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Behavior Associated with Age and Audiogenic Seizures in an Inbred Strain of Mice

By WAYNE C. BRUCE

Behavior disorders or so-called "experimental neuroses" have been observed by many investigators in a variety of species. Finger¹ indicates that convulsive behavior has been studied experimentally in such mammals as the cat, dog, mouse, rabbit and pig. Hall and Martin² refer to behavior disorders in the chimpanzee and rat. So far as is known only rats and mice have been found susceptible to audiogenic seizures.

It has been found that abnormal behavior may be elicited by a variety of stimuli such as conflict, sound, electric shock, drugs, and dietary deficiency.

Although the literature appears to indicate that a variety of species and stimuli have been used in experimental investigation, "the rat continues to hold its pre-eminent position as an animal in laboratory investigation." It is for this reason that the writer has found it necessary to refer to studies in which the rat has been used.

In this paper the writer has attempted to confine his investigation to the influence that increasing age may have on behavior and audiogenic seizures in an inbred strain of mice. Age was selected for investigation since there appeared to be little published evidence concerning the influence of this factor on behavior and audiogenic seizures.

The influence that age may have on audiogenic seizures in the rat has been investigated by several workers. It was found that the increase of age beyond a certain point was accompanied by a decline in susceptibility. Further age increments decrease still further the percentage of susceptible rats, although some rats continued to exhibit the full convulsive pattern at 510 days. With increasing age, a number of vital physiological alterations take place in the organism.

The behavior disorder investigated here has been referred to as an "experimental neurosis," "neurotic pattern," "audiogenic seizure and an "audio-epeleptic" seizure.

¹F. W. Finger, "Convulsive Behavior in the Rat," *Psychological Bulletin*, XLIV (May, 1947), 201.

²C. S. Hall and R. F. Martin, "A Standard Experimental Situation for the Study of Abnormal Behavior in the Rat," *The Journal of Psychology*, X (March, 1940), 207-210.

The behavior observed in an audiogenic seizure is episodic and convulsive in nature. It appears to consist of sudden, violent, and undirected running, jumping, stiff hopping, and tonic and clonic manifestations; this is followed by an inactive, comatose phase during which there is a lack of response to sensory stimulation, reflexes and righting responses are absent, and the animal may be molded in any direction.

In the present investigation the writer has attempted to pinpoint the mean age of death and the mean age of susceptibility to audiogenic seizures in an inbred strain of mice. An attempt was made to chart and illustrate various aspects of seizure-behavior as age increases. Comparison was made between behavior observed during the orientation and stimulation periods as age increases. Such other factors as onset of susceptibility, latency of seizures, frequency of exposures, age at fatal seizures, frequency of seizures, number of seconds in fatal seizure, and age of onset of susceptibility within litters were investigated. In each case these factors were examined from the standpoint of increasing age, the assumption being that behavior increases, decreases, or changes as age increases.

The materials used were those suggested by Scott.³ The experiment was designed to include a standard galvanized tub, two batteries connecting wires, a jack-knife switch, a door-bell, recording blanks and a stop watch. The animals used were (dba) sublime 2 stock raised by the writer at Drake University. A total of 75 animals were obtained from mating 20 females with 6 males. The original stock was obtained from the Supply Department of the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine.

Since an age was desired at which virtually no symptomatic behavior would be elicited, the experiment was begun when the animals reached 12 days of age. This age was found to be satisfactory, since there was no evidence of response to auditory stimulation.

The experiment included two specific periods, the "orientation" and the "stimulation" period. The orientation period lasted for one minute and gave the animal an opportunity to become familiar with the surroundings. The stimulation period lasted for two minutes, during which all behavior was carefully recorded and timed. Each animal was stimulated once daily for two minutes until a fatal audiogenic seizure occurred.

³J. P. Scott, "The Use as Test Material of Inbred Strains of Mice Having High Frequencies of Audiogenic Seizures," *Science*, CXI (May, 1950), 583.

DISCUSSION

Since most of the information concerning behavior associated with age appears to be from work done on rats, the conclusions that can be drawn concerning the reaction of mice must be with reference to them for comparison.

The literature indicates that the age factor may be important in the extent to which it may influence susceptibility to audiogenic seizures. There seems to be evidence that at the early ages little, if any, symptomatic behavior is observed. As age increases, however, there appears to be a rapid increase in seizure behavior. With further increment of age there seems to be a gradual decrease in the symptoms of susceptibility to audiogenic seizures. The present data are in general agreement with the trend reported by other workers, in which the rat was used. The results seem clearly to indicate that one of the intrinsic determiners of susceptibility is age.

The great age range over which first symptoms occur (from less than fourteen to more than twenty days) is perhaps surprising, but this dispersion emphasizes the fact that the age-susceptibility relationship is a highly individual matter and that only by repeated testing over a long period of time can the diagnosis of "susceptible" or "non-susceptible" be made with any degree of assurance. It is also evident that an animal once classified "susceptible" may later fail to respond to auditory stimulation, simply as the result of changes associated with increased age.

