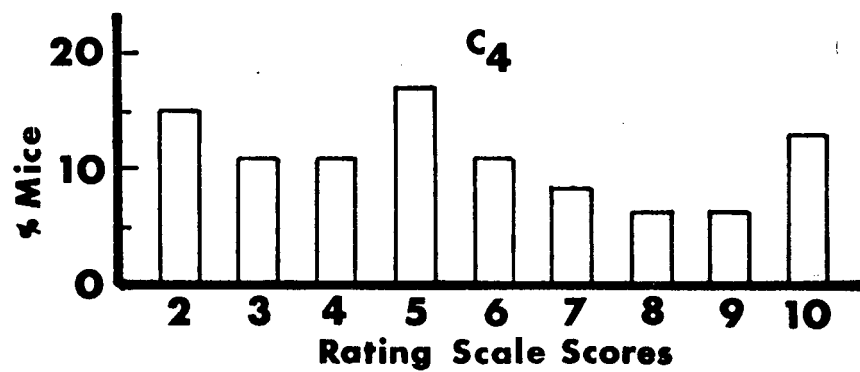
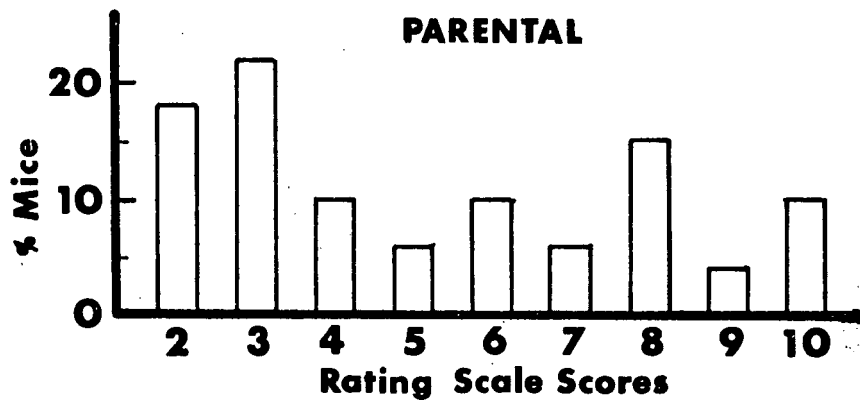
Figure 5. Comparison of variances within each line for all four selected generations.



GENERATIONS

GENERATIONS

Figure 6. Rating scale distributions based on the sum of scores obtained over the two days of testing.



these distributions are far from normal, a Chi-square analysis was done on the data (Table IV). In order to obtain sufficient numbers for the expected frequencies in each cell, the rating scale scores were divided into Low (scores 2, 3, and 4), Intermediate (scores 5, 6, and 7) and High (scores 8, 9, and 10) categories. The results of the Chi-square analyses are very similar to those obtained by analyses of variance (Table II) with only a couple of exceptions. The Chi-squares showed significance for the combined and H_2, L_2 analyses in the First Generation, whereas the F-test did not. In the Second generation, the F-test shows significant differences in the H_1, C_1, L_1 analysis. However, the Scheffé analysis (Table III) shows that this significance is not attributable to the H_1, L_1 comparison. These results agree with the Chi-square analysis in which the H_1, L_1 comparison for the Second Generation is not significant.

The scores of the S_1 Generation and the Parental Generation were used to calculate the regression of the daughters' scores on the mothers' scores. This procedure yielded a heritability estimate of .17 (Falconer, 1960). Subsequently, realized heritability was calculated for the four generations of selection. Since single sex selection was practiced, the realized heritability is equal to twice the quotient of the response to selection (R) divided by the selection differential (S) or $h^2 = 2\frac{R}{S}$. The realized heritability was calculated by plotting the response against the cumulated selection differential and fitting a regression line to the points (Falconer, 1960). The slope of the regression line is equal to one half the realized heritability. The realized heritability was .49 for the combined high lines; and .38 for

TABLE IV

Chi-square values for the First through Fourth Selected Generations. The rating scale scores were divided into Low (scores 2, 3, and 4) Intermediate (scores 5, 6, and 7) and High (scores 8, 9, and 10) categories in order to obtain sufficient numbers for the expected frequencies in each cell.

Generation	Combined Groups Analysis	Separate Groups Analysis	
	H, L	H ₁ , L ₁	H ₂ , L ₂
S ₁	7.88*	5.21 N.S.	13.50**
S ₂	10.10**	2.10 N.S.	9.34**
S ₃	46.47**	21.69**	27.45**
S ₄	48.10**	39.03**	18.17**

df = 2

* $\underline{p} < .05$

** $\underline{p} < .01$

N.S. = not significant

the combined low lines. When analyzed separately, the realized heritabilities for H_1 and H_2 were .55 and .43 respectively. Separate low lines analyses yielded $h^2 = .32$ for L_1 and $h^2 = .35$ for L_2 .

Each mouse in the study was weighed on the two consecutive testing days. The mean weights for all six lines were calculated for all generations (Figure 7). The selection procedure did not seem to have any effect on the weights of the adult mice. Weight does not appear to be a correlated character of agonistic behavior in wild female mice. There is a decrease in weight for all six lines in the Third Selected Generation. Since this decrease is constant across all six lines, it probably represents environmental fluctuation.

The mice of the Third and Fourth Generations were weighed when they were toe-clipped at seven days of age. The mean pup weights (males and females analyzed together) for all six lines were examined (Figure 8). The selection procedure did not seem to have an effect on maternal competence as measured by pup weight at this age. Mean litter size was calculated for all six lines over the Third and Fourth Generations (Figure 9). Again there appears to be no variation of litter size with respect to the selection procedure. Apparently female agonistic behavior is not detrimental to maternal behavior.

The sex ratio was calculated for each litter of the Third and Fourth Generations by dividing the number of males in a litter by the total number of individuals in the litter (Figure 10). By this calculation, a score of 50 per cent or greater would indicate that there were more males than females in the litter. Conversely, a score of less than 50 per cent would indicate more females in a litter. There

Figure 7. Weight at testing in grams for all lines and generations.

