UNIVERSITY OF CINCINNATI

May 23 1942

I hereby recommend that the thesis prepared under my supervision by William J. Griffith

entitled The Production, Persistence and Transmission of Convulsions in the White Rat.

be accepted as fulfilling this part of the requirements for the degree of Doctor of Philosophy

Approved by:

Arthur G. Bills.

Form 668—G. S. and Ed.—1M—7-37

THE PRODUCTION, PERSISTENCE AND TRANSMISSION OF CONVULSIONS IN THE WHITE RAT

A dissertation submitted to the

Graduate School
of the University of Cincinnati

in partial fulfillment of the
requirements for the degree of

DOCTOR OF PHILOSOPHY

1942

by

William John Griffiths, Jr.

A. B. Dartmouth College 1937.
M. S. The Ohio State University 1940.

Acknowledgment

I wish to express my indebtedness to Dr. A. G. Bills, head of the Department of Psychology at the University of Cincinnati, under whose guidance this study was carried out. The suggestions, criticism and encouragement which he has given have been instrumental in carrying the work to completion.

Table of Contents

4 S '42

Part V.

Tables, Graphs, and Illustrations

Part II, Section 1

Part III, Section 2

Part IV, Section 3

Foreword

Introduction of animals into the psychological laboratory for purposes of studying behavior has been a comparitively recent procedure.

Early studies of animal behavior consisted largely of casual observations and anecdotes concerning the behavior of personal pets.

With the development of experimental methods applicable to animal work, this field of psychology has made rapid strides. Such psychological functions as learning, retention, and habit formation have been investigated by ingenious devices in the animal laboratory, for the light that they may throw on similar functions in the human.

Animal studies have been occupied with the functions of the normal individual and have only recently attempted to produce and study abnormal behavior, as an aid to understanding certain forms of human abnormality.

The following Historical Introduction gives an account of the work in the field of abnormal animal behavior from early casual observations to the more recent experimental attacks on the problem.

Part I.

Historical Introduction

Status of the problem of abnormal behavior in the rat at the time of the study

Purpose of the investigation as a whole

Historical Introduction

Hooper (22) reports a peculiar breed of goats raised in central and eastern Tennessee. When suddenly frightened the hind legs become stiff and the animal jumps along until it recovers and trots off normally. If greatly frightened, the animal falls to the ground with front legs stiff also. They have received the name stiff-legged or sensitive goats.

Cole and Ibsen (7) report the birth in 1914 of two guinea pigs, one differing from the other in lacking nervous control. When this individual was placed on his feet, attempts to walk resulted in spasmodic stiffening of the legs, causing it to fall over on its side where it lay helpless, unable to get up. Further experimentation indicated that this condition, termed palsy, was inherited and followed the law of a simple Mendelian recessive. Affected individuals experience the most difficulty in control of the hind legs which appear to be in a hypertonic state and are commonly moved in a hopping fashion rather than in steps.

These investigators also reported having in their possession a rabbit several years old which, since young, showed the characteristic circus movements, or waltzing, very similar to the activities of the waltzing mouse.

Stockard (42) has described various defects in the guinea pig, the symptoms somewhat resembled congenital palsy, and were ascribed to the inherited effects of alcohol treatment of the original parents.

Lord and Gates (31), studying a stock of normal albino mice, report in two families, individuals showing distinctive behavioristic characters. This strain was inbred by MacDowell for twelve to thirteen generations. The term shaker was adopted to indicate this mutation. This mutation shows itself principally in the form of nervous head movements: rapid, successive jerkings of the head upwards, accompanied by sniffing and twitching of the vibrissae. Shakers can, for short intervals at least, cease from the head shakings and appear perfectly normal. Animals sometimes run in circles but seldom as rapidly or in as small a circle as the Japanese Waltzer. The authors feel that the entire condition is associated with the central nervous system and might be classed as a chorea. The condition was noted to be present at birth. Adult shakers show no reaction to sound. Breeding experiments done with these animals indicate a close approximation to the theoretical ratio 3:1, of a recessive.

Lush (32) reported a flock of goats showing peculiar hereditary nervous behavior. No possibility presented itself for any breeding experiments; so merely the observations made were recorded. The goats, if suddenly frightened or surprised became perfectly rigid, and in this condition were able to be pushed around or turned over. The fit lasted only a short while, 10-20"; recovery of the anterior muscles occurred first. After being thus frightened, the animals cannot be again frightened regardless of the strength of the stimuli until they have rested 2-30'. The author mentions several ways which may be used to induce fright, surprise being the principle element; loud noise, a shot, dropping of a galvanized can, men creeping up on the animals and then appearing suddenly yelling and waving their arms. These stimuli cause rigidity accompanied by prostration on the part of the animal. Occasionally animals were observed to have seizures spontaneously without general scaring of the flock. The strain was of uncertain origin.

Wortis (44) has reported on the use of a standard convulsant. Unanesthetized cats were given camphor monobromide intervenously at successive ten minute intervals. Results indicated chronic convulsive discharges in various parts of the body. The following symptoms were attendant upon the seizure: increase of deep reflexes, sweating, increased respiration and heart rate. These were followed by a temporary loss of corneal and pineal reflexes. Frothing at the mouth, tail bushing, tongue biting, and rise in blood pressure were also observed. As the lethal camphor dose was reached the animal has a tonic convulsion with extension of all limbs.

Curtis (10) reported Sutherland and Davis' training pigs over a year's period to restriction of their freedom in two controlled environments alternated daily. One environment was characterized by a continuous tone of six hundred cycles whose cessation for ten seconds was the signal for dropping an apple into a covered food box. The other environment was characterized by a tone of seven hundred and fifty cycles whose cessation for ten seconds was a signal for a mild electric shock to be applied to the foreleg. After stabilization of the performance, motor outlets were further curtailed by random opening of the food box between tests on feeding days. Punishment by shock attended such openings. As a result, the pig refused to lift the lid until the apple was dropped into the box. The experimenter then refused to drop apple until the pig opened the cover. In consequence of this last procedure, one pig developed a condition resembling an inhibitory type of experimental neurosis observed by Pavlov (40) in the dog.

The extensive researches of Liddell (28) and his associates on the conditioned behavior of sheep and swine featured Pavlov's methods, further delimited, for the production of a nervous strain. The general method was similar to Pavlov's: the animal was induced to submit to restrictions of a harness limiting freedom of locomotion and remain inert and quiet except when responding to stimulation. The response used with sheep was a delayed motor reaction reflex based on application of a mild electric shock to the fore leg. In the trained normal sheep this stimulation evolks a brisk flexion of the fore leg, but no tantrum or observable emotional behavior. Anderson and Liddell (1) have mentioned the following factors as likely to damage the nervous system of sheep:

1. Necessity of inhibiting or restraining a conditional response beyond the animal's capacity to do so.
    a. A conditioned reflex with moderate delay of five seconds between onset of the signal and application of the shock may be elicited too frequently or with insufficient rest intervals between tests.
    b. Excessive long delay between onset of signal and application of shock straining the capacity of the sheep to withhold response.

Liddell and co-workers presented sheep with auditory stimuli; one being reinforced by shock and the other not. The animal always responded positively to both tones and no evidence was obtained that there was any discrimination between them. Neurotic behavior appeared in a few weeks. After resting, the animals were trained to react to a buzzer followed by a shock with rest intervals of seven minutes. The neurosis remained unchanged. Anderson and Liddell believe that the regular temporal alteration of positive and negative stimuli placed heavy strain upon the animals' nervous system. Whatever the means of inducing the neurosis the manifestations of it are remarkably constant. The above mentioned authors have characterized them in at least three ways:

1. Behavior changes in the sheep are permanent, enduring for life of the individual.
2. They are new and do not resemble regression to an earlier habit pattern.
3. They involve not only the animal's overt adjustments to the environment, but also many of his homeostatic physiological relationships such as speed and regularity of pulse and respiration.

Liddell further reports gross changes occurring in behavior of sheep previously cooperative in the laboratory situation. The animals become refractive and resist being taken into the laboratory and harnessed in the Pavlov frame. Actual break down is usually initiated by an inhibitory phase in which conditioned responses are sometimes suppressed for a time. If the training is continued the animal passes over into an excited phase where conditioned reflexes are more violent than normal. Positive responses are given to stimuli that were formerly negative, discrimination between stimuli having completely broken down. Anderson (1) noted that animals could not maintain their former state of alertness during the interval of several minutes between stimulations, but exhibited tic-like movements of the limb which he likened to the fidgeting of a nervous child. This was probably the most characteristic overt manifestation of neurosis in sheep. Significant and enduring differences in heart rate and respiration were also reported.

Differences between the normal and the neurotic pig and sheep have been demonstrated in the barn and field life of these animals, as well as in the laboratory situation. Records indicated that activity of normal sheep is greatest during the day, rising to a peak at feeding time, but ceasing almost completely for an hour or so at a time during the night. The neurotic animals' record shows that there are bursts of activity spaced a few minutes apart during most of the day and night.

Liddell, Anderson, Kotyuka and Hartman (29) have shown that subcutaneous injection of adrenalin had the effect of depressing the conditioned leg response in anticipation of the shock, while increasing the sheep's irritability during the rest interval. Extract of the adrenal cortex had the reverse effect, quieting the sheep during the rest interval and increasing the vigor of the conditioned response to a signal. The result was to make the neurotic sheep resemble the normal.

Karn (26) has reported on a case of experimentally induced neurosis in the cat. Using the double alternation problem in the temporal maze situation, Karn has obtained positive results. Hunter (24) has indicated that solution of this problem calls for a response to temporal relations in the absence of differential sensory cues, and thus appears to depend upon an implicit symbolic process. Following the mastery of the double alternation response, one animal, a six month old cat, ceased correct performance of the response and subsequently exhibited symptoms characteristic of experimentally induced neurosis. Karn's report is concerned with a description of the behavior of this animal. The cat learned the double alternation response in 230 trials, the average accuracy reached was 90 percent. Up to this time the animal always entered the maze readily, worked rapidly and was in general a docile subject. In order to determine whether the animal could achieve still higher accuracy, training was continued beyond the 230th trial. On the second response of the 232nd trial a radical change in behavior was observed. The animal hesitated at the choice point and finally jumped to the right and then raced to the front of the maze. During the remainder of the trial he worked slowly and whimpered continuously. Five hours later when brought to the maze for another trial he refused to enter of his own accord and resisted being forced through the door. After the cat had been forced into the maze, its behavior throughout the trial was characterized by a refusal to work, at first scratching at the doors and the wire mesh, mewing loudly and urinating at various points. This behavior occurred at the most difficult point of choice reaction, at which time the animal would resolve the conflict by returning to an earlier and lower habit order; a clear case of regression, according to the author.

The Morgans (37) have reported concerning an abnormal pattern of behavior in the rat, first observed in the living cage of the rats subjected to the sound of a high pitched blast of air. These workers found that cutaneous stimuli were dispensible, while the auditory stimulation was not, for production of the abnormal pattern. The behavior pattern in each case is stereotyped and predictable. After several minutes or even one half hour, these investigators claim that the animals arouse themselves from the immobile state following convulsive seizures, and are apparently normal. To date, they reported that only 4 out of the 41 animals, given the preliminary test, reacted positively. Animals may give no observable response to one or more presentations of the stimulus and yet on a subsequent occasion exhibit the typical behavior pattern. The authors feel certain that the abnormal behavior is correlated with the auditory component of the air blast directly. The question is raised by the Morgans as to whether the abnormal behavior is properly termed neurotic. They point out that in the early stages the vigorous activity and tics resemble some of the aspects of human neurosis but in the final stages the coma seems more closely allied to the phenomenon of tonic immobility. The investigators further state that this abnormal behavior in lieu of any fundamental relation to a problem situation has little in common with neurotic behavior described by Liddell (28) and Pavlov (40). The final conclusions of the Morgans is to the effect that the behavior which they have observed is probably not to be considered neurotic behavior although perhaps significant for the study of abnormal behavior.

Cook (8) has made a survey of the methods used to produce experimental neurosis. He first presents the conditions under which chronic disturbances of behavior occurred as a result of environmental stresses produced in the laboratory. These disturbances developed at some stage in one of the following situations:

1. Continued presentation of a conditioned stimulus which not only has the effect of establishing a new association but also results in the inhibition of a strong inborn reflex.
2. Delay of the reinforcement of positive conditioned reflexes for a given time after the beginning of the conditioned stimuli.
3. Rapid transition from one conditioned stimulus to another, the two stimuli being conditioned to evolk antagonistic behavior.
4. Reinforcement of conditioned stimulus which had previously an inhibitory effect.
5. Occurrence of a very strong or unusual stimulus.

The nature of the disturbance of the behavior or the neurosis varied from animal to animal although there were certain common symptoms. Cook reports that the first case of experimental neurosis occurring in the Pavlov laboratory came during the course of an experiment attempting to generalize a positive conditioned response or reflex of salivation. When a conditioned response is associated in this manner with an electrical shock, the native defense reaction to the shock, however severe, is inhibited. The generalization in Pavlov's experiment proceeded successfully for a while, the shock producing salivation at each new point tried. When a still further point was tried, an abrupt change in the behavior occurred. The shock no longer evoked salivation, but instead caused a violent defense reaction.

Pavlov's workers trained another animal to salivate at the presentation of a circle. A discrimination between the circle and an ellipse had been established as the result of never giving food when the ellipse appeared. This discrimination was made successfully to the point where the axis of the ellipse was in a ratio of 9:8. At the time of total loss of inhibition to the ellipse the gross behavior of the animal became quite different. From normally quiet conduct, the animal grew violent and destructive. Cook points out that the first actual experiment with experimental neurosis came with the selection of two dogs for their normal excitatory or inhibitory nature. Pavlov believed that either the excitatory or the inhibitory process was dominant in the normal activity of all dogs. Cook has summarized the different symptoms displayed by Pavlov's dogs as follows:

1. A loss of a previous habit, regardless of the strength, of making responses to certain conditioned stimuli.
2. A loss of the previous habit, regardless of strength, of making response to certain conditioned stimuli unreinforced, regardless of how well or how readily these inhibitions had been acquired.
3. A loss or impairment of the capacity to reacquire these lost habits, as shown by the failure or difficulty of the retraining efforts.
4. Various degrees of restlessness and excitement when brought into the experimental room and put into the apparatus, or when presented with certain conditioned stimuli.

Drabovitch and Meger, as reported by Cook (8), have studied two further cases of experimental neurosis in dogs. Their animals had been working in experiments in which they learned to respond to the sound of a bell with flexion of the left hind leg. For three daily experimental periods, in the case of one dog, the experimentors attached the electrodes to the left front leg, and sounded the bell without giving any reinforcing shock. The dog soon became agitated, and on the fourth day of this procedure showed a continuous convulsion of the test leg. After a rest of several days, the convulsions gradually disappeared. The second dog for two years had gone regularly into the experimental room but was not experimented with for a period of one month. Each day during that time its companion was removed from the cage to be taken to the laboratory. When at the end of one month the dog was placed on the experimental table the left hind leg started a violent withdrawal reaction. This reaction spread to the leg on the opposite side, leaving both limbs in such a severe nervous condition that the animal was not able to stand. Administration of bromides brought about cessation of the convulsion within five days.

The investigators were not completely clear concerning the factors responsible for the break down. In the case of the first dog there is non-reinforcement of a conditioned stimulus over a period of time, plus a change of the electrode to the front foot; both factors may have played a part. In the second dog there is the month intervening between routine schedules. Drabovitch and Meger believe that the daily trips to the cage to get the companion dog left the second animal in a state of excitement which consisted in part of a supercharged condition of the centers for conditioned flexion movements.

The second series of major studies, as outlined by Cook (8), are those of Krasnagorski, on conditioned reflexes in children. The first technique used by this worker required differentiation between mutually antagonistic stimuli. A child developed the reaction of mouth opening to a metronome, beating at the rate of 144 beats per minute. A slower rate served as the inhibitory impulse. When, in the course of the experiment, this slower rate had reached 120 beats per minute, the child's response latencies lengthened and he became nervous and irritable and refused to come to the laboratory. When the inhibitory rate was still further increased to 132 per minute, the child responded by crying and beating other children and a strong desire to leave the hospital. In addition, the child lost the ability to discriminate between excitatory and inhibitory stimuli, responding to both with mouth reactions, though the inhibitory rate was lowered to 120 beats per minute. Krasnagorski observed similar behavior in other children making difficult discriminations between tactual conditioned stimuli. A second technique used by this investigator required the child to make delayed reactions to conditioned stimuli.

Cook summarized the results of the child experiments as follows:

1. A loss of a previous habit, regardless of strength of response to conditioned stimuli.
2. Various degrees of restlessness in the experimental situation.
3. Various degrees of sleepiness in the experimental situation.
4. Increased irritability and asocial behavior outside the experimental situation.
5. Unwillingness to return to the experimental situation.