The conviction that susceptibility to auditory stimulation is largely controlled by age appears to be confirmed by the age at which fatal audiogenic seizures occurred. Since the greatest frequency of fatal seizures occurred between sixteen and eighteen days of age, it may be assumed that susceptibility occurs at an earlier age.

The results of this investigation seems to indicate that the onset of susceptibility for (dba) subline 2 mice occurs at a somewhat earlier age than that reported by other writers. This variation may be attributed to nutritional factors, since providing vitamin B₁ supplement to the original diet tends to prolong susceptibility. The diet used in this investigation contained somewhat smaller quantities of vitamin B₁.

Throughout both the orientation and stimulation periods a general increase was observed in the percent of behavior as age increases. In the earlier days of age behavior seems to be at a minimum, with a general increase occurring as age increases.

The period of greatest mortality occurred between sixteen and eighteen days of age and the mean age of susceptibility and death

were found to occur at 15.35 and 18.68 days respectively. Since some individuals were scattered above and below the mean, it may be assured that individual differences may have some effect. It has been reported that individual variation has been reduced to the lowest possible amount in subline 2 stock.

The frequency of audiogenic seizures seems to follow the same general pattern suggested earlier, that, as age increases, behavior increases rapidly up to a certain age, then falls off rapidly.

Although some animals were observed to adapt or adjust to the stimulus, any conclusions that may be made must await further investigation.

Inasmuch as each animal was stimulated under identical conditions it might be assumed that other factors associated with age would follow the same pattern. In recording the amount of time each animal spent in a fatal seizure, it was found that no positive relationship existed between increasing age and the number of seconds an animal would remain in a fatal seizure. The average number of seconds in a fatal seizure seems to vary considerably with age. This variation may be explained by adaptation and individual differences in maturation and in susceptibility.

When the average age of onset of susceptibility within litters was determined, it was found that considerable consistency existed. The details of the records indicate that the average age of onset of susceptibility for each litter occurs between fourteen and sixteen days of age. What variation existed may be attributed to the age of the parent at conception and to intra-uterine development. No attempt was made to investigate these factors.

The latency of audiogenic seizures has been defined as the amount of time elapsing between the beginning of stimulation and the instant at which the animal goes into a violent convulsive seizure. The details of the records revealed no evidence that the age factor systematically influenced the average latency of audiogenic seizures.

When the average frequency of exposures to auditory stimulation for May and June litters, prior to fatal audiogenic seizures, was determined, it was found that no significant variation existed between litters. This portion of the investigation was carried out to determine if any significant variation in the average number of exposures could be observed as the age of the producing animals increased.

The final step in this investigation concerned the frequency of exposures to auditory stimulation as age increased prior to susceptibility. The details of the records indicate that the frequency of exposures prior to susceptibility decreases rapidly to around fifteen

days of age and decreases more gradually with further increments of age.

The age factor appears to be an important determiner of behavior and susceptibility to audiogenic seizures in (dba) subline 2 mice.

SUMMARY AND CONCLUSIONS

Dilute Brown non-agouti (dba) subline 2 mice were used in this investigation. A total of 75 animals were tested under identical conditions beginning at twelve days of age and continuing until all animals had suffered fatal seizures. During the course of the investigation consideration was given to behavior associated with age and audiogenic seizures.

1. It was demonstrated that the age at which first symptoms of susceptibility to audiogenic seizures occurred was between 13 and 15 days.

2. It was demonstrated that the age at which fatal audiogenic seizures occurred was between 16 and 18 days.

3. It was demonstrated that the percentage of behavior observed as age increases, during the orientation and stimulation periods tends to increase.

4. The percent mortality resulting from audiogenic seizures as age increases was demonstrated to be greatest between 16 and 18 days and 100 percent mortality occurred prior to 30 days of age.

5. The mean age of susceptibility and death were found to occur at 15.35 and 18.68 days respectively.

6. The average number of seconds in a fatal seizure was found to vary considerably and no positive relationship could be found between increasing age and the number of seconds an animal would spend in a fatal seizure.

7. It was demonstrated that the frequency of seizures as age increases was greatest between 14 and 16 days.

8. The average age of onset of susceptibility within litters was found to occur between 14 and 16 days.

9. No systematic increases was found to occur in average latency as age increases.

10. It was demonstrated that little difference existed between the average frequency of exposures to auditory stimulation for May and June litters.

11. It was found that the frequency of exposures to auditory stimulation as age increases prior to susceptibility, decreases rapidly from 12 to 15 days of age and more gradually thereafter.

12. When a comparison was made between the results of this investigation and those reported by other writers, no significant variation appeared to exist.

The results of this investigation appear to indicate that age strongly influences behavior and determines susceptibility to audiogenic seizures in (dba) subline 2 mice.

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