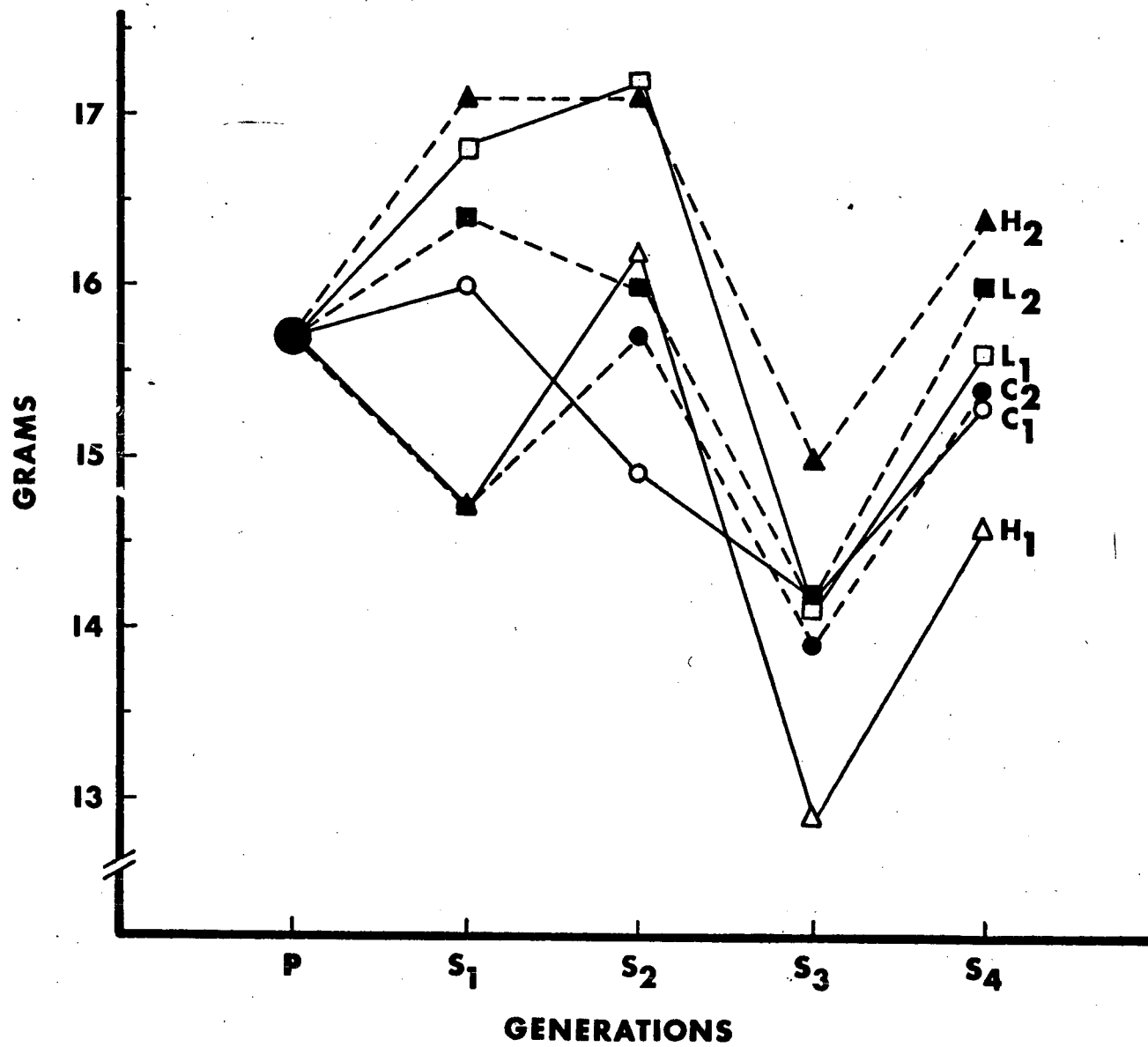


Figure 8. Mean pup weights in grams for all lines, third and fourth generations.

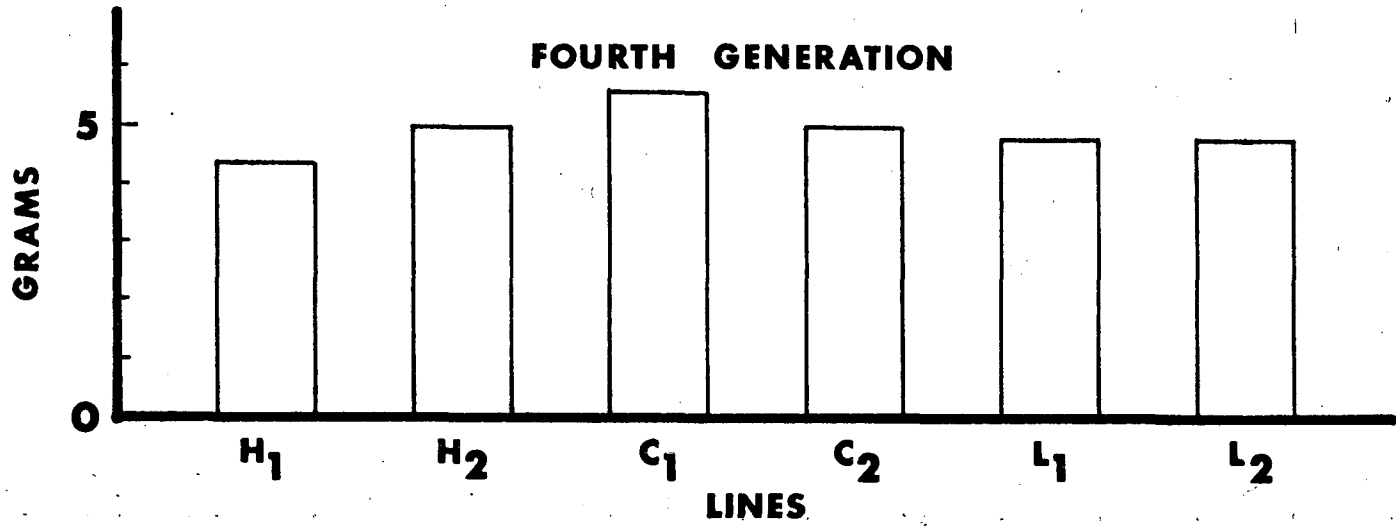
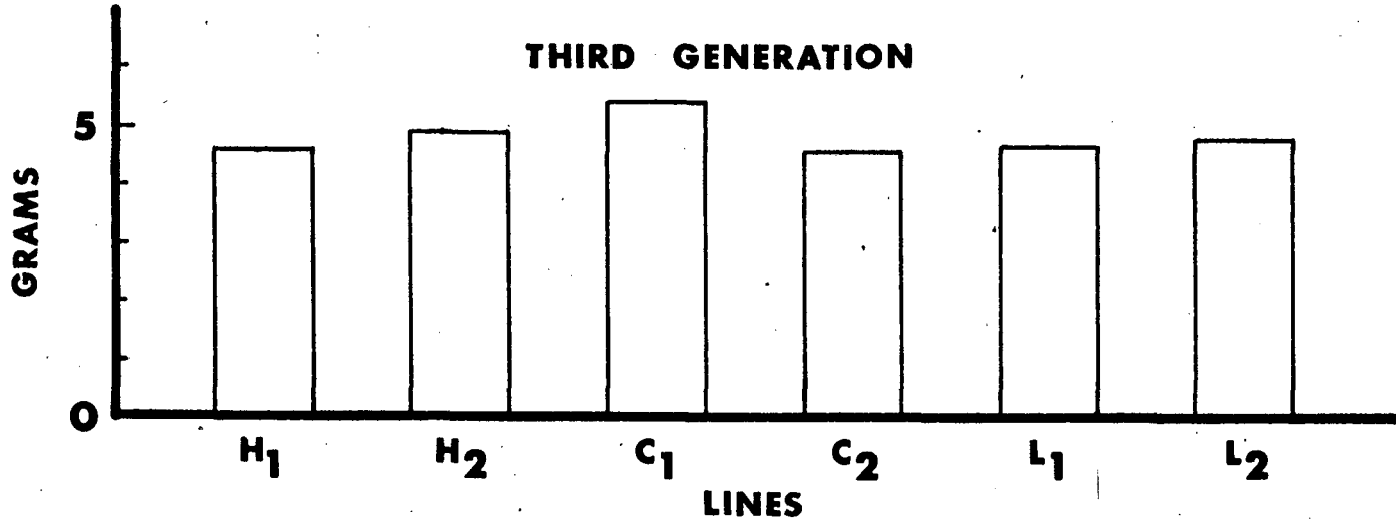


Figure 9. Mean litter size for all lines, third and fourth generations.