The third of the major series of experiments reviewed by Cook have been done by Liddell. These studies we have already had occasion to mention.

Jacobson, Wolfe, and Jackson (25), in the course of experiments on the effect of frontal lobe extirpation on behavior, observed that experimental neurosis could be developed in a chimpanzee. One item on which the post operative responses were compared was a test of recent memory. Food was hidden under one of two cups while the animal was watching. An opaque screen was then lowered for a given period. One of the animals showed no disturbance to the lowering of this blind; the other flew into a temper tantrum, rolled on the floor and defecated. After a few such responses this animal refused to respond to this particular problem at all; although she worked eagerly on other problems. By the end of three weeks it became necessary to force the animal from its own cage to the experimental cage. Retraining with the substitution of a glass door for the opaque screen proved successful in removing the abnormal reactions of this animal. After extirpation of the frontal lobe, a similar disturbance was again produced by the same procedure. Upon extirpation of the second lobe the animal assumed a friendly cheerful attitude, which was never abandoned in spite of frustrations. The number of errors made at the task attempted was, however, greatly increased.

Observations of experimental neuroses in animals have been reported by Ba^{n}jandurow (2) who accidentally produced behavior disturbances in two doves while experimenting with them on form discrimination. One dove, as the result of receiving a reinforcing shock, had developed a conditioned leg withdrawal to the presentation of a circle, while remaining quiet to an ellipse. The ellipse was then made more and more like the circle, until at a certain point the discrimination broke down and leg withdrawals were made to all ellipses.

Cook (9) has reported concerning the production of experimental neurosis in the white rat. This author defines abnormal behavior as "that which involves changes in a given animal's responses, persisting at least as long as the animal is in periodic contact with the precipitating situation". This author performed the following experiments. A small tin cup was fixed into place in the center of a wire cage two feet in area. The cup constituted the active electrode of a circuit, the cage being the inactive electrode. The circuit was made whenever the animal in the cage touched the water in the cup. Five experimental animals received all their water from this container for a period of two weeks. During the same period the rats learned to perfection a twelve unit elevated maze. At the end of two weeks the rats had formed a strong habit of rushing directly to the cup when placed in the experimental cage. The current was gradually increased from an imperceptible point to a point where the rat gradually ceased drinking from the cup and withdrew. The intensity was gradually lowered and for a given animal remained constant for the next seven days. During this time the rats drank little, if any, less water than formerly, though they frequently recoiled from the shock as they began to drink. A cautious approach to the cup was developed. For the next seven days each time the rat overcame the initial impulse to recoil, and began drinking, the shock intensity was rapidly increased serving to drive it away. The intensity was then reduced to the starting point. Approach and withdrawal behavior and occasional jumping to the side of the cage was observed, and no modification of the behavior outside of the experimental situation was noted in the maze, or in handling by the experimenter.

In a further series of experiments Cook used a modification of the Warner jumping apparatus. The animals learned to jump to the grid opposite the one on which it received a shock. Next the animals learned to jump to the opposite grid when the box was illuminated by a bulb at full intensity. A shock followed the illumination after a three second interval. An inhibitory impulse, the shining of a light at a very low intensity was then used. Co-incident with this the grid opposite the one on which the rat stood was charged; thus if a jump occurred the animal received a punishing shock as it came to rest. While this new stimulus caused a temporary disruption of the previous fast jump to the bright light, adjustment to the situation was uniformly successful. In the case of several animals the same punishing shock had been used to prevent the changing of grids in the dark. Following this the intensity of the inhibitory light was changed, being increased at each point in the lower range. Discrimination was perfected before further increase occurred. Where discrimination was too difficult the rat was most often observed to remain crouched on the edge of one grid, flexed for a jump.

No behavior change outside the experimental situation was observed.

Cook (9) then decided to construct a situation where two overt responses rather than an inhibitory one would be brought into opposition. Three grids were arranged symmetrically so that from any one of the grids an animal could jump to either of the other two across a five inch space at the bottom of which was a permanently sensitized grid. Behind each of the grids was a milk glass and a light bulb. Six rats placed in this situation learned that they could escape the shock on one grid by jumping to one of the other two. Next, the animals learned to jump to the lighted grid rather than the darker one. With the exception of upward jumping, fighting, etc., no effects outside the apparatus were observed.

Cook constructed a stand with holes through which the legs of the animal could be drawn and fastened. When in the stand the animal rested upon chest and abdomen, being held in place by a broad leather strap. The right front leg was fastened by a thong to a lever on which were balanced two mercury switches; when thrown, these switches activated either a circuit carrying a shocking device, or one carrying a foot releasing device. The active electrode of the shocking circuit was bound to the right front leg near the ankle. The inactive electrode was a wet pad under the rat's stomach. The food releasing device fed small pellets into a cup under the animal's head. One foot from the front of the stand was a single light bulb. The rat first learned the association between the shining of the bulb at full intensity and the appearance of food. This reaction resulted from the pellet being delivered automatically a fraction of a second following the light. The rat then learned that, while the light shone, flexion of the right leg brought food. An inhibitory response, the shining of a dim light, was next introduced. A right leg flexion to this light brought a punishing shock. After a discrimination between this and the bright light, the animal was trained to an inhibitory response to two dim lights in succession.

Following the learning of these habits, the intensity difference between bright and dim lights was gradually decreased by increasing the intensity of the latter. At each new level where the animal experienced any difficulty, decrease in intensity was postponed until the rat had made two-thirds, or better, correct responses. This procedure was continued until the limit of the discrimination was reached. Three out of six animals that were brought through this procedure showed behavior changes that may be called experimental neurosis. This author noted persistence of behavior changes in the form of slight jumpiness; later by very marked jumpiness to light taps of the finger, backing away when the cage door was opened, squirming and turning over on the back. Stiffening and holding poses indefinitely were characteristic behavior alterations. After being kept away from the apparatus for a nine day period, abnormal behavior completely disappeared. Three weeks following renewal of the experiments all abnormal behavior reappeared.

Page (39) has investigated, with animals, some theories of psychological importance. Among these are the possibility of conditioning of convulsions, the importance of excitement as a predisposing factor, and finally the effect of repeated convulsions upon personality changes. In this study, electrical procedure was used for production of convulsions in cats and rats. Current applied to the animal's cortex via electrodes was obtained from a sixty cycle per second transformer, delivering about six hundred volts to an undirected current regulating the network. The network was such that variation in animal resistance were automatically compensated for. The amount of shock required to produce the seizure varied considerably with the placement of electrodes, but for the particular placement the threshold was fairly constant for the individual animal. Superficially, attacks in both cat and rat resembled grand mal seizures, and were quite similar in both types of animal. Minor differences were present, however, and it was doubtful whether any two attacks were exact replicas. Closing of the circuit produced a marked "start" which sometimes lifted the animal partly in the air. The spine was flexed inward, with the hind legs drawn up and fore legs drawn down. Golla, as reported by Page (39), has interpreted this reaction as indicating stimulation of the pre-central gyrus, and compared it to the initial clonic phase of a metrazol seizure. During the duration of the shock, the body is rigid. From this point the pattern of reaction is somewhat variable. In some instances the animal passes from the shock reaction to a state of rigidity, which in turn is followed by characteristic jerking movements of the clonic phase. At other times the clonic movement may occur directly after termination of the shock, with no noticeable intervening tonic stage. When present, the tonic stage consisted in the animal's stretching out to full length with hind and fore legs extended as far as possible. The entire body is stiff and rigid and eyes are generally closed. The transition to the clonic stage is gradual; fine tremor of tonic phase giving way to rapid jerking movements of the clonic stage. Tonic and clonic phases last together about 30". Usually the clonic stage is followed by a coma-like state from which the animal recovers spontaneously in about five minutes. During this post-convulsive state it is not possible to induce a seizure, but as soon as the animal is active again another seizure may be induced.

Shocks of less than convulsive intensity elicited a somewhat milder start reaction and subsequent behavior was quite variable. Such animals appeared dazed, or had spurts of impulsive running, exhibited clonic movements or muscular twitching, vocalized, or engaged in other forms of activity. Page points out that impulsive running associated with the subconvulsive shock is somewhat more controlled and less forced than that observed in rats as a result of stimulation with air blasts or conflict situations plus air blast. Shocked rats seldom ran blindly into objects. They also tended to run in a straight line, rather than in circles. The former type of running is, as Page points out, always associated with the psychologically produced seizures.

Erickson (14) reported characteristic epileptic changes in blood flow and electric potentials during attacks induced by electrical stimulation of the cortex of a monkey.

Page (39) notes that there is some evidence that epileptic attacks in humans may be precipitated by external visual, auditory or kinesthetic stimuli. This is further confirmed both by history of the seizure and the patient's statement that certain stimuli (external) tend to bring on the fit. One possible interpretation offered concerning these reflex attacks is that they are associated with specific brain pathology and are of the Jacksonian variety. A second possibility is that they are of the conditioned variety. Experimental induction of seizures in hypnotized epileptics, of non-Jacksonian variety, by verbal stimulation would favor the latter view. With these factors in mind Page has attempted to produce seizures in five cats and ten rats. The usual conditioning procedure was followed. Immediately after sounding the bell for two seconds, shocks sufficient to produce grand mal convulsion was applied to the cortex. Each animal was given one or two trials per day for at least seventy-five trials. During the course of the experiments many simple reactions were conditioned, but in no instance was a conditioned convulsion obtained. Page points to the loss of consciousness which occurred immediately before onset of the seizures as the most probable explanation for lack of success in production of conditioned convulsions.

The author further points out that emotional disturbances, exclusive of aura of an affective nature, often precede the onset of an epileptic seizure. Clark (6) has interpreted the epileptic attack as a method of escape from an intolerable unconscious conflict, a flight into a fit. Clark has stated that, "No doubt, of course, can be entertained that incidental circumstances of a psychical kind, fright, grief, anxiety and other effective elements frequently act as precipitants, and are potent in immediate causation of the fit."

On the assumption that excitement is a predisposing factor, or a precipitating factor in convulsions, Page (39) felt that perhaps less current would be needed, in the excited condition to produce the reaction. His findings with ten animals were negative; the same amount of current was needed.

Page made an attempt to produce emotional disturbances by means of drugs. He used adrenalin and ethyl alcohol. Page found that larger doses than 25 cc had anti-convulsive property in the case of alcohol. The narcotic effect of the alcohol in the doses given was recognized by the author. Adrenalin also gave negative results, as far as reducing shock intensity for fit precipitation, was concerned.

Watson (43), as reported by Maier (34), made a more detailed study of the strain of mice reported by Dice (13), who had previously observed and studied the effects of auditory stimulation as a means of producing abnormal responses in mice, which he called epilepsy. Watson took Dice's strain of mice and discovered that a characteristic of both epileptic and waltzing mice is that they become totally deaf at the average age of six months, with gradual loss of hearing. The abnormal behavior also disappeared. In addition to keys, other stimuli used by Watson included the electric door bell, a police whistle and the high tone of a piccolo. The latter stimulus proved ineffective. Neither Dice nor Watson observed any adjustment to the situation with repeated stimulation.

Maier (35) used keys and air blasts and found that seizures could be produced in rats. His study was primarily concerned with conflict. Maier used direct auditory stimulation on control animals. He pointed out that, whereas auditory stimulation with an air blast was effective only a few times, whereas the conflict situation produced many seizures. Humphrey and Marcus (23) found that auditory stimulation by means of door bells produced seizures in 11 out of 23 animals. These workers pointed out the importance of the fact that supplementary conditions, such as oscillation of the cage, and previous development of nervous conditions in another test situation increased the number of animals having seizures.

Maier (35) reported that although auditory stimulation was adequate for production of violently abnormal behavior in the rat, the number of animals having an attack, and the frequency of the attacks are increased when conflict is introduced into the situation. Regarding effectiveness of auditory stimulation, the quality of noise, rather than intensity was the important factor in production of a convulsion. Maier found that when direct stimulation alone was used there occurred a reduction in the frequency of attacks as the testing proceeds. He further states that adjustments are reduced by a period of no testing, so that attacks could be re-instated in animals that showed continued periods of freedom from attacks. The pattern of seizure was found to vary somewhat according to the form of stimulation, the individual stimulated and the history of previous attacks. None of these factors were found sufficiently influential to determine the form that an attack would take on a given occasion. Maier indicated that conflict was an important determiner of seizures by showing that the negative card of a discrimination pair, was more than twice as likely to produce an attack as was the positive one. He further stated that the importance of conflict was greatest for animals not reacting to air alone.

Maier felt that the results of this study pointed to the following conclusions:

1. Auditory stimulation was basic in production of abnormal behavior.
2. Auditory stimulation does not arouse abnormal behavior as a reflex, but rather seems to furnish the emotional background

for the abnormal reaction.

In general, Maier considered that the evidence indicated that a conflict between excitation and inhibition was present in all situations in which attacks occurred. The auditory stimulation seemed important only as an exciting agent.

Maier (34) further studied the inheritance of the neurotic pattern. He used key jingling in a soundproof box as the critical stimulus. Animals were stimulated two minutes on five successive days to determine susceptibility. Animals which showed neurotic patterns of any form on any of the stimulations were considered abnormal. Various crossings of susceptible and non-susceptibles were then made, and on reaching the age of twelve weeks, offspring of these crossings were tested in a manner similar to the above mentioned parental testings. Since Maier experienced difficulty in getting neurotic animals to mate the same neurotic male fathered six litters. Three mating combinations were found to produce the following proportion of offspring.

1. Neurotic x neurotic, 25.7% normal, 74.3% neurotic.
2. Neurotic x normal, 48% normal, 52% neurotic.
3. Normal x normal, 100% normal, 0% neurotic.

Thus Maier concluded that the neurotic pattern is heritable as a unitary, dominant trait.

Maier (33) has reported concerning the relation of behavior which he has termed abortive, to the neurotic attack. The rats used in this experiment had each been previously taught to discriminate between negative and positive cards, and each had a record of attacks in the one window situation. Maier noted the necessity of continuing experiments, to determine the ability of abortive behavior to alleviate neurotic attacks, over a long period of time, due to fluctuations in susceptibility of the individual rats. He used three situations in this experiment. A discrimination test during which positive and negative cards of the original training series were presented; the one window situation in which case the animals were required to jump to a card, irrespective of whether it was positive or negative, and the two negative card test. The jumping apparatus hitherto used by this investigator, was modified in this experiment so as to permit the escape of the animal either from the starting box or by jumping over the stimulus card.

In this situation, one rat had, as Maier stated it, "what might be called attacks." Abortive behavior prevented the appearance of attacks in 13 out of 58 trials. The attacks were explained by the author as, "products of the necessity of responding to a situation in which a mode of response is unavailable." As further evidence of the ability of abortive behavior to eradicate the neurotic pattern, Maier stated that rats could be caused to have attacks when the old apparatus, which did not provide possibility for abortive jumping was used. When confronted with the same problem on the new apparatus, abortive jumping prevented the seizure.

Another rat is reported by Maier in this paper to have fewer seizures when allowed to make abortive jumps either to the right or left of the stimulus cards, or over them. Retraining experiments with this animal re-instated the attacks, and "in all cases the attacks occurred immediately after the critical situation was reintroduced." The author stated that, "since the exposure to air in the situation was less before an attack than on controlled test days, one cannot argue that manipulation of the situation increased the delay in response and thus increased the period of confinement in the jumping box."

The record of a third rat is reported by the same author to demonstrate the relation between abortive behavior and attack frequency. Its record furnished evidence, according to Maier, which indicated that the attack is partly a function of the reaction to cards, rather than a direct response to an air blast. Maier felt that this fact was demonstrated by the fact that all the animal's attacks in the one window situation occurred in response to the negative card, and all the attacks in the discrimination situation were in response to the negative card when it conflicted with a position habit.

Maier and Glaser (35) have concluded that even exposure to direct auditory stimulation could be regarded as a conflict situation, since "Auditory stimulation in such cases gave rise to no specific response, but was excitory in nature." The major conclusion which Maier has drawn from experiments on abortive jumping, related to the effectiveness of the latter as a cure for the neurotic pattern.

In a review of Maier's studies Hampton (19) has pointed out that rats have presented the most difficult problem to the psychologist studying neurosis, since they appear to adjust better than other animals in conflict situations. In discussing Maier's experimental methods of inducing abnormal behavior in rats, Hampton stated that Maier used a modified form of a discrimination technique. Maier changed the cards so that the rats were no longer able to use previously learned cues to make a choice of the card which would lead them to the food. At this point the animal refused to jump and an air blast or electric shock was applied to force the rat to jump. A number of animals developed neurotic attacks either before or after the jumping was forced. These attacks occurred only when the air blast was used to force jumping, and never with shock alone. Maier explained this fact by stating that, when the shock was applied, the animals managed to avoid the issue of jumping. This was not the case with the air blast for it was continuous on some occasions. Some rats were reported having attacks merely from seeing or hearing other rats being forced to jump by the air blast. Maier felt that this evidence suggested that neurotic attacks may be brought about when no conflict situation existed.

Hampton (19) further reported investigations by Humphrey and Marcuse which purported to place doubt upon the possibility of putting a rat into a neurotic state without producing a conflict situation. Humphrey pointed out that he and Marcuse discovered that adaptation to the stimulus situation played a very decided part in the rats' susceptibility to attacks. These authors further pointed out that wild rats that have had much less handling were more susceptible than the tame animals. The tamer the rat was, the less likely he was to succumb and fall into a seizure, according to Humphrey and Marcuse. These investigators further stated that, "tame or wild, all animals that developed the fit showed clear signs of undergoing a conflict." Thus, in accordance with this view, the rats which in Maier's experiment fell into a neurotic state by merely seeing or hearing other animals, actually shared the conflict situation in which the former animals found themselves. As Hampton pointed out, there is lack of agreement between Humphrey and Marcuse and Maier on the claim of Maier that the more emotional the animal, the less subject it is to attack, and conversely the more phlegmatic the rat is, the more susceptible to attack. Humphrey and Marcuse intimated the opposite view point.

Recently Maier (36) has published a report dealing with permanence of behavior tendencies in "fixated and nonfixated" animals. In this report the author referred to metrazol as having a therapeutic effect on abnormal behavior, stating that "the fact that metrazol failed to disturb the learned patterns, some of which were abnormal adjustments, in any observable manner is inconsistent with any theory which makes the therapeutic effect of metrazol dependent upon a disruption or disorganization of past experience." Maier also concluded, in this publication, that predisposition to the development of fixations and showing of neurotic seizures are unrelated factors. Further experimentation prompted Maier to state that "a number of factors must operate together, and these become clear only when we grant the role of conflict," and again, "...only when resistance was broken by an additional agent that seizures occurred in any number." Maier also felt, as a result of his work, that since electric shock is not an effective manner for producing seizures "mere overcoming of resistance to jumping does not guarantee a seizure."

Maier then gave metrazol to animals, obviously for the purpose of determining whether it had any therapeutic value for attacks in psychological tests. He found that metrazol reduced the relative frequency of attack to the negative card. Maier stated, in addition, that the metrazol, rather than its convulsion, seemed to be the active agent. In another part of the same paper, Maier suggested that a non-convulsing dose of metrazol is more disturbing, psychologically, than the convulsing one. He further suggested that, the effect of metrazol seems to be that of producing a temporary psychological condition that increases the animals' irritability.

In the eighth article of the series entitled "Studies of Abnormal Behavior in the Rat" Maier, Sacks and Glaser (36) reported concerning "influence of metrazol on seizures occurring during auditory stimulation." It was the stated purpose of the authors to further elucidate the mechanism concerned in the seizures. More specifically, they wished to determine whether the convulsions had a structural or functional basis. Three groups of animals were described. The first group consisted of animals which came from a stock resistant to convulsions, the second group was made up of animals from a convulsive stock, and the third group was composed of rats taken from matings of the first two groups. Animals in groups one and two were given a series of metrazol fits, until their threshold for the drug was lowered. On the test day they were given a sub-convulsive injection of metrazol and then subjected to auditory stimulation. The second group of rats were similarly dealt with. The third group received no previous metrazol convulsions before being injected with the sub-convulsive dose of metrazol and subjected to auditory stimulation. Maier found that a large percentage of groups 1 and 2 could be subjected to seizures by the above mentioned procedure, group 3 did not react so strikingly. From these results the authors felt justified in concluding that previous convulsive experience with metrazol may increase the tendency of a rat to react to auditory stimulation. The authors offered the further conclusions that auditory fits are functional.

Humphrey and Marcuse (23) have reported a technique for inducing chronically disordered behavior in the rat. Ten rats were trained by daily runs for twenty-five days in a Warner-Warden multiple Y-maze. The food box had no bottom, so that the rat and its food were in direct contact with the floor of the room. With six of the animals the food box was moved along the floor after the animal was in the food box and the door closed. The extent of movement varied from four to ten feet and had no appreciable effect on the immediate behavior of the animals except that they refused to eat until the movement ceased. The remaining four rats were trained in the ordinary way with the stationary food box. The six rats whose food box was moved were consistently above the four unmoved controls in their scores both for learning time and error. The curves for experimental animals were more irregular both in time and errors. At the same time, the authors reported that there appeared activities significant of disorder; belly crawling, loud gnashing of teeth, spasmodic starts from one side to the other of the cul-de-sac, shivering and a type of withdrawal reaction described by the authors as follows, "When half-way to the food box would frequently withdraw and rerun the maze with or without errors, and then return to the food box with or without errors." None of the above reactions were observed in the control animals.

In discussing the results of their work, Humphrey and Marcuse stated, "It is difficult not to use anthropomorphic terms in description of these animals, the most natural explanation seems to be that the animals knew their way to the food box, but were prevented from entering it by some conflicting motive." These workers also felt that the conflict was one which was very difficult or perhaps impossible for the animal to resolve.

Freeman (16) has reported concerning the adaptation of Pavlov's general method of frustration with human subjects. In Freeman's study the motivating condition was desire to escape shock rather than the desire for food. The subject was trained to make finger reactions signaling whether the second pair of near threshold visual stimuli is lighter or darker than the first. Failure to react within ten seconds following presentation of the stimuli is punished by shock, as were incorrect reactions. The author reported a trend toward disorientation as the problem became too difficult. Breakdowns of specific differentiations were reported along with concurrent rise in general bodily excitement as indicated by decreased palmar resistance. As in other experimental studies on frustration, Freeman's results indicated individual differences in ability to withstand the experimental conditions.

Hall, and Martin (18) have proposed that an air blast be used as the standard method of producing abnormal behavior. These authors felt that the air blast method provided a tool for understanding causes, prevention and cure for gross behavior derangements. In the standard procedure suggested by Hall and Martin, the rat was placed in a circular enclosure, brightly lighted, seven feet in diameter with a surrounding wall of galvanized iron 30 inches high.

Compressed air was released into this field from an air chuck attached to rubber hose leading from a portable air compressor. The air blast was continued for two minutes. The attack consisted of a disoriented hyperactivity followed by tonic or clonic convulsions, or both, terminating either in coma-like states during which the rat could be moulded. Gradually these states passed off and the animals apparently returned to the normal condition. Hall and Martin pointed out the similarity of the above pattern to epileptic seizures.

Erickson (14) has reviewed the epileptic literature in summary fashion. Bravais, an early investigator in this field, had no conception of a physiological basis of epileptic form of fit and merely defined a variety considered more curable than the ordinary form. Jackson thought that the spread of epileptic discharge took place through the arteries. Karplas felt that spread occurred through the cortico-tegmental path to the brain stem. Gibbs found a general increase in blood flow through the brain during a convulsion. Kornmuller stated that activity induced by stimulation of one center may spread by neuronal and not vascular pathways. Erickson stated in his paper that spread of an epileptic after-discharge induced in monkeys by electrical stimulation of the cortex was attended by several indices of epilepsy. Local changes in the cerebral blood flow during the fit helped indicate how the fit discharge was spread. Section of the corpus callosum and transcortical sections at right angles to the central sulcus of Rolando enabled Erickson to state that, "the after discharge induced by electrical stimulation of the cortex is the counterpart of clinical types of epilepsies. Changes in the blood flow of the animals during a fit are the same as those in man during an epileptic fit. Changes in the electrical potentials during and after epileptiform fits are the same in monkey as following an epileptic fit in man. The corpus callosum plays a definite part in spread of the epileptic discharge from one hemesphere to the other."

Notkin (38) made a study of the personality make-up in 75 male and 75 female epileptics. This study revealed a definite correlation between age of onset of the seizures and the type of personality known later. Epileptic make-up was apparent in cases in which there was an early onset of the seizures. This constituted 16.6 percent of the cases. Notkin noted, however, a considerable variation in personality types among the epileptic patients.

Status of the Problem of Abnormal Behavior In the Rat at the Time of this Study

Surveying the foregoing literature, it appears that several aspects of the general problem of abnormal animal behavior needs the elucidation which further experimentation may supply. As we have noted, the status of auditory stimulation as a requisite for producing convulsive seizures in the animal is unsettled. The effects, if any, of the convulsions on previously learned habits have not been satisfactorily determined. Investigation of the heritable factor or factors concerned in convulsive seizures has only recently been undertaken and needs further study.

Purpose of the Investigation as a Whole

This entire study has been divided into three sections. Section 1, titled The Production of Convulsions in the White Rat, deals with the following major questions:

1. Is auditory stimulation an essential requisite for obtaining seizures in the rat by the conflict method?
2. Are the convulsions evidenced in the presence of auditory stimulation actually audiogenic?
3. What is the actual role of conflict in the production of convulsions?

Supplementary to the above questions, we attempted to find psychological and physiological methods of alleviating the seizures.

Section 2 of the investigations titled The Persistence of Convulsions in the White Rat, is concerned with the nature of the seizure itself. The question before us is, are these convulsive seizures, evidenced in the white rat, fundamental enough to leave any lasting imprint on the animal which might be detected by testing the retention of a previously learned habit?

Section 3 of the work, titled The Transmission of Convulsions in the White Rat, deals with the heritable factor or factors of the convulsion, looking toward the possible production of chronic animals who would exhibit abnormal behavior outside of the stimulus situation.

Part II.

Section 1. The Production of Convulsions in the White Rat

Purpose and Method of Section 1

This section is primarily concerned with the following questions:

1. Are convulsions evidenced in the presence of auditory stimulation actually audiogenic?
2. What is the actual role of conflict in the production of convulsions?
3. Is it possible to differentiate clearly convulsive from non-convulsive rats?
4. What effect does continued stimulation over a considerable period of time have on the onset, duration, and post-convulsive stages of the seizures?
5. Is it possible to produce convulsions without employing auditory stimulation (exclusive of electrically induced seizures)?
6. Corollary to this, are combinations of two ineffective stimuli effective in producing seizures?
7. What factors may be utilized to alleviate the seizures?

The investigation is divided into three experiments, utilizing, in all, 97 white and black-and-white rats. *Experiment 1* was carried out in the following manner:

Eighteen animals, 8 males and 10 females, were placed individually on the floor of a small room (4'x6'). A double coil electric door bell, affixed to a ledge approximately 4' above the animal's head, was rung for a 3' period to induce seizures. Animals were stimulated an average of 91 times during trials spaced at intervals of one day. As Table 1, page 78, indicates rat R-6, female, and R-16, male, were stimulated by key jingling instead of the usual bell.

Rats not succumbing to a seizure after 3' stimulation were considered negative on that particular trial. No attempt was made to divide animals into "normal" and "convulsive" classes until every rat had received at least 60 stimulations.

The length of time that the bell had been ringing before the animal began the running phase of the fit, (Running, at first oriented, then "blind" and random was recognized in the literature and by the experimenter as the first stage of the convulsive pattern), was recorded with a stopwatch, and considered as "onset time". The period actually spent in violent muscular spasm was similarly recorded as "duration of seizure", and the period immediately following the violent muscular activity of the duration stage, was recorded as "post-convulsive" stage. In all cases the bell was discontinued at the close of stage 2 (Duration) of convulsive seizures. Consequently, stage 3, or the "post-convulsive" period was considered as extending from the end of stage 2 up to the first voluntary movement on the part of the animal.

Experiment 2

This experiment was conducted with 10 animals, 6 males and 4 females, using a series of discrimination problems. Each animal was trained on a different discrimination series. Each discrimination series, designated A-J, consisted of 7 cards. Five of the cards were "positive" stimuli in the form of circles, the remaining two were "negative" stimuli. The latter, although identical with each other, were either circles of a given diameter, or a blank card with no circle upon it.

For presentation of the stimulus cards in the discrimination series, a modification of the Lashley jumping apparatus was constructed. This consisted of a jumping platform 33" high guarded on three sides by cardboard blinds. The fourth side was open and faced the stimulus windows. The two stimulus windows, which held the discrimination cards were square openings 5"x5", cut in an easle 41"x36", and equipped with hinged wooden shutters which could be closed and locked. The top of the jumping stand, upon the surface of which the animals were placed, was a square platform measuring 10" per side. The stimulus windows opened onto a food platform extending the entire width of the easle, and being itself 12" wide. The surface of the jumping platform, ledges surrounding each stimulus window, and the top of the easle were electrically charged, as was the moveable grid placed on the table top, upon which the apparatus rested. Current from three dry cells flowed through the system.

Depending upon age and size, animals were required to jump 12-20 cms (distance of jumping stand from stimulus windows could be varied as desired by moving either easle or jumping platform). Training was begun when animals reached the age of 90 days.

Rat BF, a male animal, may be used to illustrate the procedure which was adhered to with all animals used in this experiment. Table 5, page 82 , may be referred to for clarification of the explanation. From the left side of this table it is noted that rat BF was trained on discrimination series A. The right side of the same table indicates that the "positive" cards (cards toward which rat is to jump) consisted of white circles on a black background. The "negative" cards were plain black with no figure. The animal was trained to avoid or withdraw from the black card. The "critical" test (test designed to produce "conflict") for this animal was presentation of the black (negative) card in both stimulus windows. The card board blinds fixed to the three sides of the jumping stand, and the grid systems which we have previously described were designed to prevent the animal from escaping from the apparatus during the "critical" test, or during the training periods.

In the case of rat BF the training series began with the largest circle of the 5 which composed the "positive" stimuli (10 cms. diam.). In successive training periods the diameter of the white circle was diminished in steps of 2 cms. until the circle was no longer evident, at which point the rat was forced to face two negative black cards. Incorrect reactions were punished by shock.

The actual training was carried out in the following manner. Previous to the first day of the training period the animal was starved and kept without water for a 24 hour period. During the preliminary training period food and water were placed on the ledge behind the stimulus windows. The rat was placed on the jumping stand and the jumping stand was moved adjacent to the windows and the animal permitted to walk back and forth from the jumping platform, through the open stimulus windows to the food shelf. A small amount of food and water was permitted the animal after each excursion. This procedure was engaged in until the rat walked readily through the open windows when placed upon the jumping platform. One of the stimulus windows was then closed and locked and a negative black card placed on the front of the closed shutter. The next several trials consisted in teaching the animal to walk through the open window and avoid the closed shutter with its black card. The negative black card was placed on right and left windows in random order to prevent learning of position habits. Food and water from the food shelf was permitted only when the animal went through the open window.

Following the establishment of a definite avoidance reaction to the negative black card, the animal was ready for presentation of the first positive card of the discrimination series. In the case of rat BF, this card contained the white circle with largest diameter (10cms.) of the five contained in its series (A). This card was referred to as circle range 1, positive.

At this point we shall digress for an explanation of the terminology used with reference to the stimulus cards composing a discrimination series. The discrimination problems consisted of series of circles painted on cardboard squares, of a size permitting insertion in stimulus windows, or on the closed shutter of a stimulus window. (Approx. a square of cardboard 5"x5"). Discrimination problems were grouped into series A-J, dependant upon color of circle and background upon which it was painted. For example, series A (Table 5) contained discrimination cards composed of white circles on a black background. Series B consisted of black circles on white backgrounds, etc. Each series contained 7 discrimination cards. In the event that a card contained a circle on it, reference was made to it by range, which indicated the diameter of the circle. For example, circle range 1, referred to the first discrimination card upon which the animal was trained. Depending upon the particular training series range 1 could indicate either the largest, or the smallest circles of the series. In any event the rest of the circles composing the series progressed, or regressed in their ranges, from that of circle range 1 toward the negative card. As mentioned, circle range 6 was identical with the negative stimulus. In this respect it might be better to speak merely of card 6, since in some of the discrimination series the negative card (of which card 6 was a duplicate) was plain with no circle upon it.

Reference may be had to the right side of Table 5, page 82 , in clarifying the above description. We note from this table that series A consisted of white circles on a black background for the positive stimulus and a plain black card for the negative member. This indicates the direction of progression, in this case regression, in the ranges (diameters) of the circles 1-5. Since black card is the negative member and since the sixth card of any series is identical with the negative member of the series, hence the discrimination cards included in series A vary from a large white circle (range I) through 4 intermediate ranges, to a plain black card (card 6); or from a circle of range 1, diameter (10cms.) to one of range 5, diameter (2cms.).

Discrimination series I, B, D, F, and E (Table 5) follow this regression from range I (10 cms.) to range 5 (2 cms.), from large to small diameter circles. Conversely, discrimination series C, G, H, J, progress from smallest diameter at range I to large at range 5. Range 6, being equivalent to a negative card, was thus the largest circle of the series.