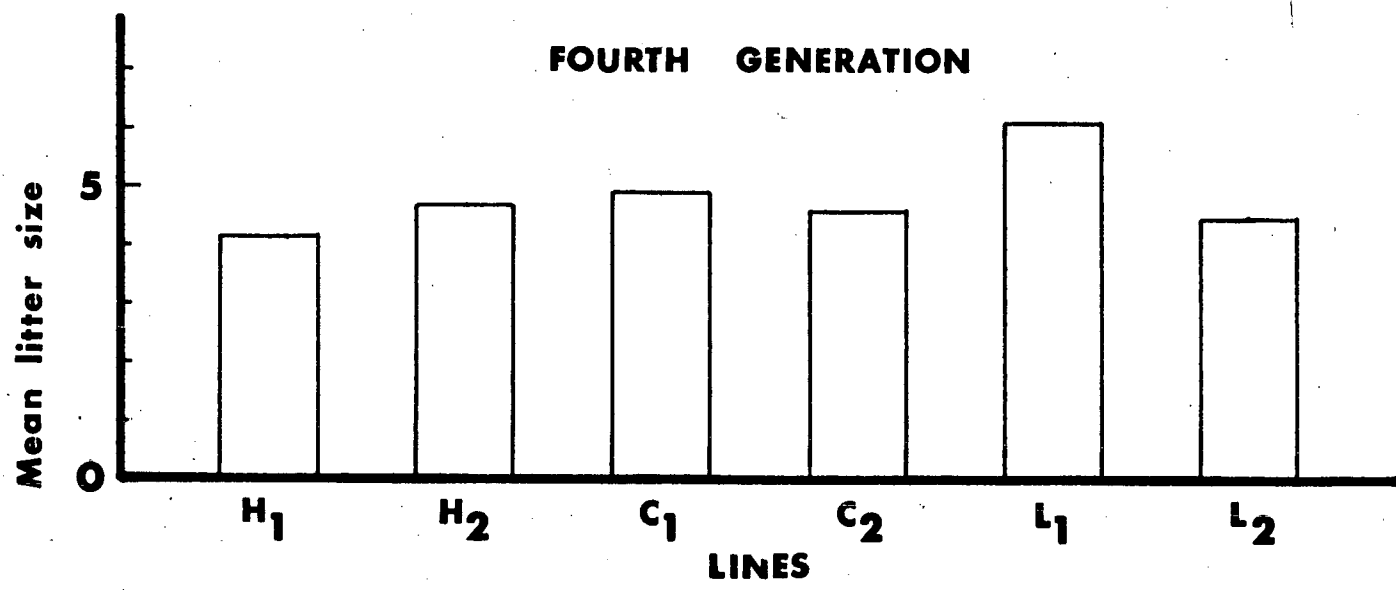
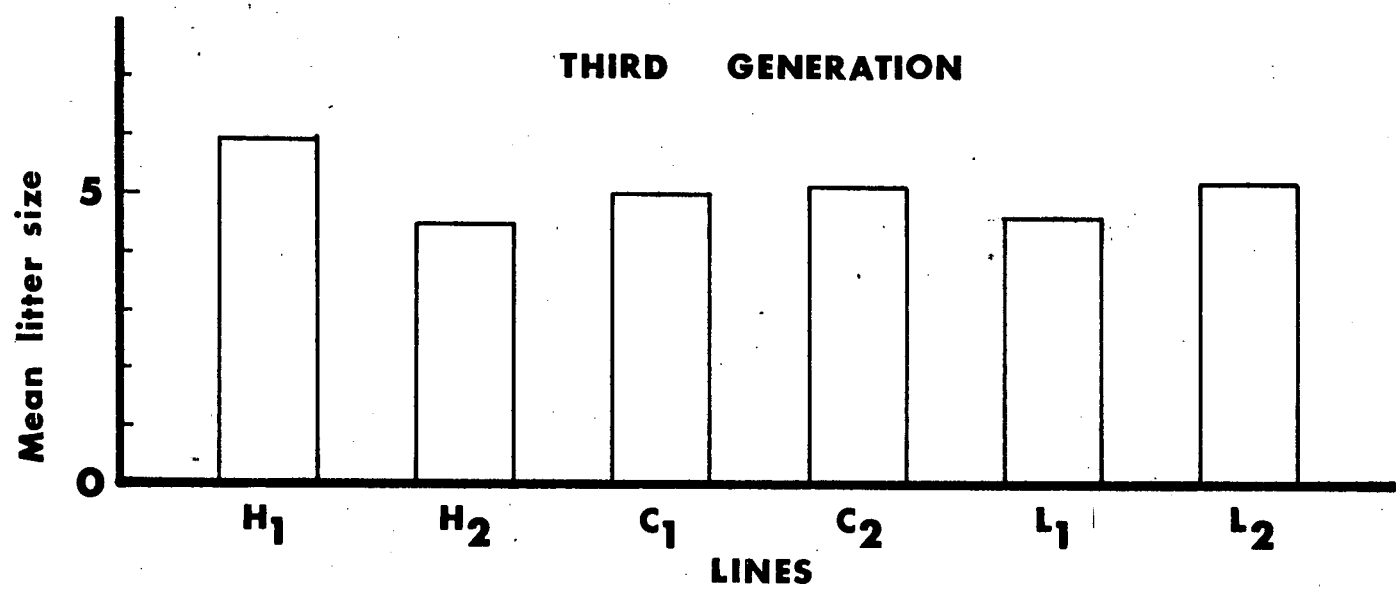
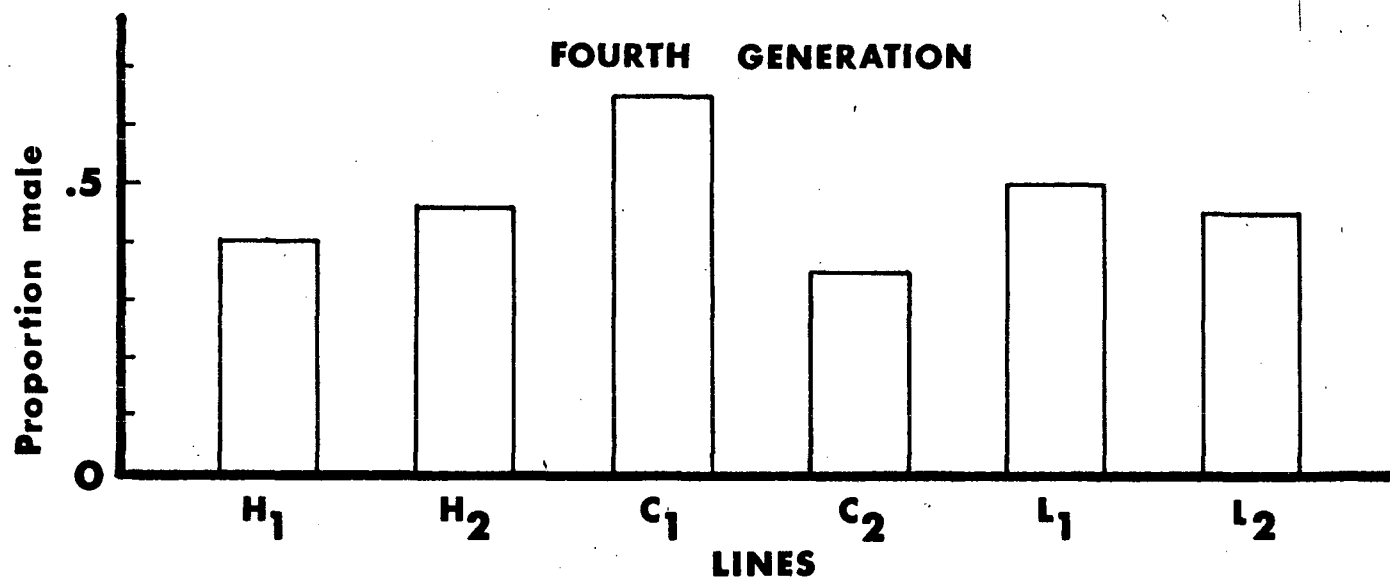
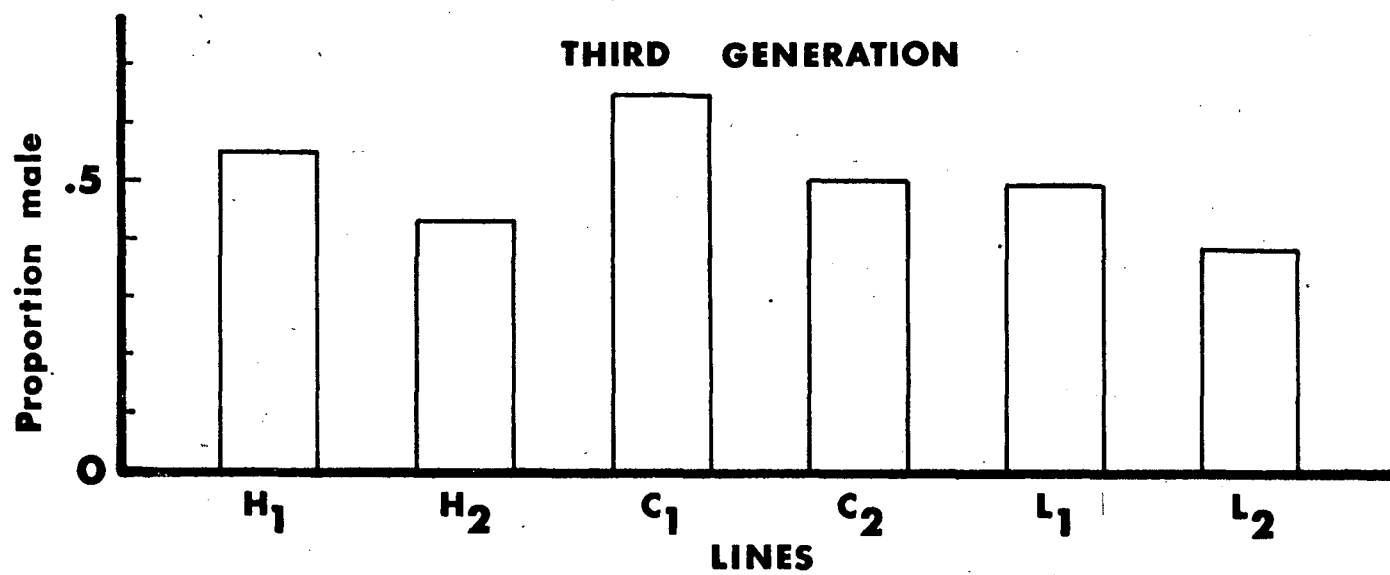