We return now to rat BF, which we were using as an illustration of method of training animals used in this experiment. After having established a withdrawal response to the "negative" stimulus (black card), by the procedure outlined, the first "positive" card was leaned against the open window (circle range 1, series A). In the training of BF, then the card with large white circle on black background was leaned against the open window in such a way that the animal could walk from the jumping platform to the food shelf by merely pushing over the card with a white circle on it. Positive and negative cards were, of course, shifted at frequent intervals to avoid position habits from becoming established. After the animal had correctly differentiated "positive" circle range I from the "negative" black card several times, the "positive" card was fitted snugly into one window, "negative" card similarly placed in the remaining window and both window shutters were raised. The jumping stand was moved back to a distance of approximately 21 cms. from the easle windows. This point marked the close of the preliminary training period, which, as we have indicated, served to acquaint the animal with the apparatus and to establish the approach-withdrawal reactions to their proper stimuli. The animal was then replaced in its cage, starved and kept without water for 24 hours.

Following this rest period, and the preliminary training period, the rat entered upon training day 1. Using again circle range 1 as the "positive" card toward which the animal was to jump, and the plain black card, as the "negative" stimulus from which the rat was to withdraw, BF received 28 trials at 10 A. M., 4 trials at 2 P. M. and 30 trials at 3 P. M. The positive and negative cards were presented in random order to avoid position habits. Food and water in small quantity were permitted only when correct reactions were made. It may be mentioned that animals seemed to perform the discrimination reactions as a type of "trick" after they had learned what was expected of them, and ate very little even following a starvation period. Occasionally tapping, pushing or slight shock was necessary when animals exhibited signs of lethargy or negativism.

On training day 2 (following immediately training day 1, with no cage starvation period) an identical procedure was followed using again circle range 1 as "positive" card and the plain black card as the "negative" stimulus. On day 3 the rat was again left in its living cage without food or water. Training days 4-5 were repetitions of the procedure recorded for days 1-2 with the exception that "positive" circle range 2 replaced "positive" circle range 1. The rat was left in its cage on day 6 without food or water. Training days 7-8 were repetitions of procedure indicated for 1-2; 4-5 with the exception that "positive" circle range 3 replaced "positive" circle range 2, used during days 4-5.

Training days 10, 11, 13 and 14, and starvation-rest days 9-12 and 15 followed in due order. Each two training days saw a reduction in range of the "positive" stimulus (this of course was true only in the case that the discrimination series regressed.) In progressive discrimination series each two days saw an increase in range or diameter of the "positive" stimulus. By training day 14, the last range (5) of "positive" circle was reached. In the case of BF, under consideration, this would mean that the smallest diameter circle of the discrimination series A was presented on training day 14.

When the animal had mastered the discrimination of this small diameter circle from the black card we were ready to prepare the rat for the "critical test " with two black cards. Prior to presentation of the two negative cards, the animals were given intensive re-training (on consecutive days) on circles ranges 1-5 which they had been previously trained on. In accordance with this procedure, BF was starved and kept without water on day 15 and, on the following day (16), was re-tested with "positive" circle range 1 and the "negative" black card; which, as will be noticed, was the same procedure as carried out on training days 1-2. On such re-test days the rats were given 52 trials distributed throughout the day as follows: 20 trials at 10 A. M., 2 trials at 2 P. M., 30 trials at 3 P. M. On days 17-18-19-20, 52 trials were given, re-testing the animals on all 5 ranges of the "positive" circle opposed to the black card.

On day 21, the rats were faced for the first time with a "negative" black card in each stimulus window; immediately preceding this exposure, animals were given a preliminary test of 20 trials on circle range 5 with the black card. The animal's reaction to presentation of the two negative cards was carefully recorded, and no electric shock applied. On day 22 the procedure outlined for day 21 was repeated and in addition the electric shock was applied to the rat. Again the animal's reactions were recorded. Day 23 was a rest-starvation period, during which time the rat remained in its cage without food or water. On training day 24, the animal as usual was given the preliminary 20 trials on positive circle range 5, and then faced with the two negative cards, without electric shock. Day 25 was a starvation period and, on day 26, the usual procedure was repeated, this time with the electric shock.

This procedure was continued as outlined with all animals until they had 15 exposures to the two negative stimuli; shock being used on alternate days.

Experiment 3

This experiment was titled Production of Convulsions by Sensitization. The subjects were 19 males and 17 female rats. We desired to determine whether animals, whose histories indicated only a very small percentage of seizures when subjected to bell stimulation, would exhibit an increased percentage of convulsions when the rather ineffective bell stimulation was combined with another equally ineffective stimulus.

The thirty-six animals were divided into two major groups. Animals in the first group received sub-convulsive doses of metrazol as the "sensitizing" agent before being stimulated with the bell. Rats in the second group were subjected to the stimulation obtained by beating upon a strip of galvanized iron in combination with bell ringing.

Group 1 (F_1 animals) was further divided into 3 sub-groups (Table 6, page 83) on the basis of genetic histories. All the parental animals of this group were non-convulsives. The offspring of these animals (F_1 used in this experiment) had themselves only a very low percentage of seizures when stimulated with bell alone, and none at all when subjected to the sound of striking on a galvanized tin strip. This group was composed of 6 males and 2 females. Sub-group 2 consisted of 9 animals, 4 males and 5 females, F_1 generation of convulsive parents. (As Table 6 indicates, animals RT and RH were exceptions to the general rule mentioned above, that F_1 animals had very few seizures, stimulated with bell alone.) Sub-group 3 consisted of 5 animals, 3 males and 2 females, F_1 generation of parents, one of which was convulsive, and the other non-convulsive. Procedure for administration of metrazol was the same for all three sub-groups and was done as follows: all rats were stimulated for 5' with the bell. Failing to succumb to a convulsion, the animals were given sub-convulsive doses of metrazol. (cf. Table 6) After an interval of 5' the animals were again subjected to bell stimulation (not in excess of 5'), and results recorded in Table 6.

Group 2 was composed of 17 rats. Of these, 6 were males, 11 were females. The experimental procedure was in general the same as that used with Group 1, with the exception that the animals were stimulated by beating with a stick upon a galvanized iron strip during the ringing of the bell (in place of metrazol injection). These animals were all given pre-tests to determine effectiveness of "extra" noise, and electric bell, presented separately. In no case was extra noise alone effective. In a few cases the bell alone was effective a small percentage of the time. (Table 7, page 84.)

From observations made during experimentation with stimulation of rats by bell to obtain convulsive seizures we designed a final experiment to investigate possibilities of psychological means of alleviating the seizures. We had observed that animals, which, during the "oriented" stage of running, occurring during a typical seizure (cf. discussion, page 93), succeeded in hiding behind the photographic curtain, or wedging themselves into a crevice in the cardboard retaining wall, guarding the stimulus area, never had convulsive seizures.

We constructed an apparatus, which incorporated this "shelter" factor, for the purpose of determining its value in alleviating the convulsions. We selected 12 rats, 7 females and 5 males, from amongst the convulsives produced in

Experiments 1 and 3 of this research, to be tested in the "shelter" situation. The animals were placed in a galvanized iron cylinder with the stimulus bell hanging 4' above their heads. The cylinder enclosed an area of 20" on the floor where the animal was placed for stimulation. On one side of the galvanized enclosure a 3"x5" opening was cut, level with the bottom of the cylinder. This opening could be closed at will by a shield, operated by the experimenter. The 3"x5" hole led to an open runway, 3'x1', ending in an experimentally constructed "rat hole". The latter was constructed by splitting two ordinary galvanized iron pipes, bolting them together and covering the open top with wire netting. The pipes thus formed a space of about 10" within which an animal could hide. The distance from bell to center of "rat hole" was approximately 4' (equal to distance from bell to center of galvanized cylinder). The experiment with this "shelter" apparatus was carried out in the following manner. The rat was placed in the galvanized iron cylinder and the bell was turned on. At a given point in the "oriented" running phase of the convulsive pattern, the experimenter removed the shield, thus exposing the opening in the galvanized cylinder. The number of times the rat took advantage of the altered environment and ran through the 3"x5" hole, along the runway and into the "rat hole", was recorded. The number of seizures exhibited by animals making this "shelter" reaction was also recorded.

Corollary to the above experiment, 3 female and 1 male animal were selected from the convulsive rats used in experiment 1 to serve as subjects in the "binding" experiment. This experiment was conducted in the following manner. The rats were rolled up in bandage cloth with head and ears protruding. The cloth was kept in place by two cloth bonds in the vicinity of fore and hind limbs. Animals thus restrained were held 4' from the ringing bell. Three of the 4 subjects were anaesthetized prior to binding to negate struggling reaction. Suitable time, of course, elapsed between anaesthetic and stimulation. Following exposure to bell, the animals were unbound and placed in a previously learned maze to indicate presence or absence of refractory period ordinarily following a convulsion.

Both "shelter" and "binding" experiments were presented a number of trials, equal to the total number of times the animal was stimulated in absence of these conditions (cf. Total Stimulation in Tables 1 and 7). In cases of rats from Experiment 3, which were used in the "shelter" experiment, the "sensitizing" combination was employed as stimuli, not merely the bell alone.

Results of Section 1

From Table I, page 78 , we note that the rats may be divided into general classes of convulsive and non-convulsive. Certain animals, namely, RX, R-12, R-LHL, and R-BW, however, cannot definitely be classed as non-convulsives. Although the percentage of seizures in the above mentioned animals was small, as the Table indicates, yet due to the presence of these convulsive tendencies it would be misleading to call these rats non-convulsive, or normal. Table 4, page 81 , indicates the importance of prolonged test periods in determining the convulsive tendencies of rats. Rat RX, for example, never showed any signs of a seizure until the 57th trial; thereafter, as the Table indicates, it had seizures 4 percent of its trials. Excluding the border-line cases mentioned above, we have considered Rats 6, 16, 18, 72, 14, S-SC, L-AS, RA, and R-FF definitely convulsive, and hence these animals formed the experimental group. Animals R-71, R-B2, R-LE, R-BW, and R-RE were considered definitely non-convulsive, and hence formed the control group.

Table 2, page 79 , indicates the effect, on the speed with which a convulsion may be induced, occurring from continued stimulation of animals over a long period of time in the absence of prolonged rest periods. Without exception, the average onset time for a given rat's last 10 seizures was less than that necessary for the same animal's first 10 seizures. As the table indicates, the percent difference in time necessary to elicit a seizure, in first and last ten seizures, varied from 3 to 64 percent in favor of less stimulus for the last 10 seizures.

Conversely, Table 3, page 80 , shows that prolonged, continuous stimulation of convulsive animals leads to an increase in amount of time spent by the animal in the post-convulsive, or coma state, following a seizure. Without exception, the average number of seconds spent in abnormal behavior following cessation of the stimulus bell was greater during the last ten seizures than was this period during the first ten convulsions. As Table 3 indicates, the percent differences, between average post-convulsive periods of first and last ten seizures, were uniformly high, being in most cases above 50 percent. Rat R-18 was the only exception to this statement.

Results of administration of sub-convulsive doses of metrazol, combined with bell stimulation, as a method of producing convulsions in refractory animals is indicated in Table 6, page 83 , It is at once evident on examination of this Table that the method was most effective with animals whose parents were both convulsive. Conversely the method proved least effective in animals, neither of whose parents were convulsive. Judging from the seizure percentages following injection of metrazol recorded in the last column of Table 6, page 83 , it appears that animals which are offspring of one convulsive and one non-convulsive parent show most variability regarding the effectiveness of metrazol as a sensitizing agent.

With two exceptions (R-6 and R-3, Table 7, page 84) combination of two stimuli in the form of bell ringing and beating on a galvanized tin strip with a wooden mallet, proved more effective in inducing seizures in refractive animals than was the case when one stimulus only was used. This fact is evident by comparison of seizure percentages prior to addition of the extraneous noise, recorded in column 5, Table 7, page 84 , with those following addition of the sensitizing agent, recorded in column 6 of the same Table. Considerable variability as regards the reactions of individual rats to the sensitizing agent used with Group 2 of Experiment 3 is noted in Table 7. Extraneous noise plus the bell is no more effective in producing seizures with Rats 3 and 6 than was ringing of the bell alone. In the case of Rat 14, the combined stimuli proved only slightly more effective than the bell itself. This was likewise true of Rats 12, 15, and 16. The remaining animals, Rats 1, 2, 5, 8, 10, 11, 13, and 17, however, showed a considerable increase in percentage of seizures following addition of extraneous noise as a sensitizing agent.

The results of our attempt to produce convulsions by the so-called "conflict" method were uniformly negative with one exception. The most common reaction to presentation of two negative cards in absence of shock was withdrawal. When shock was added in presence of the two negative cards, the animal's reaction was variable. In some instances, animals would exhibit marked signs of emotionality when two negative cards were presented. In other cases, emotional behavior was evidenced only when shock was applied with negative stimuli. With other animals, no emotionality was evidenced either with negative cards plus shock, or negative cards alone; rather these animals seemed to manifest a general negativism. For a clearer picture of the actual results obtained in Experiment 2, excerpts from our original records may prove helpful. Table 5, page 82 , may be consulted for additional information. As the Table indicates, Rat BF made 733 correct reactions to discrimination problems presented him (possible 824 correct reactions could be made). Column 5, Table 5, page 82 , indicates that this rat's reaction to two negative stimuli was not a convulsive seizure. Similarly, application of the electric shock in combination with negative cards failed to produce a seizure. Consulting our original records on Rat BF, we find the following notations regarding its behavior:

4/21/40 "Animal (Rat BF) faced for the first time with two negative cards. Rat walks to far edge of jumping stand. Neck stretched toward stimulus card. After brief period in this position, animal backs up slowly pressing himself against side walls of jumping platform and remains motionless for duration of period. No clear marked signs of emotionality. Respiration apparently normal; slight movement of vibrissae."

4/26/40 "Rat races to front of the jumping stand, shock applied while animal is in this position. Animal jumps slightly and begins 'weaving' movement of the head. Respiration appears to be considerable increased. Audible teeth chattering. This type of behavior continued for approximately 4'30". Animal then starts to the back of the stand. At this point the shock is again applied. Animal quickly runs to front of the jumping stand and repeats 'weaving' movement."

5/10/40 "Rat BE, faced with two negative cards. Animal goes to edge of the jumping stand; leans far out, wavers from one side to the other; teeth chattering clearly audible. Animal retreats to middle of jumping stand, paces from one side to the other. This reaction lasted approximately

5'30". Animal then retreats to back of the jumping platform and remains motionless for rest of test."

5/12/40 "Negative cards presented rat BE. As animal starts toward sidewall of jumping stand shock is applied. Animal 'vocalizes'. Respiration is increased. Tail is partially lifted free of ground and rat begins to hurry back and forth on the front part of the jumping stand. Occasionally animal stops this type of behavior and engages in 'head weaving'. This reaction continued for approximately 7' 32" followimg application of the shock. As animal started again toward back of jumping platform shock was applied a second time. Rat raced to front of jumping platform 'vocalizing' even after cessation of the shock. Rat remained on edge of stand leaning toward stimulus windows and 'weaving' head."

6/16/40 "First reaction on presentation of negative cards to rat BT was an 'about-face'. Animal turned back to stimulus windows and pressed itself against side-walls of jumping platform. Animal stayed in this position ignoring stimuli."

6/17/40 "BT presented two negative cards. Begins 'weaving' motion of head. At this point

> while animal is fairly close to the front of the jumping platform he is shocked. Violent respiration is at once visible. Vibrissae move rapidly, slight eye 'bugging' noted. Movements to and fro on edge of jumping platform increase, as does rapidity of head movements. Reaction continues 2' 14" after shock given. Following this activity animal turns to center of jumping stand and sits motionless faced with two negative cards. Respiration and vibrissae movements normal. Shocked again in this position, animal emits a squeal, runs to front of jumping stand and repeats above reactions."

The above excerpts give a general idea of the type of reaction obtained using "negative" cards alone, and negative cards plus electric shock to induce convulsions. As Table 5, page 82 , shows, Rat BA, a male animal, trained on discrimination series F, showed the only exception to the type of reaction recorded above. This animal, as indicated in column 6, Table 5, page 82 , succumbed to a convulsive seizure upon presentation of "negative" cards and application of the electric shock. Our records read as follows concerning this rat:

> 4/19/40 "Upon presentation of two negative cards, animal BA commences quick circular turns.

> Violent increase in respiration, eye bugging, vibrissae twitching. Attempts to escape from jumping apparatus. Reaction lasted 5' 38". Animal then retreated to center of jumping stand, apparently disregarding negative stimuli."
>
> 4/20/40 "Animal BA gives evidence of great excitement when presented with negative cards. Subsequently rat appears to become acclimated and starts toward rear of jumping stand. At this point the electric shock is applied. Signs of excitement increase. Animal jumps to top of easle, shocked again, jumps to table top. Shocked on moveable grid; jumps to floor, begins to run in wide circles, blindly, culminates in convulsion lasting 17' 30" complete pattern."