Figure 10. Sex ratios for all lines, third and fourth generations.



appears to be very little fluctuation in sex ratios over the six lines, and none corresponds to the selection procedure.

DISCUSSION

The present study was successful in establishing significant differences between the high and low lines in the expected directions. The replicated high and low lines all showed a response to the selection process. The response of the unselected control lines is somewhat more difficult to explain. Both unselected control lines show an upward trend in scores which overlaps the high lines in the Second Generation.

There are two possible explanations for this overlap. The selection procedure may have been effective only for the low lines, and the apparent rise in the high and control lines due only to environmental factors or testing procedures. If this were true, it would be difficult to explain why the control lines show a downward trend in the Third and Fourth Generations. Also, the variances for the high lines show a trend toward decreasing size (Figure 5) over the four selected generations. The control lines show no such trend.

The second possible explanation for the overlap of high and control lines would be random drift of the control groups' scores. This explanation seems more likely since the control lines eventually separate out in the Fourth Generation. However, it is unusual that both control lines would drift in the same direction.

It is also unusual that the low lines do not show a trend toward decreasing variance as do the high lines (Figure 5). Such a decrease in variance is usually thought to indicate that the limits of selection

are being approached. The reason for the lack of decreasing variance in the low lines may be due to the rating scale itself. Lagerspetz (1964) reported that her low line did not respond to further selection after the first generation. This lack of response might be due to the failure of the rating scale to adequately discriminate among lower levels of agonistic behavior. Since the present study used the same scale for the lower levels of agonistic behavior, there might have been a floor effect due to the rating scale which made it impossible to approach the limits of selection in the low lines. Of course, the trend of decreasing variances would not be expected in the unselected control lines.

The distribution of scores in the Parental Generation is spread widely (Figure 6). There two modes--one at "three" and the other at "eight." The high and low distributions of the Fourth Generation are both skewed in the expected directions. The mode for the low lines is the "two" score which substantiates the possibility of floor effects in the lower end of the rating scale. It is interesting to note that the mode for the high lines is "eight" which was the second mode in the parental distribution. A score of eight usually indicates that, on both days of testing, much contact and following was observed, but that no actual fighting took place. It may be that it is easier to select for increased contact and following than for actual fighting, although there does seem to be an increase in the "nine" and "ten" scores which would indicate an effect upon actual fighting behavior. The distribution for the combined control groups in the Fourth Generation, although somewhat different from the Parental Generation, is also widely spread.

The heritability estimate of .17 obtained by calculation the regression of the daughters' scores on the mothers' scores greatly underestimated the realized heritability values. The realized heritability values for the high lines were consistently higher than those of the low lines. This finding may be a further indication of the rating scale's inability to discriminate among lower levels of agonistic behavior.

None of the weight or fertility measures displayed any line differences that could be related to the selection procedure. These findings indicate that the different levels of agonistic behavior obtained in this study did not seem to affect the health or maternal competence of the wild female mice or the health of their offspring.

The finding of genetic variability in agonistic behavior in females leads to the question of what adaptive function, if any, agonistic behavior has for a wild population of mice. One possibility is that female agonistic behavior might be related to maternal defensive behavior. The St. John and Corning (1973) study indicated that the two behaviors might be related. Since mice are capable of existing in many different kinds of environments, and of displaying many different types of social organization, it seems likely that it would be adaptive for the population to incorporate some variability with respect to maternal defensive behavior. That is, maternal defense might be extremely adaptive under certain environmental situations, but relatively unimportant or even unadaptive in others.

This explanation can be extended to account for the disappearance of female agonistic behavior in domestic stocks. In a confined

situation, such as the laboratory, a number of breeding females might be caged together in a small area. Under these conditions, females who displayed little maternal defensive behavior would be favored as breeders so that highly defensive females, who might also display agonistic behavior in certain situations, would be eliminated from the population.

In order to substantiate the above explanation, the next step would be to test the lines obtained in this study for maternal defensive behavior. If maternal defensive behavior can be shown to be a correlated character of female agonistic behavior, this would be good evidence for at least one adaptive function of female agonistic behavior in a wild population of mice.

Since different levels of agonistic behavior have been established for the females in the high, low, and control lines, it would be informative to test their male siblings for agonistic behavior under similar conditions of isolation and later pairing with a C57BL/6 mouse of the same sex. If line differences in male agonistic behavior corresponding to the female's were found, it would seem that agonistic behavior was influenced by the same genetic factors in both sexes. The next step would be to look for physiological correlates of agonistic behavior common to both sexes. Although similar directional differences might be found in both males and females, the overall level of agonistic behavior in males might be greater, presumably due to the effect of testosterone.

The lines of mice established by this study could also be used to examine other forms of fighting behavior in the mouse which involve

test situations different from the one employed in the present study. These tests would determine if the results of this study were generalizable to other forms of fighting in the mouse. It might also shed some light on possible relationships among different kinds of fighting, again indicating the possibility of common physiological correlates.

In conclusion, this study represents a unique application of the behavior-genetic technique of artificial selection to agonistic behavior in female mice, a phenomenon which has received little attention in the past. It also represents one of the few studies to apply behavior-genetic techniques to a laboratory-reared population of wild Mus musculus. These studies are important because one would expect to find more genetic variability in a wild population than a domestic one, and because the frequencies of genes in a wild population should be related to their adaptive function in a natural environment. Since this study was successful in establishing lines of mice which differ in levels of agonistic behavior, these lines can be used to further the understanding of the mechanisms and functions of agonistic behavior in mice. An increased understanding of agonistic behavior in mice may, in turn, lead some direction to future research on fighting in other mammalian species.

APPENDIX A

The Selection Study in Behavior Genetics Research

Selection, as defined by Lerner (1958) is the non-random differential reproduction of genotypes. That is, certain individuals, because of their particular genotype, will be more likely to produce viable offspring than other individuals. Thus, over a period of generations, a change in the composition of the gene pool will occur. An artificial selection study, such as the one discussed in this paper, involves the arbitrary determination of which individuals in a population will become the parents of the subsequent generation.

Since it has been shown that many behavioral traits have a demonstrably strong genetic component, it becomes possible for an investigator to select individuals on the basis of certain behavioral traits. This process results in the production of lines which contain a larger percentage of individuals with the selected trait than in the original population. It is also possible to select bidirectionally or for more than one qualitatively different trait. Most behavior-genetics selection studies involve both a high and low line which eventually differ considerably in the percentage of individuals displaying the selected behavioral trait.

Behavioral Traits

There have been a number of behavioral traits which have served as the basis for the selection technique. Among these are simple tasks, activity level, mating speed and ability, emotionality, intelligence

or learning ability, seizure susceptibility, and agonistic behavior. Some of these traits are more easily defined, quantified, and measured than others. Traits which describe broad hypothetical constructs such as activity, emotionality, and intelligence are particularly difficult to study.

Ewing (1963) attempted to select for "spontaneous" activity in Drosophila. This attempt was inspired by Manning's 1961 study in which he reported that the lines he had selected for fast mating speed showed a decrease in activity while the slow mating lines showed an increase in activity. This observation was based on the behavior of the flies in their bottles after the bottles were handled by the experimenter. Ewing made several attempts at measuring "spontaneous" activity, but was decidedly unsuccessful, which is not surprising considering the ambiguity of this trait. However, he did manage to obtain different levels of reactivity, which was probably a trait more similar to the phenomenon that Manning had reported. He also observed that flies that were highly reactive showed a decrease in courtship efficiency, which again is compatible with Manning's findings.

Continuing the interest in Drosophila activity, Connolly (1966) obtained differences in locomotor activity by selecting flies on the basis of their performance in an open-field apparatus. He selected for 25 generations and calculated a heritability of .51. He also tested his active and inactive lines in three different apparatuses and found that the active line was always more active under the different test situations. This finding is extremely important since it shows that the selected trait is somewhat general as opposed to being highly

situation specific. Activity in Drosophila can be used as a basis for selection if it is carefully defined and measured.

Emotionality in rats has served as the basis for two selection studies. Both Hall (1951) and Broadhurst (1960, 1962), operationally defined this construct as amount of defecation in an open-field situation. Although both studies obtained increases and decreases in defecation rate, the question of whether or not defecation in an open-field is an index of emotionality is definitely open to debate.

Dawson (1932) reported his findings on the inheritance of what he called wildness and tameness in mice. He defined wildness as having a fast time in running to the end of a 22 foot runway which again is a questionable definition of a complex, ambiguous trait.

There have been several studies dealing with the inheritance of intelligence or brightness and dullness in rats which will be omitted from this review. In these studies maze-learning ability was the basis for selection. Searle (1949) emphasized the pitfalls of this kind of research when he demonstrated that the "Bright" line that he tested did not appear to display greater global intelligence. Searle took samples from Tryon's Brights and Dulls and sample of non-selected rats and ran them through a battery of tests in order to determine whether or not the Brights had a greater level of "general intelligence" than the Dulls or the non-selected rats. He came to the conclusion that this was not the case, although there was a slight tendency for the Brights to perform better overall. However, the two selected lines did show distinct differences in patterns of behavior. For example, the Dulls seemed to be below average in strength of food drive. Food, of

course, was the reinforcement in Tryon's maze. The Dulls also seemed to have a specific fear of unstable platforms. Similar platforms were part of Tryon's mechanical maze. The Brights, on the other hand, were consistently inferior in tasks involving escape-from-water motivation.

More recently, two studies have reported what is perhaps a more realistic approach to selection for learning ability. Bignami (1965) using rats, and Bovet et al. (1969) using mice selected for high and low rates of active avoidance conditioning. Both of these studies were highly successful in obtaining results from selection, and neither involved the interpretation of a vague hypothetical construct.