Twelve such reactions were obtained with this animal out of fifteen exposures to shock plus "negative" cards.

Table 8, page 85 , indicates the effectiveness of the "shelter" reaction as a method of reducing percentage of seizures in convulsive rats. Column 3 shows the percentage of convulsions succumbed to by the rat previous to introduction of shelter. Column 4 indicates percentage of times that a given animal took advantage of escape possibility and ran to "rat hole". The fifth column shows percentage of convulsions experienced by the animal notwithstanding the "shelter" reaction. A glance at Column 6 of this Table is sufficient to indicate the effectiveness of this psychological method of reducing the percentage of convulsions. As is noted, this last column shows difference in percentage between pre- and post-shelter conditions. Without exception, seizure percentages are reduced, on an average of 57.8 percent by addition of the "shelter".

Table 9, page 86 , merits little explanation. Without exception, binding alleviates convulsive seizures. Also, without exception, animals show no refractory period when placed in a previously learned maze. Rats run this maze without error or delay, a fact not characteristic of animals experiencing convulsive seizures.

TABLE I.

Total Stimulations and Seizures.

Rat	Sex	Total stimulations.	Total seizures	Percentage seizures.	Stimulus
R-6	♀	60	54	90.0%	Keys
R-16	♂	75	62	82.6%	"
R-18	♀	65	55	84.6%	Bell
R-72	♂	103	73	70.8%	"
R-14	♀	108	77	71.3%	"
R-X	♀	100	4	4.0%	"
R-71	♂	75	0	0.0%	"
R-B2	♂	100	0	0.0%	"
S-S6	♂	100	65	65.0%	"
L-AS	♀	60	35	58.3%	"
R-LHL	♀	70	3	4.3%	"
R-LE	♀	70	0	0.0%	"
R-BW	♀	209	10	4.8%	"
R-FF	♀	105	74	70.4%	"
R-BW	♂	100	0	0.0%	"
R-RE	♂	72	0	0.0%	"
R-12	♀	75	5	6.0%	"
R-A	♂	100	78	78.0%	"

TABLE II.

Average Time of Onset in First Ten Seizures Compared with Average Onset Time in Last Ten Seizures.

Rat	Sex	Onset in seconds of first ten seizures.	Onset in seconds of last ten seizures.	Difference in onset time between first and last ten seizures.	Percent decrease in seizure time of last ten seizures.
R-6	♀	100.6"	93.7"	6.9"	7%
R-18	♀	54.4"	31.1"	23.3"	43%
R-14	♀	22.4"	17.8"	4.6"	20%
L-AS	♀	42.0"	30.9"	11.1"	26.4%
R-A	♀	29.3"	10.4"	18.9"	64%
R-FF	♀	52.4"	23.9"	28.5"	45%
R-16	♂	42.7"	21.1"	21.6"	50%
R-72	♂	52.3"	21.3"	31.0"	59%
R-SSC	♂	81.8"	79.2"	2.6"	3%

TABLE III.

Average Post-convulsive Period of the First Ten Seizures Compared with That of the Last Ten Seizures.

Rat	Sex	Average duration of the post convulsive period in first ten seizures.	Average duration of the post convulsive period in last ten seizures.	Difference in seconds	Percent increase in duration of post convulsive period in last ten seizures.
R-6	♀	29.4"	46.3"	16.9	57%
R-18	♀	31.2"	36.4"	5.2	16%
L-AS	♀	28.9"	57.3"	28.4	97%
R-A	♀	73.4"	152.9"	79.5	108%
R-FF	♀	56.0"	129.9"	73.9	131%
R-14	♀	22.2"	42.8"	20.6	94%
R-165	♂	48.0"	73.5"	25.5	53%
R-72	♂	28.0"	43.2"	15.2	54%
R-SSC	♂	21.5"	52.0"	31.5	141%

TABLE IV.

Percentage of Seizures Obtained in Animals with Delayed Onset.

Rat	Sex	Trials in which first seizure occured.	Total number of seizures.	Total number of trials.	Percent of seizures.
R-X	♀	57th	4	100	.04±.019
R-12	♀	21st	5	75	.06±.027
R-BW	♀	8th	10	209	.048±.014
R-LHL	♀	14th	3	70	.043±.024

Table V

Record of Production of Convulsions by "Conflict" Situation

Series	Rat	Sex	Correct reactions	Reactions to negative card	Reaction to shock plus negative card	Series	Positive		Negative		Direction
							Background	Circle	Background	Circle	
A	BF	♂	733	-	-	A	black	white	black	none	regress
C	BT	♂	765	-	-	C	black	gray	gray	none	progres
E	BH	♂	623	-	-	E	BW	large BW	BW	small BW	regress
G	BM	♂	554	-	-	G	white	small CH	white	large CH	progress
I	BX	♂	576	-	-	I	white	large VH	white	small VH	regress
B	BE	♀	569	-	-	B	white	black	white	none	regress
D	BS	♀	574	-	-	D	BW	gray	BW	none	regress
F	BA	♂	595	-	+	F	gray	large white	gray	small white	regress
H	BL	♀	662	-	-	H	gray	small black	gray	large black	progress
J	BZ	♀	694	-	-	J	white	small HB	white	large HB	progress

Key
BW--Black & White
CH--Cross Hatched
VH--Vertical Hatched
HB--Half Black

Table VI

Production of Convulsions by Metrazol Sensitization in First Generation Animals

Rat	Sex	Age	Gms. body wt.	Previous trials	Percent seizures	No. of injections	Amount of injection	Percent seizures
RS	♂	7 mo.	339-472	35	0%	45	30-80 mg.	2%
RB	♀	5 mo.	200-261	30	0%	43	40-50 mg.	2.3%
RF	♂	5 mo.	198-301	30	0%	43	30-70 mg.	13.0%
RB	♂	5 mo. 6 da.	125-167	30	0%	21	20-30 mg.	0.0%
RLE	♂	6 mo. 4 da.	204-268	33	0%	37	30-50 mg.	8.0%
RS	♀	7 mo. 3 da.	197-211	39	0%	10	20-30 mg.	0.0%
RF	♂	5 mo.	154-253	26	0%	36	20-50 mg.	2.0%
RH	♂	5 mo.	200-348	32	3%	31	30-70 mg.	6.0%
RT	♂	5 mo. 4 da.	200-253	26	46%	19	10-30 mg.	54.0%
R2T	♀	5 mo.	174-303	26	0%	53	30 mg.	73.0%
R2B	♀	5 mo. 12 da.	198-281	29	0%	43	20-30 mg.	63.0%
RT	♀	6 mo.	130-163	38	0%	34	20-40 mg.	70.0%
RRE	♀	10 mo.	264-273	56	0%	27	30 mg.	100.0%
R2E	♀	10 mo. 2 da.	153-186	56	0%	26	30 mg.	83.0%
RB	♂	4 mo.	169-251	20	0%	22	30 mg.	74.0%
RLE	♂	4 mo.	127-314	20	0%	38	20-40 mg.	50.0%
RH	♂	7 mo.	324-341	34	60%	29	50 mg.	79.0%
BF	♀	7 mo.	210-253	58	0%	25	30-40 mg.	28.0%
BWT	♂	8 mo.	249-	50	0%	20	40-50 mg.	0.0%

			wt.					
RS	♂	7 mo.	339-472	35	0%	45	30-80 mg.	2%
RB	♀	5 mo.	200-261	30	0%	43	40-50 mg.	2.3%
RF	♂	5 mo.	198-301	30	0%	43	30-70 mg.	13.0%
RB	♂	5 mo. 6 da.	125-167	30	0%	21	20-30 mg.	0.0%
RLE	♂	6 mo. 4 da.	204-268	33	0%	37	30-50 mg.	8.0%
RS	♀	7 mo. 3 da.	197-211	39	0%	10	20-30 mg.	0.0%
RF	♂	5 mo.	154-253	26	0%	36	20-50 mg.	2.0%
RH	♂	5 mo.	200-348	32	3%	31	30-70 mg.	6.0%
RT	♂	5 mo. 4 da.	200-253	26	46%	19	10-30 mg.	54.0%
R2T	♀	5 mo.	174-303	26	0%	53	30 mg.	73.0%
R2B	♀	5 mo. 12 da.	198-281	29	0%	43	20-30 mg.	63.0%
RT	♀	6 mo.	130-163	38	0%	34	20-40 mg.	70.0%
RRE	♀	10 mo.	264-273	56	0%	27	30 mg.	100.0%
R2E	♀	10 mo. 2 da.	153-186	56	0%	26	30 mg.	83.0%
RB	♂	4 mo.	169-251	20	0%	22	30 mg.	74.0%
RLE	♂	4 mo.	127-314	20	0%	38	20-40 mg.	50.0%
RH	♂	7 mo.	324-341	34	60%	29	50 mg.	79.0%
BF	♀	7 mo.	210-253	38	0%	25	30-40 mg.	28.0%
BWT	♂	8 mo.	249-328	50	0%	20	40-50 mg.	0.0%
RA	♂	7 mo.	342-365	40	0%	28	50 mg.	75.0%
R2S	♀	6 mo. 2 da.	158-193	33	3%	25	20 mg.	33.0%
RBW	♂	10 mo. 2 da.	322-348	50	4%	26	30-50 mg.	0.0%

TABLE VII.

Production of Convulsions by Auditory Sensitization.

Rat	Sex	Age at treat-ment.	Previous trials.	Percent seizures.	Percent seizures after sensiti-zation.	Difference	$D/\sigma D_p$*
R-1	♂	121 da.	23	.13	.35	..22±.122	1.80
R-2	♀	121 "	25	0	.75	.75	
R-3	♀	152 "	25	0	0	0	
R-5	♂	120 "	25	.36	.70	.34±.131	2.59
R-6	♀	130 "	27	0	0	0	
R-8	♀	124 "	26	.23	.80	.57±.260	2.19
R-10	♀	140 "	29	.27	.60	.33±.122	2.70
R-11	♂	139 "	29	.20	.70	.50±.112	4.46
R-12	♀	134 "	28	0	.04	.04	
R-13	♂	120 "	25	0	.50	.50	
R-14	♂	135 "	28	0	.01	.01	
R-15	♀	120 "	25	0	.02	.02	
R-16	♂	130 "	27	0	.05	.05	
R-17	♀	125 "	26	0	.75	.75	

*Based on standard error

TABLE VIII.

Effectiveness of "Shelter" in Alleviating Convulsions.

Rat	Sex	Percent seizures	Percent adient responses to shelter.	Percent seizures after shelter.	Difference
R-6	♀	90%	40%	10%	80%
R-16	♂	82.6%	35%	15%	67%
R-18	♀	84.6%	62%	21%	63.6%
R-72	♂	70.8%	70%	25%	45.8%
R-14	♀	71.3%	20%	0	71.3%
R-2	♀	75%	32%	15%	60%
R-5	♂	70%	50%	25%	45%
R-8	♀	80%	25%	0	80%
R-10	♀	60%	90%	38%	22%
R-11	♂	70%	40%	12%	58%
R-13	♂	50%	30%	3%	47%
R-17	♀	75%	65%	20%	55%

TABLE IX.

Effectiveness of Binding in Alleviating Seizures.

Rat	Sex	Percent seizures	Percent seizures when bound	Percent closed maze refractory.
S-SC	♂	60%	0%	0%
L-AS	♀	58.3%	0 %	0%
R-A	♀	78.0%	0%	0%
R-FF	♀	70.4%	0%	0%

Fig. 1. A Convulsive Animal.

Discussion

A point of major controversy in the general field of Production of Convulsions in rats has centered around the so-called "audiogenic" as opposed to "functional" points of view regarding causation of fits manifested by some rats subjected to auditory stimulation. Another factor concerning which there is considerable lack of agreement relates to the role of "conflict" in production of a seizure.

Investigators at Queens' College (23) feel that it is unlikely that any convulsive seizures could be produced without the factor of "conflict".

Maier (35) definitely feels that, of the components "air-blast" and "negative card" situation, which form the convulsive producing stimuli employed in his investigations, the latter is of far greater importance than the former.

Morgan (37) states, on the other hand, that, "...it is certain in our case that the abnormal behavior is connected with the auditory component of the air blast directly."

In addition to the above factors our work with metrazol, given refractory animals in sub-convulsive doses, and Maier's (36) recent publication of results obtained with sub-convulsive doses of this drug, makes it necessary to generally clarify the role of metrazol in production of convulsions in the white rat.

We first draw attention to Experiment 1 (Table I, page 78), wherein 18 rats were stimulated with a bell in order to obtain convulsive seizures. It should be noted that no attempt was made to divide these rats into "convulsive" and "normal" or "control" and "experimental" until each animal had a minimum of 60 stimulations. Our stimulation period of 3 minutes was likewise longer than that of most workers, with the exception of Humphrey and Marcuse (23). Maier (34), for instance, differentiated "neurotic" from "normal" rats on the basis of a two minute stimulation period over five successive days. Animals selected by this investigator as abnormal were those exhibiting the convulsive seizure on any one of these occasions. As we have previously indicated, in dealing with the results of this experiment, such a procedure admits the possibility that a number of Maier's so-called "normal" animals were actually susceptible to convulsive seizures and would have exhibited the reaction had they been tested over a longer period of time. The initial failure to differentiate the two types of animals would naturally vitiate any conclusions drawn from future experiments with these rats. This would be especially true as regards studies of the heritable factor of the seizures. The above mentioned failure is likewise probably the explanation of Maier's statement that "the convulsive pattern is not completely accounted for in terms of heredity".

As an example of the necessity of more preliminary tests on animals which are to be used in experiments on abnormal behavior than have ordinarily been given, we mention the case of Rat BW. Stimulation of this animal over a period of one year led to 50 percent seizures, whereas the percentage after the first nine trials was only 20 percent. We also point out that the same animal may change the pattern of its convulsive seizures so that we cannot speak of "typical" patterns without having adequate records on each individual rat.

In experimenting with the bell as a means of inducing convulsive seizures we made several observations which led to the formulation of the last experiment reported in this paper in the section of results (Page 77). These observations, in conjunction with the results reported on the "shelter" reaction may clarify the disputed question previously mentioned concerning causation of the seizures attending auditory stimulation. We employ the term "audiogenic" as indicating that an auditory stimulus itself, acting as a sort of "electric" generator, "touches" off a convulsion. Inasmuch as our results have indicated, (cf. problem discrimination experiment (2) and sensitizing experiment (3)) that convulsions may be produced in instances where the auditory stimulation is distinctly the subordinate factor, or is not required at all, the question at issue is, in cases where auditory stimulation is used exclusively for eliciting a convulsion, are the attendant convulsions "audiogenic"? The "affective" tone of the animals under bell stimulation was one of the first factors which impressed us. Susceptible animals appeared "scared to death". Such rats seemed to be vainly attempting to escape from a highly undesirable and frightening stimulus, in the form of the ringing bell. The shaking, running, teeth chattering, etc. observed in the animals used in Experiment 1 seemed indicative of a general fear reaction.

Some animals seemed to find an outlet for their nervous energy by engaging in violent face washing behavior, backing against corners of the room, flattening against the wall, hiding behind the photographic curtain, or wedging themselves into a crevice in the cardboard retaining wall. Animals making such reactions never had convulsive seizures. In the event the rats were forced to the center of the room where all kinesthetic sensations were lacking, many of the animals evidenced convulsive seizures. Observing such reactions it seemed unlikely that the nature of the stimulus could be in itself an adequate explanation for the presence or absence of convulsive seizures, since the source of the stimulation remained at practically the same distance from the animal regardless of whether he was in the center of the room or wedged behind one of the above mentioned "shelters". The above observations led to the experiments on "shelter" reactions and "binding" of animals reported in the foregoing section of this paper. From the results of these experiments, i.e. effectiveness of "shelter" and "binding" in alleviating convulsions, it would seem that the "affective" tone of the animal is altered depending on whether he is in an "open" or a "sheltered" field. This affective disposition would then be paramount in importance for determining whether a given animal would succumb to a seizure when stimulated with the bell. Narrow enclosures, such as those formed by galvanized iron cones, are said to be more effective in producing seizures than larger spaces. The lack of adequate kinesthetic sensations, or "security" feeling aroused by pressure sensation, in the unprotected field formed by the galvanized iron, is a possible explanation of the superiority of small enclosures over a larger area in producing seizures.

Another observation made by us, which we feel throws doubt upon the validity of an "audiogenic" theory as explanation for the phenomenon of convulsions in the rat, is the considerable variability of the seizures. An animal which succumbed to a seizure on Monday may not do so on Tuesday or Wednesday. It is difficult to conceive of the auditory system itself varying so considerably as regards susceptibility to the same stimulus.