In conclusion, any behavioral trait which is to serve as the basis of selection should be carefully defined and quantified before the selection procedure is instigated. After separation is obtained, the lines can be tested in different situations in order to determine the generality of the selected trait.

In all of the above studies, the selection involved different amounts of the behavioral trait, or selection on a quantitative basis. In fact, there is only one reported study of selection based on qualitative distinctions. Frings and Frings (1953) used a random bred stock of albino mice to produce four lines of mice with predictable susceptibilities to audio-genic seizures. These differential susceptibilities involved both types of seizures (clonic vs. clonic-tonic) as well as differences in the ages for greatest susceptibility. This kind of selection method makes it possible for the investigator to develop the specifically desired phenotypes that are necessary for future research.

Genetic Variability and Quantitative Inheritance

In addition to defining and quantifying the behavioral trait which is to be the basis of a selection study, it must also be assumed that a fair amount of genetic variability with respect to the trait can be found in the foundation population. The greater the variability, the greater the response to selection will be. Another related assumption that is usually made is that the behavioral trait involves a polygenic mode of inheritance. In other words, it is assumed that many genes contribute additively to the expression of the behavioral trait, and that the selection procedure will bring about differential changes in the distribution of these genes in the selected lines. Consequently, the selection procedure should bring about a gradual divergence in the lines over several generations. If only a few genes were involved, the limits of selection would be reached after very few generations. Also, the use of quantitative genetic statistics such as heritability depends to a certain extent on the assumption of a large amount of additive, polygenic variability.

Most selection studies reported in the literature seem to support these assumptions, since a gradual divergence of lines is usually obtained over a period of several generations. Further support for these assumptions is sometimes demonstrated after divergence is obtained. One method of demonstrating polygenic inheritance is through the use of hybrid analysis. Hadler (1964) tested hybrids from his Drosophila lines which had been selected for positive and negative phototaxis. He found that the hybrids were intermediate between the two selected lines. This finding does not necessarily eliminate the possibility of other

modes of inheritance. Incidentally, one of the reasons that phototaxis was first used as a basis for selection (Hirsch and Boudreau, 1958) was the amount of variability in the base population. The other reason was that the trait was highly amenable to mass testing in a maze-like apparatus.

For the same reasons, positive and negative geotaxis later served as the basis for selection studies of Drosophila (Hirsch and Erlenmeyer-Kimling, 1961). Positive and negative geotactic lines were also used by Hostetter and Hirsch (1967) in another attempt to support the polygenic hypothesis. After divergence was obtained, both lines were divided into forward and reverse selection groups. After several further generations the forward group of one line phenotypically resembled the reverse group of the other. Complementation tests were then performed by crossing members of the reverse group of one line with members of the forward group of the other. Therefore, the parents were phenotypically similar. The assumption was made that if the parents were genotypically as well as phenotypically similar, then the offspring should phenotypically resemble the parents in this trait. However, it was shown that the offspring did not resemble the parents in this case, in fact they showed considerable variability. This study shows that phenotypic similarity does not necessarily imply genotypic similarity, and that geotaxis is influenced by many genes.

If a polygenic mode of inheritance is assumed, and if greater genetic variability means greater response to selection, then it would be to the advantage of the investigator to begin selection on a population thought to contain genetic variability. Ginsburg (1967)

reported a series of three selection studies attempted on a population of C57Bl/10 mice. Since an inbred strain of mice should contain no genetic variability, selection for any trait within the strain should be impossible. Indeed, the attempts to select on the basis of agonistic behavior, emotionality, and susceptibility to audiogenic seizures were all dismal failures.

Some of the selection studies in the past have reported the use of inbreeding within a selected line at some point in the study. Theoretically, this is a very dangerous procedure since it would decrease the genetic variability within the line. Lagerspetz (1964) inbred some of her mice selected for agonistic behavior early in her study in order to obtain a quick response to selection. Rundquist (1933) and Broadhurst (1960) state that an unspecified amount of inbreeding did occur in their studies. Obviously, some degree of inbreeding will occur in any artificial selection study since all of the subjects will be members of a confined laboratory population. Also, as the limits of selection are approached, one would expect to find a decrease of genetic variability within the lines. However, it is probably to the advantage of the investigator to avoid any systematic inbreeding.

When a selection study is begun, the usual procedure is to close the lines. That is, the lines themselves become segregated gene pools, and animals in one line never become parents in another. Rundquist (1933) selected for high and low levels of "spontaneous" activity in rats as measured by scores on a revolvable drum. For the first four generations of selection, the two lines were not closed, so that the highest and lowest scoring rats were always selected no matter from which line their parents came. This procedure led to an upward shift

in means for both lines. Starting with the fifth generation, the lines were closed, and divergence was obtained.

Use of Replicated and Control Lines

In most of the studies discussed so far, only two lines selected in opposite directions were employed. Although good divergence is usually obtained by this procedure, it is not always possible to make strong statements about the generality of the findings. If, however, two or more replicated lines selected in the same direction are a part of the design, the investigator can be more confident in his results if the two lines show an identical response to selection.

Craig et al. (1965) selected both White Leghorn and Rhode Island Red chickens for high and low levels of dominance ability. Although different realized heritabilities were computed for the two breeds of chickens, the response to selection was very similar. Hadler (1964) selected Drosophila for high and low phototaxis on two different mazes. After selecting for 30 generations, he found similar but slightly different heritabilities for the two different mazes. This also demonstrated that heritability was not a characteristic intrinsic to a particular trait, but to a particular population with respect to a particular testing environment.

Manning (1961) reported the results for 25 generations of selection for fast and slow mating speeds in Drosophila. In this study he not only used replicated high and low lines, but also used a non-selected control group. Hirsch and Erlenmeyer-Kimling (1961) also used a non-selected control group in their geotaxis selection study. The use of non-selected control groups allows the investigator to examine the

effects of microenvironmental variation between generations, and to determine the degree of symmetry of the divergent lines to selection. DeFries (1967) stated that this design should serve as a prototype for future selection studies.

In a selection study for open-field activity in mice, DeFries and Hegmann (1970) followed that suggestion and employed replicated high, low, and control lines. They also employed a within-family selection procedure. This procedure involves the selection of the highest scoring male and female offspring from each mated pair in the high lines and the selection of the lowest scoring male and female offspring from each mated in the low lines. Brother-sister matings are, of course, never done. One advantage of this design is that it keeps inbreeding to a minimum since each mated pair contributes a male and female to the subsequent generation. Also, this design results in control for maternal effects since all maternal genotypes are contributing an equal share of selected offspring.

Asymmetrical Response to Selection

A number of selection studies have reported asymmetrical response to selection for high and low lines. Three possible explanations are offered for these results, which are by no means mutually exclusive. The first two explanations involve the actual mode of inheritance. If one line reaches the limits of selection after fewer generations than the line selected in the other direction, it may be that fewer genes were involved in the first direction, or that there was more homozygosity and fewer dominant genes in that direction. The third explanation involves

an evolutionary point of view. That is, one would expect to find it easier to select for a behavioral trait in an adaptive direction than in an unadaptive direction. For example, Manning (1961) found a greater response to selection for fast mating speed in Drosophila than for slow mating speed. It can be assumed that slow mating speed is not very adaptive for the species. However, in 1963 Manning reported on another study for selection of mating speed in Drosophila. This study employed a different procedure for selection. In the 1961 study, male and female flies were placed in a bottle, and the first ten pairs to mate and the last ten pairs to mate became parents in the subsequent generation. In the 1963 study, Manning selected individual male flies rather than pairs of flies in both fast and slow directions. He was successful in obtaining only slow mating lines of males.