As Table 9, page 86 , has indicated, convulsive rats exhibit neither seizures, nor the after-effects of fits, when wrapped in a cloth and held under the bell. Such animals certainly received no different auditory stimulation (being kept the same distance away from the source of stimulation as when in the center of the room), yet the maze retention test indicated no refractory period, characteristic of animals recovering from a convulsive seizure. Lindsley and Finger(30) have reported that encephalograms of bound animals indicate that no convulsion has been experienced. If the audiogenic theory is correct then it is difficult to see why such animals give no evidence of having experienced a seizure. We believe that it is not out of the question to conceive the bound animal as being affectively in a different condition from the rat which in its terror is vainly attempting to escape the fear-provoking stimulus. This is evidenced by an initial running period, which appears quite oriented, as evidenced by the fact that the animal directs his efforts to the corners of the room, where possible escape might be accomplished. Failing to find an outlet, the oriented running stage passes into a blind, probably "unconscious" wild thrashing about the enclosure. This stage is followed by the actual spasm or seizure, composed of clonic and tonic convulsions ending in coma-like rigidity. The bound animal may be just as much "afraid" as the free-running individual in the presence of the bell; yet his affective condition may be more like a person "paralyzed" by fright, rooted to the spot, incapable of moving and still in full possession of his "mental" processes.

We may, of course, dispense with the term fear used in the above discussion, and substitute "emotionality". This as a concession to those individuals who object to the use of words like "consciousness" and "fear" when speaking of emotional reactions of animals. Of the various types of emotions we are familiar with, and from close observation of the reactions of the animals to bell stimulation, it is our opinion that "fear" is the proper term to use referring to these rats. If we ignore the "affective" tone of the animals, or deny that such a term has meaning when applied to rats, then we must either make our terminology more general, and consequently more vague, or else assume that not only does auditory stimulation itself contain a convulsion producing factor, but also that it has a factor which produces running. We have observed that in all cases of non-drug fits, running is an essential part of the pattern. Oriented running followed by blind running, as mentioned in the above description of a typical seizure, is essential if the animal is to have a seizure. We have found the maxim "no run, no fit" to hold true. Bound animals cannot run, hence do not experience a convulsion in the presence of the bell.

As previously pointed out, we cannot explain "audiogenically" the running phenomenon, nor the variability of reactions of the same animal to the same stimulus on different days. Nor does the "audiogenic" theory explain the variability of the pattern of the convulsion. We could hardly assume that the same stimulus acting on the same system in the same animal would act so differently from day to day. The above phenomenon, observed by us, could only be explained by assuming that variability arises from individual animals' particular psychological condition, or "affective tone", on the day of stimulation. On some days, dependent on the rats' general emotional level, it is easier to elicit a fear response than on others.

The importance of the running phase of the convulsion as well as the beneficial effect of Cortin and Dilantin (17) in alleviating seizures points to functional rather than structural interpretation of the fits which we have produced in the rat. It is not likely that these substances are specific for one portion of the nervous system (such as the auditory system). It seems more probable that they have a general effect on the nervous system and perhaps a particular action on the emotional centers.

Experiment 1 of our research has indicated that with successive seizures the period of the running phase is diminished. This may be interpreted to indicate a general increase in the emotional tone of an animal which has been repeatedly thrown into convulsions. Such an increased emotionality in turn would render the animal capable of being frightened, to the extent of precipitating a fit, without the need of the preliminary running period, which may function to increase emotionality to the level concomitant with a convulsive seizure. We may mention that the reduction of the running period and the increase in time spent in the post-convulsive or coma stage in the parent animals enabled us to breed from them "chronic" animals which exhibited abnormal behavior from birth or shortly thereafter without the need of stimulation of any type (Page 154).

Experiment 1 has shown that 50 percent of our animals had seizures when placed in the presence of a ringing bell. This percentage agrees well with that found by Humphrey and Marcuse (23) but does not support the statement of Maier (35) that, of the various types of stimuli used to produce experimental convulsions, the bell is least effective. We would agree with Morgan (37) that the tone of the auditory stimulus is of importance in inducing a seizure; but we do not feel that the tone in itself acts as an audiogenic "spark-starter" for the convulsion. Rather the auditory stimulus is merely the most effective way of inducing emotionality of fear reactions in the animals. Unless the emotional centers are aroused there will be no seizure regardless of how long the auditory centers are stimulated. We can agree with Hall (18) that excessive activity on the part of an animal may be interpreted as a mechanism of protective nature serving to "blow-off" excess nervous energy which otherwise would expend itself in a convulsive seizure. We cannot support this author in a further supposition that so-called nervous animals are, in view of the above statement, more resistant to seizures than are the "phlegmatic" rats. Our reasons for disagreement on this latter point will be considered at a later point in this discussion.

Briefly summarizing the factors brought out in Experiment 1, which we feel strongly suggest a functional rather than structural interpretation of convulsions produced in this experiment, we would emphasize again:

1. Variability of both seizure and seizure patterns in individual animals.
2. Prolonged stimulation of animals showed that some rats exhibited seizures only after many trials covering many months.
3. Audiogenic theory cannot explain the running phase of convulsive patterns satisfactorily.
4. With auditory stimulation kept constant, manipulation of the environment proved an

effective method of reducing the seizures.

5. Certain non-specific substances such as Cortin and Dilantin were effective in reducing convulsive seizures (17).

With the above factors in mind, we offer the following as the best explanation of the convulsions produced by us in Experiment 1. Animals placed in the presence of a ringing bell seek escape from the stimulus, which through excitation of the thalmic and hypothalmic emotional centers produces a fear (or increased emotional) reaction in the rat. This fear-escape reaction manifests itself in running. The running is divisible into oriented and "blind" phases. The tone of an auditory stimulus is important only in so far as it is optimum for producing the fear reaction. If "shelter" is achieved during the oriented stage of the running phase, or if it is experimentally provided, the probability of the animals' having a seizure is reduced. The fact that animals are reported to have a greater proportion of seizures when placed in a confined field is due in all probability to the lack of "shelter" possibilities.

We have made the observation that, although the "shelter" itself is a confined space, animals very seldom have seizures if they seek out the shelter in their oriented state. If, on the other hand, an animal is placed in the confines of a "shelter", and escape blocked, the probability of his having a seizure is increased. We again point out, that although physical stimulation of the auditory system under the above two circumstances cannot account for the variation in reactions, the difference in psychological condition, or affective tone of the animal, is very probably the explanatory factor.

Although, as mentioned, the running stage is of paramount importance in the pattern of the non-drug fits obtained by us in Experiment 1, there is still a question as to whether an animal fails to succumb to a convulsion solely because the musculature is inhibited from as great a discharge as a fit warrants. In the case of our binding experiments, some animals exhibited no tension, no struggle to free themselves from the bonds, which were loose enough to allow such a procedure, and which they certainly could have accomplished under pressure of as much muscular discharge as ordinarily accompanies a convulsion. Such animals, when forced out of their bonds to the floor, in the presence of bell stimulation, in some instances have seizures, in others remain quiet and do not have a seizure. We feel that these reactions to binding are explainable, at least in part, in terms of the psychological effect on the animal. The major factor appears to be the kinesthetic sensations which the rat experiences from the binding. Such sensations possibly add to a feeling of "shelter" and protection, similar to those experienced by the animal in the tunnels of its native haunts, or by the laboratory rat crouching in an experimental "shelter". We do not feel that rats used in the binding experiment worked off so much energy struggling against the binding procedure that it was unnecessary for them to succumb to a fit in order to relieve the nervous energy. Since, as we have pointed out, the bonds were very loose, the animal could have escaped with very little expenditure of energy, and also, since the majority of animals were anesthetized before binding, the explanation of Hall (18) set forth above is not tenable.

As already mentioned, the effectiveness of Dilantin and Cortin in alleviating convulsions evidenced in the presence of bell stimulation strongly argues in favor of functional factors being the most important as regards causation of the convulsive seizures obtained by us. We would like to differentiate between the shelter reaction, which we have found effective in reducing convulsive seizures in animals subjected to bell stimulation, and the "abortive" jumping reaction developed by Maier (32) as a method of producing similar alleviation of the fits. In Experiment 2 of our research, dealing with the use of discriminatory problem reactions as a means of inducing convulsive seizures in the rat, the animal reported as succumbing to a fit when presented with two negative cards and stimulated with electric shock, jumped clear of the discrimination apparatus and had a convulsive seizure on the floor. This jumping clear of the apparatus was also observed in two other animals reported in the section of this research titled Transmission of Convulsions. Such reactions obviously occurred while the animal was still in an oriented condition, else the jumping could not have been properly directed to enable escape from the situation. The actual seizure thus took place on the floor, and not while the animal was in the apparatus proper. The animals then, actually made what Maier would term an "abortive" jump, and yet such a reaction had no effect in alleviating the convulsive seizures which these three animals underwent on the floor. Maier's reports concerning the reactions of his animals to the air blast coupled with negative card situation do not make it clear as to the actual manner in which animals had seizures in the discrimination problem situation. If his rats reacted as we have described above, then some differentiation must be made between jumps preceding actual convulsive seizures, and jumping which he has described as "abortive".

If we assume for the moment, as Maier does, that a "conflict" brought about by the presentation of negative cards in conjunction with an air blast, is the fundamental factor in causing convulsions, then if we remove the animal or allow him to physically remove himself from facing the critical situation, he should have no seizures. The reactions of the three animals described above are in direct contrast to such an explanation. Unless we assume that the reaction of jumping free from the apparatus, exhibited as a fore runner of a convulsive seizure in our animals, was actually part of the pattern of the convulsion, we have no explanation to offer regarding the phenomenon. However, were we to open the door of our experimental room and allow the animals to physically remove themselves from the presence of the exciting stimulus it is doubtful whether they would succumb to a seizure. We wish merely to emphasize that our animals were not permitted physical escape from the stimuli in the "shelter" reaction experiments; rather they were provided with psychological escape; which we feel constitutes an argument in favor of a functional basis for the convulsions evidenced in the presence of bell stimulation.

That "conflict" is a common characteristic of emotion was recognized by Dewey in 1895. Darrow (12) points out that the same theme has since been elaborated by McLennon, Kantor, Howard, and Luria. These men have emphasized the confusion, dissociation, blur, and disruption of behavior during emotional stress. Destruction of equilibrium and competition between the impulses typical of the excited emotion are pointed to. They look upon the above phenomena as the consequences or manifestations of an emotional state.

Darrow (12), on the other hand, emphasizes that the outward manifestations listed above are symptomatic of something taking place within the central nervous system and especially the brain. This author has pointed out that conflicting processes in the brain are conceivably of far reaching effect in other ways than mere production of motor impulse situations, essential to release of subcortically controlled emotional behavior. If the cortex does, except in emotional conditions, maintain a high degree of selective inhibitory control over the subcortical automatic mechanism, the probable neural mechanism of release of emotion by ideas is at once suggested.

Morgan (37) feels that the emphasis on adjustment as a form of response has led to a misinterpretation of the significance of the experimental production of neurosis. This author points out that, in the development of experimental neurosis, the experimenter discards some rule that the animal has learned. The old rule, according to Morgan, is not changed to any new one which the animal might learn, since, if this were the case, the animal would not become neurotic. Instead, Morgan states, of a situation in which the animal changes his routine and attempts to find a new set of rules, his behavior becomes erratic and he develops what experimenters have called a neurosis. Morgan feels that this is a poor term, since in his estimation, the animal has no disease of the nervous system but is merely thrown into a state of non-adjustment. (We digress a moment for comment on this last statement. While the body of the theory presented above may be sound, our results with breeding experiments and production of chronic animals stand out strongly in opposition to any supposition that the nervous system of convulsive animals is unaffected; whether one wishes to title this effect a disease or not is an open question.) Morgan further states that when forced by the experimenter into a situation in which he knows he will fail it is natural for an animal to seek to avoid the situation.

The role of shock therapy is to overcome a patient's inertia and complacency, disturbing perfect adjustment by substitution of non-adjustment.

Maier (35) has placed great emphasis on the "conflict" situation, produced by a "negative" card situation. As a "motivating" stimulus this investigator has used an air blast. He has claimed that of the two factors, auditory and discriminatory, the latter plays the more important role in production of seizures of a convulsive nature, being actually indispensible for obtaining the seizure in some animals. In Experiment 2 of our research we have attempted to duplicate Maier's "conflict" situation with discrimination cards. We have, however, changed the so-called "motivator" from the air-blast to electric shock, for the purpose of discovering whether the negative card conflict situation actually is as important as Maier would have us believe. As we have reported, one animal out of ten subjected to the negative card situation plus the shock had a seizure. None of the animals had seizures when only the cards were used.

Subsequently, by selective breeding experiments, we produced two more animals reacting positively to the "conflict" situation.

Among those workers placing importance on "conflict" as being one of the necessary factors for the production of convulsions in rats, it seems to be tacitly assumed that the same reasoning which applies to one animal making discrimination choices, likewise applies to "conflict" in the negative card situation. In the discrimination-problem procedure the animal is taught a series of reactions and avoidances. He connects an adient response to one card and an abient one to another. He then goes through a series of reactions where the situation confronting him is one of adience and abience. Now when the rat is confronted with two "negative" or abient stimuli, the situation, in our estimation, is at once changed. With due respect to Morgan's theory reported above, it is our opinion that the experimenter has changed the "old rule to a new one", i.e. adient-abient reactions change to abient-abient. This situation has never before confronted the animal. At the point of presentation of the two negative cards we contend that the situation has changed, the psychology of the rat is entirely different. We may even assume that, immediately the two negative cards are presented, the situation is comparable to one in which the rat has been removed from the problem discrimination test. The animal was, in the latter mentioned tests, engaged in actively choosing his reactions in accordance with the stimulation. In this entirely new situation an external stimulus in the form of an air blast or an electric shock is introduced. We cannot agree with Maier that these external stimuli are forcing the animal to solve an unsolvable problem, presented by the negative card.

No problem exists when the two negative cards are presented to the rat. As we have reported, the final reaction of animals faced with the negative cards is an abient one, which is correct. It is true that some evidence of emotionality is exhibited, but certainly is too small to act as much of a factor in the production of a convulsive seizure. The addition of an external agent in the form of shock or air-blast cannot, we believe, transform a no-problem situation into a problem situation. It is probably true that the shock has the function of substituting maladaptation for adaptation as reported in human studies. Our former statement would also not indicate that the external stimulus does not create a new and entirely different problem, concerning which we shall speak presently. We would point out that if there were any serious problem connected with presentation of the negative cards, in the sense of "conflict" due to an unsolvable situation, animals should precipitate themselves into a fit trying to solve the "impossible" without the need of adding an external stimulus. If this additional agent in the form of shock or air blast is functioning as a motivator, what has happened to the potency of hunger and thirst, used throughout the training period as motivators? Certainly these two ordinarily effective motivators cannot become suddenly less effective when the animal is presented with the two negative stimuli.

If the role of the external stimulus, introduced at the point of presentation of the two negative cards, is not that of a motivator, then what function does it perform? In our opinion, the shock or the air blast plays the same role as the "sensitizers" used by us in Experiment 3 of this research. The "conflict" if such exists is brought about by the presence of an unpleasant situation, created by being placed in a closed field, being increased to an unbearable point through addition of the external stimulus in the form of shock or air blast. Thus, the so-called "conflict" is between remaining in an unbearable environment and the possibility of escape from that environment. The problem thus changes, as we should expect, in as much as the two negative card situation is a change from the original problem where the task confronting the animal was one of making a correct choice in order to obtain the desired reward.

We may summarize our discussion of Experiment 2 in the following manner. The rat faced with two negative cards finds himself in a closed field from which he cannot escape. This very fact is sufficient to create a certain degree of nervousness in some animals, but entirely insufficient to be of primary importance in producing a convulsive reaction. If an additional stimulus in the form of an air blast or electric shock is introduced in conjunction with the negative card situation the emotional level is still further increased as a result of this added unpleasantness to the extent that in a few cases convulsions are actually precipitated.

It would seem that, since our experiments have merely substituted a different external stimulus in conjunction with the negative cards for the air-blast and card situation used by Maier in his studies, the percentage of seizures obtained in the two investigations should be somewhat comparable. We have seen that this is not the case. The obvious reason for the discrepancy between Maier's claims of considerable success with the "conflict" method of producing abnormal behavior and the fact that our more detailed studies failed to substantiate this claim returns to the fact mentioned previously that Maier did not give his experimental animals sufficient preliminary trials to demonstrate conclusively their negativity to the air-blast.