Hall's (1951) study on emotionality in rats indicated asymmetrical response to selection. The limits of selection for the non-emotional line were reached at the first generation while the emotional line showed a monotonic response up the ninth generation. It is interesting to note that Broadhurst (1960, 1962), using a very similar testing procedure, found symmetrical results through fifteen generations. Again, the use of replicated lines would have been advisable.

Lagerspetz (1964) reported that her non-aggressive line stabilized after the first generation, but that the aggressive line had not reached its limits of selection by the eighth generation. It is, of course, very tempting to speculate on the adaptivity of agonistic behavior on the basis of this study. However, a replication of these results is obviously necessary. Also, as mentioned above, deliberate

inbreeding was practiced at the beginning of this study. The rating scale which was the criterion for selection in this study might also have been responsible for this effect.

Single Sex Selection Studies

In the cases of some behavioral traits, measurement can be obtained for only one sex. Manning (1963) would have preferred to select both male and individual flies for mating speed, but, alas, the females would become pregnant during the preliminary test. When selection pressure is placed only on one sex, the response to selection should be the same, but should occur at one-half the rate that it would for both sexes. Other single-sex selection studies include Wood-Gush's (1960) study on the selection for high and low copulation frequency through three generations of cockerels, and Siegel's (1965, 1972) more comprehensive study of mating ability in roosters. Lagerspetz (1964) selected levels of agonistic behavior in males only, since no female aggressiveness could be elicited in her population of random bred albino mice. Females, however, were chosen for mating on the basis of their brothers' scores. This procedure should have the effect of increasing the response to selection.

Correlated Characters

Once significant divergence has been obtained in the selected lines, it is sometimes desirable to test for possible correlated characters. Correlated characters are traits which are systematically related to the selected traits. There is a danger in attempting to examine these characters in selection studies in which no replicated

lines were included in the design. That is, if it is observed that a trait corresponds to selected behavior, there is no way of disproving chance association of the two traits. If, however, the same association can be demonstrated in replicated lines, one can have more confidence that the association is a true correlated character and not an effect of chance. Manning's (1964) study on selection for mating speed gave some indication that the slow mating lines showed more activity when their bottle was handled by the investigator, although this was not systematically measured. This relationship is somewhat substantiated by Ewing's (1963) observation that his highly reactive line showed a decreased courship efficiency.

There is also indication that activity is related to fertility in female rats. Rundquist's (1933) inactive line died out after the 25th generation, apparently due to infertility of the females. Brody (1959) developed a new line of inactive rats to continue the research. For males, the level of inactivity reached that of the original line after 10 generations. However, the females' activity was somewhat higher than that of the original line, and there were no problems with fertility.

The two studies on mating behavior in chickens also indicated the presence of correlated characters. Although the Wood-Gush (1960) study lasted only through three generations, he did report a tendency for high copulation frequency to be associated with an increase in the number of cloacal contacts which occurred before actual copulation took place. Also, the high frequency line was found to produce a lower semen yield. In the Siegel (1965, 1972) study, good separation

of lines was obtained only by the fourth generation, and no indication of the existence of correlated characters was found until after the sixth generation. Siegel found that low line males had a greater volume of semen than the high line males. This finding was, of course, consistent with Wood-Gush's findings. Also, by the seventh generation, high line males were showing significantly more courts than low line males. These two studies point to the possibility of compensation in the selected lines. That is, the modification of mating behavior might have very little effect on actual fertility in either high or low lines.

Collins (1970) found that aggressiveness could possibly be a correlated character of brain weight in mice. Using well-established selected lines for high and low brain weights, she found that mice with high brain weights showed significantly less aggression than those with low brain weight. Her criterion of aggressiveness was amount of scarring found in mice that were housed together.

DeFries and Hegmann (1972) examined defecation scores in their mice selected for open-field activity over all selected generations. The results indicated a consistent inverse relationship between activity scores and defecation scores. Since this study employed replicated high, low, and control lines, the results are convincing. Happily, they did not make any statement concerning emotionality.

APPENDIX B

Agonistic Behavior in Mus musculus

The purpose of this review is to discuss some of the known mechanisms involved in agonistic behavior in mice. In particular, mechanisms which can be related to the genetic and physiological makeup of the mouse will be emphasized. More comprehensive reviews of the literature are Scott (1966) and Ebert (1972). The reason that genetic and physiological aspects are being discussed in this paper is that they may eventually be shown to be related to the agonistic behavior in female mice which served as the subject of the present study.

Genotype

Genotype (other than sex) has been shown to have an influence on agonistic behavior. Most of this work, other than Lagerspetz's (1964) selection study, has been done with inbred strains of mice. Scott (1942) was the first to report differences in agonistic behavior among C57BL/10's, (Bagg) albinos, and C3H's. However, as Scott stated in his 1966 review, strain differences in agonistic behavior usually do not indicate that one genotype is consistently more aggressive than another, but that differences will occur in one particular test situation.

Isolation Effects

Ginsburg and Allee (1942) were the first to isolate their subjects before testing them for agonistic behavior. Since that time isolation has become a common treatment for increasing agonistic behavior in mice.

Sigg et al. (1966) attempted to explain why isolation facilitated agonistic behavior in terms of endocrine factors. In their study, they isolated mice at twenty-five days of age. At the end of three months, all of the intact males that were isolated showed agonistic behavior, whereas none of the mice in the control condition of group rearing did. The intact isolated males also showed an increase in adrenal weight, and increase in testicular weight, and a decrease in splenic weight. The finding of increased adrenal weight in isolates is somewhat uncommon. Adrenalectomized mice fought after isolation, but castrated and hypophysectomized mice did not. They concluded that an intact pituitary-gonadal axis is a prerequisite for the development of isolation induced agonistic behavior.

Archer (1970) compared adrenal weights of mice which were either isolated or trained as fighters. One group of isolated mice was then subjected to defeat by a trained fighter once a day for seven days while the others were left isolated. One group of the trained fighters was allowed to win encounters twice a day for seven days while the remaining trained fighters were left isolated. The four groups were then sacrificed, and the adrenals removed and weighed. The group which had been isolated and then defeated had significantly heavier adrenals. This study is extremely interesting since animals which are thought to be stressed--especially by defeat--show increased

adrenocorticoid activity. (See Brain, 1972 for a review of the literature.)