In concluding the discussion on "conflict" as a means of producing seizures of a convulsive nature, it seems rather evident that if the external stimulus were acting as Maier has assumed, that is as a motivator, then any potent motivator should, in combination with the negative card situation, produce a comparable percentage of seizures. Especially should this be the case in the event that the "motivation" factor is the less important of the two as far as production of convulsions in the rat is concerned. Since our experiments have failed to produce a comparable number of seizures, using the "conflict" method, two possible explanations may be offered. Either the seizures reported by Maier were actually due to the air blast which as we have previously mentioned is a possibility due to failure to separate experimental from convulsive animals on the basis of sufficient trials, or the nature of construction of our apparatus was such as to inhibit convulsive seizures. As we have pointed out, running, both oriented and "blind", is a definite stage of the convulsive seizure. The three animals reacting positively to the negative cards in conjunction with shock jumped free of the apparatus and succumbed to a seizure on the floor. Animals not reacting positively remained in the apparatus. It is possible that, were the apparatus so arranged as to permit running, the number of seizures would be increased. To our knowledge, Maier's apparatus did not permit this running stage to any greater extent than the one employed in our experiments.

To obtain acutely disordered behavior, stimuli of three grades were used by Humphrey and Marcuse (23), one in which an electric door bell was rung for three minutes on the floor of a carton, on the top of which an animal was placed; secondly, ringing of the bell close up to the cage from side to side along with ringing of the bell with the bell in position two. These investigators found that while the third procedure induced seizures in 50 percent of the normal male rats, procedure 1 had no effect on 24 males and induced seizures in only 26 females. Procedure 1 did induce seizures in 50 percent of the chronically disordered males. The chronically disordered animals were produced by these authors by a procedure of maze training involving the moving back of the food box in successive trials just as the animals were about to complete their run and enter the box for the reward.

We would point out that these workers have actually done a "sensitizing" experiment similar to the ones which we reported in this research, although Humphrey and Marcuse seem to have overlooked the significance of their results. Previous emotional reactions obtained in the maze situation, although failing to actually produce convulsive seizures, did serve to "sensitize" or increase the general emotional tone of the animals, so that when additional stimuli, in the form of bell ringing and cage swinging were introduced, convulsive seizures were precipitated. In the other instance, bell ringing plus cage swinging composed the "sensitizing" and "precipitating" stimulus combination. In Experiment 3 of this research we have reported success in precipitating convulsions by injections of sub-convulsive doses of metrazol in combination with bell stimulation, in cases of animals refractory to bell alone. Similar success was obtained by combining extraneous noise and bell stimulation with animals refractory to either stimulus alone.

We point out the impossibility of reconciling these results with Hall's (18) previously mentioned theory that "nervous" animals tend to be more refractory to production of convulsions, than is the case with the so-called lethargic rats. In Experiment 3 of this research, we deliberately selected animals of "nervous" temperament (never actually having had a seizure) as indicating the possibility, that since a single stimulus raised the emotional tone to a point at which signs of emotionality were evident, an additional stimulus, having itself the same effect, might when in combination with the first stimulus precipitate a seizure. Such a theory justified itself as the results of Experiment 3 have indicated. Likewise, in the case of animals studied by Humphrey and Marcuse (23), the animals previously excited through the maze situation were the ones reacting positively to a subsequently exciting stimulus. Phlegmatic animals in our experiments proved so well adjusted as to require doses of metrazol bordering on the convulsive amount, before bell stimulation proved effective in causing a seizure. Of course, as we have previously mentioned, the nervous activity of some animals may prevent them from succumbing to a seizure when a single stimulus is used, but this does not negate the importance of nervousness as an indicator of subsequent convulsive seizures, when the proper stimulus or proper combination of stimuli is found.

Recently N. R. F. Maier (36) has presented his eighth publication dealing with the abnormal behavior in the rat. In this paper Maier reports concerning the action of convulsive and subconvulsive doses of metrazol in production of convulsive seizures in the rat. Referring to the literature offered by this investigator in the general field of abnormal behavior in the rat, we find that the following statements have been made by Maier regarding the drug's action:

1. "...effective in creating fits in animals not before reacting positively, because such animals have previously been subjected to drug seizures. Animals not so treated are not so definitely affected by the sub-convulsive doses..."
2. "...the metrazol, as such, acting as a temporary excitant enables animals not before succumbing to fits to do so when their excitation level is raised by metrazol..." Seemingly the drug itself and not the actual metrazol seizure is the important factor.
3. "...metrazol has a therapeutic value presumably lowering the excitation value of the negative card situation."

From these statements it is evident that the true action of the drug is hopelessly confused. This state of affairs arises from failure in the first instance to separate properly animals into control and experimental groups on the basis of previous extended stimulation. As we have had occasion to mention, use of such animals, especially in drug work, would naturally give so many different reactions that any attempted explanation would lead to the hodgepodge of inadequately supported conclusions or suppositions noted above. This condition arises naturally from the use of animals whose previous histories were either not adequately determined or inadequately studied. In this paper which we have been discussing Maier reports concerning the differential action of metrazol on three groups of animals. Group 1 consisted of rats from "stocks in which the absence of convulsions was the rule". Group 2 contained animals from "stocks in which presence of convulsions was the rule". The rats making up Group 3 were those from matings of Groups 1 and 2. Maier points out that the outstanding difference between the two groups lay in the fact that the animals in the first two groups had had "previous metrazol experience"; in other words a history of convulsive seizures induced by metrazol; Group 3 had no such experience. Subsequently this author finds that rats of Groups 1 and 2 react positively when given sub-convulsive doses of metrazol and then subjected to auditory stimulation. The animals of Group 3 give inconclusive results with this same procedure. From this evidence Maier concludes that metrazol convulsions must lower resistance to fits attending auditory stimulation, and further that convulsions evidenced in the presence of auditory stimulation are functional and not structural in nature.

We do not feel that either of the above mentioned conclusions is justified on the basis of the evidence presented by Maier in his eighth publication. The conclusions that previous metrazol convulsions are the potent factor in reducing resistance to auditory stimulation could only have been drawn had no injections of the drug been administered on the day of the critical test with the auditory stimulus. Since, however, metrazol was administered on the test days, our contention, that combinations of ineffective stimuli, one acting as sensitizer, the other as precipitator, caused the convulsions, is borne out by Maier's own results. The fact that small amounts of the drug were effective is of no importance, since one would expect that such would be the case in the event that animals were previously thrown into metrazol convulsions.

From our work we may suggest three reasons which might explain Maier's lack of convincing evidence regarding the action of metrazol on rats not previously subjected to the drug seizures. Comparison of the amount of metrazol which Maier has given animals in his Experimental Group 3 with Table 6, page 83 , of our research indicates that he has failed to use sufficient amounts of the drug. This table also indicates that there is a differential reaction on the part of the animals to the drug attendant upon their genetic histories. The last section of Table 6, page 85 , composed of animals which were offspring of one convulsive and one normal parent, would correspond with rats making up Group 3 in Maier's experiments. It is at once evident, on comparison of animals in section three of Table 6 with those of the first two sections of the same table, from which they differ only as regards genetic history, that they give the most variable reactions to the drug. This fact would indicate that the variability found by Maier in reactions of animals which were offspring of one convulsive and one non-convulsive stock has nothing whatsoever to do with presence or absence of previous metrazol seizures. The third (and in our estimation weakest, in the light of the data of Table 6) possible explanation of differential reactions of Maier's three groups of animals to metrazol given in sub-convulsive doses would be that author's own interpretation that Group 3 had no previous metrazol experience.

Regarding the phenomenon of "sensitization" reported by us in Experiment 3 of this paper, it is our feeling that the genetic history of convulsions in the family of the individual rat is the primary factor in explanation of differential reactions to a combination of sub-convulsive doses of metrazol and auditory stimulation. Metrazol, as extraneous noise, and electric shock used in other of our reported experiments, merely serve as "sensitizing" agents to increase the animals' emotional threshold, to the point where, when an additional excitant is added (ringing bell), a convulsion is precipitated.

As we have noted, Maier has confused this issue by stating at one point that it is the metrazol itself which is the important factor in causing a seizure in refractory animals; suggesting on the basis of grossly inadequate evidence that the drug may act as a temporary excitant through the sympathetic nervous system. We believe that our work has clearly shown that metrazol given in sub-convulsive doses does act as a sensitizer or temporary excitant; enabling refractory animals with certain genetic histories of convulsions to succumb to convulsive seizures. Obviously, if the drug acts as we have determined, then it is impossible for it to have therapeutic properties regarding seizures as Maier has claimed in another portion of his research. Our results are likewise clearly in opposition to Maier's insistance that previous metrazol seizures are required in order for sub-convulsive doses of the drug to be effective in producing seizures in refractory animals.

We do not feel that any conclusion can be definitely drawn, from the fact that sub-convulsive doses of metrazol are effective, when combined with another exciting agent, in precipitating convulsions in hitherto refractory rats, regarding the structural or functional foundation of convulsions attending auditory stimulation. More complete proof of this fact lies in the demonstration that proper manipulation of the animals' environment, keeping them still in physical contact with the exciting stimulus, is effective in reducing the percentage of seizures experienced. We have presented such evidence based on "shelter" reactions reported in this paper (cf. Table 8, page 85).

Summary and Conclusions of Section 1

The experimental production of convulsions was studied in 120 White and Black and White rats over a period of 2 years. The research is divided into 3 major experiments. In Experiment 1, animals were stimulated for a prolonged period with an electric bell. It was found possible to divide subjects into "convulsive" and "normal" only after at least 60 stimulations. Complete division into the above groups was entirely impossible in the case of a few animals even after the prolonged test periods. The electric bell proved an effective method of inducing a convulsion in 50 percent of the original stock. Continued tests over a long period rendered animals less resistant to the bell, as evidenced by a decrease in the length of the stimulation period, and an increase in the post-convulsive period.

Experiment 2 indicated that the so-called "conflict" method of producing convulsions, when not employed in combination with auditory stimulation, was effective in only 10 percent of the cases. While auditory stimulation is not an essential factor in production of fits by non-drug and non-electrical methods, it is certainly the most effective method.

Experiment 3 indicates that two ineffective stimuli, may, in combination, prove effective in producing seizures in resistant rats. The degree of emotionality as evidenced by reactions to either stimulus alone, as well as genetic histories of the individuals, are primary factors in determining the effectiveness of "sensitization" or combined stimuli as a means of experimentally inducing seizures.

Results of the foregoing experiments and observations of animals during the two year period over which research was conducted led to the development and support of a non-audiogenic theory as to the causation of the fits produced. The theory is developed and supported that the convulsions produced in this study are functional, due to stimulation of emotional centers, and not structural. Fear and escape are the basic principles underlying the seizures. Certain psychological and mechanical methods of alleviating the convulsions add support to our theory.

From the results of these experiments, more particularly from the success of dilantin sodium (17), reported by us in a separate paper, in alleviating the convulsions, we offer the suggestion that the seizures produced and studied in our laboratory are epileptoid reactions precipitated by the emotion of fear.

Part III.

Section 2. The Persistence of Convulsions in the White Rat

Historical Introduction to Section 2

Humphrey and Marcuse (23) in inducing chronically disordered behavior in rats, trained 10 rats by daily runs, for twenty-five days, in a Warner-Warden multiple Y maze. The food box in this maze had no bottom, so that the rat and its food were in direct contact with the floor of the room. With six of the animals the food box was moved along the floor, after the rat was in the box, and the door closed; movement was effected so as not to cause pain, the extent of the movement varied from 4 to 10 feet. This movement of the food box had no appreciable effect on the immediate behavior of the rats, except that they did not eat until the movement had stopped. The remaining 4 rats were trained in the ordinary way with a stationary food box.

The 6 rats whose food box was moved were consistently above the 4 unmoved controls, both for learning time and errors. The 4 controls satisfied the critera for learning of five errorless runs, in a period of sixteen days but not one of the experimental animals did so in a period of 25 days.

The curves of the experimental animals were more irregular both in time and errors than those of the controls. At the same time there appeared in the experimental group the following activities, which Humphrey and Marcuse consider as indicative of behaviorial disorder; belly-crawling, loud gnashing of the teeth, spasmodic starts from one side to the other of the cul-de-sac, shivering, etc. When some of these animals were half way to the food box they would frequently withdraw, and re-run the maze with or without errors, reverse their field, and run to the food box with or without errors. The investigators observed all these reactions in their experimental group during the 25 days of training, but none were observed in the control animals.

Further analysis by Humphrey and Marcuse indicated that while the experimental animals never learned to run the maze, in the sense that they achieved five errorless runs to the food box, yet five out of the six learned to run as far as the door of the food box. These rats would run to the door of the food box, even to within sight of the food, without a mistake, then they would re-trace the maze, exhibiting the abnormal behavioral reactions noted above.

Commenting on their experimental results, Humphrey and Marcuse say: "It is difficult not to use anthropomorphic terms in the description of these animals. The most natural description seems to be that the animals knew the way to the food box, but were prevented from entering it through some conflicting motive. The conflict is one which is very difficult, perhaps impossible, for the animal to resolve.

It apparently induces a condition of nervous strain, which results in chronic-disordered activity."

To obtain acutely disordered behavior, these same investigators used stimuli of three grades; one in which an electric bell was rung for three minutes on the floor of a carton, on top of which an animal was placed; secondly, the ringing of the bell close to the cage, and on the same plane with it; thirdly, swinging the cage from side to side along with the ringing of the bell in the second position. It was found that while the third procedure induced seizures of a convulsive nature in 50 per cent of the normal male rats, the first procedure had no effect on 24 males, and induced seizures in only 1 of the 26 females. The first procedure did induce seizures in 50 per cent of the chronically disordered males.

Cook (9) has performed the following experiments: a small tin cup was fixed into place in the center of a wire area two feet high. The cup constituted the active electrode of an electrical circuit, the cage being the inactive electrode. The circuit was made every time the animal in the cage touched the water in the cup. Five experimental animals received all their water from this container for two weeks. These animals were fed dry food in their own cages. During the same period the rats learned to perfection a twelve unit elevated maze, with a wet mash as incentive. At the end of a two week period the rats formed a strong habit of rushing directly to the cup when put in the experimental cage; the current was then gradually increased from an imperceptible point, to a point where the animal gradually ceased drinking from the cup and withdrew. The intensity was gradually lowered, and for any given animal remained constant for the next seven days. During this time Cook reports that the animals drank little, if any, less water than formerly, though they frequently recoiled from the shock as they began to drink. The rats developed a cautious approach to the cup developed. For the next seven days the shock was increased in intensity each time that the animal overcame the initial impulse to recoil, and started to drink from the cup. The intensity was then reduced gradually to the starting point.

Approach and withdrawal behavior, accompanied by jumping to the side of the cage was observed by the investigator ,to develop from the above procedures. Cook reports that no modification of the behavior was observed outside the experimental situation, nor was there any modification of the maze learning ability.

Purpose and Method of Section 2

In this investigation we desired to determine the effect, if any, of a convulsive seizure, on a previously learned habit. The 40 white rats used in this experiment were all taught a standard "habit" in the form of a maze, learned to 3 errorless runs. Since we had previously found (page 120) that fear seemed to be an important factor in the precipitation of convulsions, and that such seizures could be alleviated by allowing the animals to "hide" in variously constructed "shelters", two types of maze were used for studying the problem. Maze 1, was of the "closed" variety, in which an animal ran through various "alleys" to the food box. Maze two, of identical pattern with Maze 1, was of the "open" or "elevated" variety, in which animals ran on the surface of the sections composing the maze.

Both mazes were of a modified "Hampton-Court" variety, consisting of 15 blind alleys, involving the sequence of turns, L, R, L, R, L, L, R, L, L, R, L, R.

The forty subjects, were of an age, at the beginning of training of not less than 65 days, but not more than 100 days. Following the method of classification used by us in the investigation titled "Transmission of Convulsions in the White Rat" (page 143), the animals were divided into a non-convulsive or "L" group, and a convulsive or "H" group, twenty animals in each group. These two groups were subdivided into 10 "Z" animals, trained on the "closed" maze, and 10 "Z" animals trained on the "open" maze; similarly with the "H" group, 10 being trained on the "closed", and 10 on the "open" maze.

Since we were not interested, in this study, in determining differential learning ability, as such, between the convulsives and non-convulsives, but only in the effect of seizures on the animals' ability to repeat a previously acquired habit, all animals were trained to the criterion of learning, by the "massed" trial technique. The rats were kept without food and water for a 48 hour period before training began. They were then removed from the living cages, placed in the food box of the maze until they had "whetted" their appetites, and returned to the start of the maze for the first training trial. Animals were allowed a very small amount of food and water following each successful trial, and the training was continued until 3 successive errorless runs had been accomplished. Time records were kept as a measure of the animals' progress in the learning of the maze. Wherever possible, litter mates of the two groups of animals were used, one being trained on the "open" elevated maze, the other on the "closed" maze.

Following mastery of the maze the animal was placed under auditory stimulation for precipitation of convulsive seizures (page 54). After the rat had recovered from the seizure (providing he belonged to the "H" group), and appeared to be normal (page 55), it was replaced again in the maze which it had previously learned. A stimulation period of 3 minutes was used with animals of the "Z" group, and a further 20 minute period elapsed before the rat was re-tested on the maze.