In a series of more complex physiological analyses of the effects of isolation and grouping on endocrine function, Brain and Nowell (1971a) grouped or isolated male mice starting at different ages and extending over different periods of time. They found that in all categories there was a lower adrenal weight in isolated males as compared to their grouped counterparts. Also, all of the isolated mice showed a lower level of plasma corticosterone. They also found some evidence that the isolated mice had elevated levels of androgen. This is especially interesting since it is known that androgens depress adrenal function by inhibiting ACTH secretion. The fact that isolation induced fighting is strongly related to the presence of male hormone, as will be discussed later, makes it seem possible that the suppression of adrenal function by increased androgen accounts for the lack of increase in adrenal size for isolated and victorious mice.

Brain and Nowell (1971b) also tested female mice using a design similar to the one in the previous study. They found that isolated females showed higher adrenal weights, but concluded that these were due to increased levels of estrogen and not to the stress of being isolated.

Burge and Edwards (1971) studied the effect of adrenalectomy on pre- and post-castrational agonistic behavior. Their conclusion was that adrenal secretions had no effect on the agonistic behavior of inexperienced fighters or on the maintenance of agonistic behavior of experienced fighters which had been castrated.

Welch and Welch (1971) attempted to relate the literature on adrenal effects of grouping to the metabolism of amines which have been implicated as neurotransmitters or modulators in the brain. Their hypothesis was that if isolated mice have lower basal levels of adrenal cortical activity, then isolated mice might metabolize the catecholamines in the brain more slowly than mice that live under the higher level of environmental stimulation provided by grouping. They confirmed this hypothesis by studying the effects of several drugs which have known effects on catecholamine metabolism. Female catecholamine activity was essentially the same as that of the males, although females in this study showed no actual fighting after isolation. It seems that adrenal activity alone cannot account for isolation induced aggression. What seems more likely is that changes in adrenal function only reflect changes in sex hormones and possibly central nervous system activity which more directly affect agonistic behavior in mice. These internal changes may, in turn, affect the production of and response to olfactory cues which will be discussed later.

Sex Hormones

The effects of sex hormones on agonistic behavior have been fairly well studied. Since it had long been recognized that female mice would very rarely fight in test situations in which males would very readily be induced to fight, it would seem logical that the male hormone would have an influence on agonistic behavior in mice. Beeman (1947) found that fighting behavior could be restored to castrated males through the use of subcutaneously placed pellets of

testosterone propionate (TP). At that time it had long been recognized that castration drastically reduced agonistic behavior in male mice. In another early study, Tollman and King (1956) gonadectomized both male and female mice at thirty days of age and then gave them TP. They found that the females still fought less than the males. Whalen and Edwards (1966) found that when estrogen was injected into neonatally castrated male rats, they developed female characteristics.

More recently, Bronson and Desjardins (1968) and Edwards (1968) independently discovered that females could be induced to fight like males if given TP on the day of birth or shortly after. These investigators have extensively elaborated on their early studies (Bronson and Desjardins, 1969, 1970; and Edwards, 1969, 1970) and have reached similar conclusions: It seems that there is a critical period around the time of birth when the nervous system of the mouse can be primed by the male sex hormone to respond as a male to the male sex hormone at sexual maturity. In normal development, the mother's gonadal-stimulating hormones activate the gonads of the fetus to produce the appropriate sex hormone for a short period of time. Thus, the male's nervous system is different from the female's, and the male hormone will affect the male's agonistic behavior when he matures.

The effects of neonatal estrogen on agonistic behavior are still somewhat questionable. Bronson and Desjardins (1968) and Edwards and Herndon (1970) reported that the administration of estrogen to neonatal females facilitated the differentiation of androgen sensitive mechanisms for adult agonistic behavior. That is, adult females that had been given the neonatal treatment with estrogen responded like males to

subsequent injections of TP. However, females castrated as adults showed no response in terms of agonistic behavior to estrogen replacement while castrated males increased fighting after being given estrogen (Edwards and Burge, 1971). So it seems that estrogens can mimic the effects of TP under certain conditions. Progesterone, on the other hand, is reported to inhibit the effect of strong androgens in castrated male mice (Erpino and Chappelle, 1971).

The fact that there seems to be a critical period immediately following birth for neonatal TP to affect subsequent agonistic behavior has generated research concerning the nature of this period. Peters et al. (1972) found that the organizational period for isolation induced agonistic behavior was completed between two to six days after birth. Whitsett et al. (1972) were concerned with brain uptake of TP in female mice and how this corresponded to later agonistic behavior. They found that as the time after birth elapsed, the amount of hormone required to be effective in producing later agonistic behavior increased. Uptake rates in the brain were also increasing during this period.

Another line of research concerns the reactions of non-treated male mice to mice treated with TP. The administration of TP quite possibly affects the olfactory cues emitted by the treated mice, and as will be discussed below, olfactory cues have been shown to be extremely important in agonistic behavior. Lee and Brake (1972) treated castrated males with either TP or oil. When these mice were paired with trained fighters, the fighters showed a greater amount of aggressive acts toward hormone treated castrates than to oil treated castrated. Mugford and Nowell (1970, 1971) treated females with TP and subsequently

found that the injected females would be attacked by normal males. Since the injections did not seem to alter the behavior of the females, it seems likely that the treated females were emitting aggression eliciting cues which were quite likely olfactory in nature.

Obviously, sex hormones play an important role in agonistic behavior in mice, but genetics still influences how this behavior is expressed. Vale et al. (1972) found a genotype by environment interaction when neonatally androgenized females of three different inbred strains were tested for agonistic behavior. They found that BALB/c females who had been given neonatal androgen fought more than either A's or C57BL/6's with the same treatment. This strain relationship was identical for intact males under the same test conditions. Similar results were found for females of the same strains when given neonatal estrogen (Vale et al., 1973).

Pheromones

As mentioned earlier, olfactory cues have been shown to be important in agonistic behavior in mice. Ropartz (1968) found that agonistic behavior could be eliminated in a trained fighter by bulbectomization. He also found that agonistic behavior could be decreased through the use of a heavy masking scent like perfume. Krames et al. (1969) found that male rats from stable hierarchies could discriminate between dominant and submissive rats from strange hierarchies and preferred the strange submissives. Connor (1972) swabbed either male or female urine on both male and female intruder mice. Both males and females swabbed with male urine would elicit agonistic behavior,

while both males and females swabbed with female urine would elicit sexual behavior.

Another newer line of research on olfactory cues deals with the determination of whether the agonistic behavior is elicited merely by the ability of a mouse to smell the opponent or by some process at a higher level in the central nervous system. Rowe and Edwards (1971) castrated male mice at thirty days of age. The mice were then subjected to bilateral or unilateral bulbectomy or a sham operation. Upon subsequent TP administration, the controls and unilaterally bulbectomized mice showed no difference in agonistic behavior. The bilaterally bulbectomized mice, however, showed virtually no agonistic behavior.

In another study Edwards et al. (1972) rendered mice anosmic by means of peripherally administered zinc sulfate. After determining that these mice would not respond to the olfactory cues emitted by a buried cookie (thus indicating anosmia), they tested the mice for fighting and found that many of the anosmic mice would indeed fight. However, it must be remembered that this technique for inducing anosmia is new, and more experiments should be conducted before any definite conclusions are drawn.

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