Results of Section 2

Table 1, page 132, indicates the results of re-testing convulsive and non-convulsive animals on a previously learned maze, following auditory stimulation. It will be noted from Column 4 and Column 7, that "H" animals re-tested on a closed maze are the only exception to the general result which indicates that convulsions have no effect on retention of a previously learned habit. It can be seen that, barring the exception mentioned, auditory stimulation, whether of convulsive or non-convulsive rats, instead of inhibiting repetition of the maze habit, has actually facilitated it. Both groups "Z" and "H" run the maze with greater speed, following the auditory stimulation, than previous to it. The range of reactions recorded in columns 2, 3 and 6 of table 1 is sufficiently great to indicate that the differences recorded in columns 4 and 7 are probably significant. However, we are not primarily interested in the fact mentioned that the re-test trials for animals of both "Z" and "H" groups, with the exception mentioned, are completed in shorter time, than the average of the last three training runs. Motivational factors were probably not controlled well enough to hazard an explanation of the above mentioned fact. We wish to emphasize only that the animals were able to repeat a previously learned habit following auditory stimulation, irrespective of whether they succumbed to convulsive seizures, with no refractive period.

Column 3, Table 1, wherein the average of last 3 re-test runs for the "H" group on the "closed" maze indicates a considerable refractive period, deserves special mention. Animals of the "H" group, trained and re-tested on the "closed" maze were observed to react very differently from animals of either group trained on the "open" maze. These rats, when replaced in the maze, following a convulsive seizure, remained entirely motionless. They manifested no interest in their surroundings, nor did they make any attempt to re-run the maze. Extra motivation in the form of pushing, or beating, merely resulted in the animals' slowly walking to the closest cul-de-sac, proceeding to the farthest corner of this blind alley, huddling pressed against its side-walls, and refusing to move further. No amount of punishment was effective in forcing the animal to run the maze, once this attitude had been assumed. That the animals were not "unconscious", or in a coma stage, such as is manifested following a convulsive seizure, was proved by the fact that they immediately resumed normal behavior when removed from the maze and allowed to walk about the table on which the maze was placed. After a considerable "refractive" period, measurable in hours, these rats did repeat the maze, in most cases without a mistake.

Discussion

From the above results it is obvious that convulsions do not affect maze retention. It is likewise obvious that even in the case of the animals exhibiting along refractive periods ("H" group on "closed" maze) it was the characteristics of the maze itself, rather than any "blotting" out of "traces" formed in learning the habit, by the subsequent convulsion which inhibited the rat from repeating his previously learned performance. We have already shown (page 66) that animals, excited emotionally by auditory stimulation, tend to take advantage of any "shelter" in the field to alleviate a fit. In the case of the closed maze there were ample opportunities for this "shelter" reaction to manifest itself. Having undergone a severe emotional "storm" in the form of a convulsive seizure, it is likely that the "shelter" reaction was called out by the very nature of the "closed" maze, causing the large refractive period on re-test which we have noted. The animal did not refuse to run the maze, when re-tested, because he had forgotten it, due to after effects of a convulsion, but rather because he was inhibited from running it by the strength of the "shelter" reaction.

Although, as we have mentioned, our experiment was not planned with a view to ascertaining the differential learning ability of convulsive and non-convulsive rats, study of the progress of both types of animals from records based on time taken to complete three errorless runs, indicates little essential difference in the learning ability of the two groups. Both types seem to find the elevated maze slightly easier than the "closed" maze.

We would agree with Cook that convulsions do not appear to affect maze performance, but would add that the type of apparatus used to determine the effect of seizures on psychological functions must be taken into consideration.

TABLE I.

Effect of convulsive seizures on retention of the maze habit

	"Closed" maze			"Open" maze		
Group	Ave. Secs. of last 3 runs	Ave. Secs. of last 3 re-test runs	D.	Ave. Secs. last 3 runs	Ave. Secs. of last 3 re-test runs	D.
"Z"	83.6"	77.1"	6.5"	66.9"	43.2"	23.7"
"H"	95.2"	8,549.0"	8,453.8"	82.3"	28.1"	54.2"

Summary and Conclusions of Section 2

Forty white rats, twenty convulsive and twenty non-convulsive were taught two mazes, one "open" and elevated, and the other "closed".

Following mastery of these mazes, the animals were subjected to auditory stimulation and subsequently re-tested on the maze previously learned, to determine the effect of auditory stimulation and convulsive seizures on retention of a previously learned habit.

It was found that:

1. Convulsive and non-convulsive animals had no difficulty in repeating an "open" elevated maze following subjection to a convulsion producing situation.
2. Convulsive animals showed considerable refractive periods when re-tested on a previously learned "closed" maze, following a seizure.
3. There appears to be no essential difference between learning ability of convulsives and non-convulsives, measured by time necessary to learn a maze to the criterion of three errorless runs.

It was suggested that:

The type of apparatus used to test learning and retention of convulsive rats is an important factor in determining the effect of convulsive seizures on these psychological functions.

Part IV.

Section 3. The Transmission of Convulsions in the White Rat

Historical Introduction to Section 3

Waltzing and epilepsy in mice have been extensively studied, and have been shown, by Dice (13) and Watson (43), to be transmitted as Mendelian recessive traits. A similar behavior pattern in rats in response to continuous auditory stimulation has been reported by Maier (35), Morgan and Morgan (37), Humphrey and Marcuse (23), Hall (18), Bayroff (3), and Maier and Glaser (34). Maier and Glaser have suggested that the reaction in mice is probably hereditarily determined. This reaction is characterized by violent undirected running about an enclosure and is frequently followed by a convulsion involving the head and fore legs primarily. Sometimes a state of coma follows the attack, but often the animals remain in a state of heightened tension. Maier has characterized the abnormal behavior as a neurotic pattern. We have, in a preceding section of this paper, expressed our preference for the term epileptoid reaction, precipitated by the emotion of fear, as the best characterization of convulsions exhibited in the presence of auditory stimulation.

Maier found that stimulation by key jingling was the most effective method of obtaining the seizures; hence this stimulus was employed by him in investigating the inheritance of the abnormal pattern. His apparatus consisted of a sound proof box with double walls containing felt between, and divided into two parts. The animal was observed through double-walled glass doors in the top of the apparatus and the keys were suspended on a rod driven by a motor. Animals were stimulated for two minutes on five successive days for determination of susceptibility to the attacks. Animals showing the behavior in any form on any of the stimulations were considered susceptible. Various crossings of the susceptible and the non-susceptible rats were made. On reaching the age of twelve weeks, the offspring of these animals were tested in a similar manner. Results are given for 35 offsprings whose parents were both convulsive; 25 offspring one of whose parents were convulsive, and the other normal; and 18 offspring of 2 normal parents. It was noted that the same neurotic father sired 6 litters due to the fact that these investigators experienced difficulty in getting the neurotic males to mate. From the three mating combinations mentioned, the authors reported the following percentages of offspring:

neurotic x neurotic,	25.7% normal,	74.3% neurotic
neurotic x normal,	48.0% normal,	52.0% neurotic
normal x normal,	100.0% normal,	0.0% neurotic

Maier explains these results by assuming that the neurotic trait is transmitted as a dominant character and that the neurotic parents were primarily heterozygous. The authors make the assumption that the expected distribution would yield the following percentages:

Nn x Nn, 25% normal (nn) and 75% neurotic (Nn and NN)
Nn x nn, 50% normal and 50% neurotic (Nn)
nn x nn, 100% norman (nn)

Maier points out that the fact that the neurotic parent should appear as heterozygous is not surprising since the trend of the results may be due to the limited number of cases. When the litters were studied separately it was found that two sets of neurotic parents produced no normal offspring, which would indicate that the females involved in this cross were homozygous. Since all the mixed crosses produced normals, the authors supposed that all of the neurotics were heterozygous. Regarding the trait as recessive, Maier gives the following percentages as the best expectation from his matings:

nn x nn, 0% normal, 100% neurotic (nn)
nn x Nn, 50% normal, (Nn), 50% neurotic (nn)
Nn x NN, 100% normal, (Nn and NN), 0% neurotic (nn)

It is noted that Maier's first crossing does not fit the findings and he explains the discrepancy by the assumption that 25 per cent of the individuals did not express the trait.

Cole and Ibsen (7) have reported concerning inheritance of congenital palsy in guinea pigs. The factor for normality appeared to be completely dominant, and it was found impossible to distinguish animals carrying the defective trait from those that did not, on the basis of observable behavior or any other characteristic. Breeding tests were found to be the only method of separating the two classes. These workers have carried out experiments to determine the ratio of palsied offspring to normal offspring when two heterozygotes are mated. The ratio of homozygotes to heterozygotes when these two classes were crossed. Of the total number of offspring from the mating of two heterozygous animals, 183 were normal and 63 palsied, an almost exact 3 to 1 ratio. The assumption made by Cole and Ibsen was that the palsied condition was based on a single unit-factor difference. The authors present further proof that a single factor was being dealt with by tests of the normal offspring from the matings of heterozygote with heterozygote. These workers made a further type of test consisting of the use of normal offspring resulting from the mating of homozygote with heterozygote individuals. The expectation in this case would be equality of the classes. The actual numbers found in 25 tests made were 14 NN and 11 Nn, instead of 12.5 in each case, as should be expected. The conclusion drawn by these investigators was that palsy in the pigs was inherited in a simple Mendelian fashion, depending on a single unit-difference; the normal condition being completely dominant to the heterozygote.

Some of the various defects in the guinea pig have been described by Stockard (42) and attributed to inherited effects of alcohol treatment of the parents. The animals reported by this investigator have symptoms that somewhat resemble the conditions found in congenital palsy. Stockard has obtained a wide variety of defects of both nervous and anatomical types. Among these various disorders, he speaks of the animal being very shy and excitable. He points out that all the young animals that died showed the nervous disturbance. He mentions an animal that died when one day old after having been in a constant tremor since birth, another that lived for nine days, but whenever it tried to walk was seized with spasmodic contractions; the third specimen mentioned exhibited the same nervous manifestations and was completely eyeless. Stockard further mentioned that paralysis agitans was very common among the F-1, F-2, and F-3 animals, with individuals being unable to stand or walk. No definite conformation to Mendelian inheritance was reported.

Lord and Gates (31), have reported concerning the "shaker", described as a new mutation of the house mouse. As described by these workers, the mutation shows itself principally in the form of nervous head movements; rapid successive jerking of the head upward, accompanied by sniffing and twitching of the vibrissae. The "shaker" is able, for short intervals at least, to cease from head shakings and appear perfectly normal, as in the case of eating and drinking and defensive reactions. The animals sometimes were reported to run in circles. Individuals heterozygous for the "shaker factor" alone were reported as being normal in all their reactions to sound, at least up to the age of one year. "Shaker" mothers are good mothers and were found to breed normally, no noticeable difference being found between them and the average of the colony either with respect to breeding capacity, size of litter, or the ability to raise young. They report that the "shaker" trait behaves like a single Mendelian recessive. It was further reported by Lord and Gates that the "shaker" character is not sex-linked. They conclude that the trait is a type of transmissible nervous disorder similar to the circus movements reported by Fortuyn (15) and Bonhote (4), in rats, and the ataxia in pigeons reported by Riddle (41).

Laanes and MacDowell (27) have reported concerning "Circling, a two-gene trait of the Mouse". This character, as reported by the authors, combines the horizontal whirling of the Japanese Waltzers and the "Shakers" with the violent reactions to sound, such as erratic leaps and somersaults. These found that the first generation by a normal strain resulted in all normals. Backcrosses resulted in 244 normals to 65 circlers, the expected proportion of circlers being 64.9. The F-2 generation resulted in 184 normals to 8 circlers in place of an expected proportion of 10 circlers. They conclude that circling appears to depend on the combined action of two recessive genes.

Purpose and Method of Section 3

In the first section of this paper we have indicated that the convulsions, manifested in the white rat when subjected to auditory stimulation, are primarily of the epileptoid type, precipitated by the emotion of fear. In this portion of our study we investigated the following question: given a normal stock of white rats from which a number of convulsive and non-convulsive animals are selected, is it possible, by selective breeding of the chosen group, in which the percentages of convulsives and non-convulsives are known, to produce a strain of animals having a significantly larger percentage of convulsives? The corollary to this is: would such selective breeding enable "chronic" animals to be produced? More specifically, could we obtain, from breeding experiments, animals manifesting observable behavior abnormalities from birth, without having been previously subjected to the convulsion-producing situations?

For the investigation of this problem, ten pairs of animals were selected from stock, 45 per cent convulsive and 55 per cent non-convulsive. These parent animals were selected in the following manner: from the age of 21 days each rat was subjected to at least 60 bell stimulations, in the apparatus described in section 1 of this paper. The per cent of times that a positive reaction was obtained from these individuals was recorded and used as a measure of the animals' "convulsivity". Animals succumbing to seizure in 50 per cent or more of their trials were considered "high convulsive" (H); those exhibiting seizure less than 50 per cent of their trials were considered "low convulsive" (L); while those animals not succumbing to seizures in any of their trials were considered "zero convulsive" (Z). For explanatory purposes and analytical treatment of the results, the Z group were at times separated from the category of H. The offspring of these selected parents were studied over six generations* during a period of two years. These animals, 762 in all, were tested exactly as the parents, each being given a total of 60 trials, and then classified, on the basis of the per cent of positive reactions, into one of the above mentioned categories. As the genetic chart (page 171) indicates, three types of mating were carried out over the six generations, namely, H x H, H x L, L x L.

*Due to the excessive number of animals, H x L matings were only carried out over 4 generations.

Results of Section 3

Table 1, page 158 indicates the percentage of animals manifesting the gradations of convulsive seizures noted at the headings of the various columns. Column 2 shows that the number of animals susceptible to convulsions in 100 per cent of their trials increases from 7 to 25 per cent going from generation 1 to generation 6. It is further seen that, with the exception of generation 2, the percentage of 100 per cent convulsives in each succeeding generation is greater than in the generation preceding. Column 3 indicates that there is likewise an increase in the percentage of animals in convulsive group H, going from generation 1 to 6. Conversely, the percentage of animals in group L decreases in generation 6 as compared with generation 1. It is interesting to note that the percentage increase recorded in column 2 for the 100 per cent convulsive animals is practically equal to the percentage decrease recorded for the Z group in column 5. It should also be noted that in the second generation, the percentage of 100 per cent animals in column 2 is falling instead of rising, but the percentage of Z animals recorded in column 5, is rising instead of falling.

These results are pictured graphically in graphs 1 and 2, page 166 . The curve at the lower portion of the page, curve A, shows a steady rise in the 100 per cent convulsive animals from generation 2 to 6. Curve B indicates the mentioned rise of the H group of convulsive rats from generation 1 to 6. Curve C, indicating the trend for animals of the L class, while irregular, shows a slight overall drop from generation 1 to 6.

This general increase in percentage of convulsive animals in the H class of convulsives, and decrease in percentage of non-convulsive may be noted from the curves D and E respectively.*

Graph 2 gives us the same general results in slightly different form. We note from this graph that the positions of generations 1, 2, and 3, and 4, 5, and 6 are reversed when the animals in the Z column at the right and the 100 per cent column at the left are compared.

Consider the relation of the three main types of mating to the general results reported above. Table 2, page 159 , is concerned with the percentage of H, L, and Z animals resulting from the L x L mating in generations 1-6. Column 3 , indicates a rise from 6 to 19 per cent in the animals of class H from generation 1 to 6. Similarly, column 5 indicates a slight rise in the percentage of L animals. Conversely, column 7 shows that the percentage of Z

*Curve D obtained by combining proportion of animals in 100 per cent, H and L classes. Curve E obtained from proportion of 3 animals in population.

animals has fallen at the end of the sixth generation. However, it will be noted that within any given generation the percentage of Z animals (Column 7) exceeds the percentage of convulsives in either column 5 or 3. In fact, the percentage of Z animals exceeds the sum of the convulsives in columns 3 and 5 in every generation except the fifth. Consulting the genetic chart (page 171) we see how this exception to the general results of mating of two L animals may have been brought about. We note that generation 5 has a higher percentage of animals whose seizure percentage places them in group H than is true of generations 1-4. This tendency may be explained by the high percentage of convulsions in their ancestral background. Generation 6, although possessing about three times the percentage of H class animals in its genetic history, has 81 rats to balance this factor.

Graph 3 (page 168) illustrates the above mentioned facts. The general trend of the graph resulting from the mating of two L class rats is from right to left; that is, toward a larger percentage of Z offspring than H offspring. The justification for considering animals below 50 per cent convulsive as L group is evident from this graph. If this group of "low convulsives" had been added to the H group of rats, graph 3 would have been still further displaced from its theoretical course of high right to low left. The relative positions of the 6 generations on the right as compared with the left hand scale, indicating a fall in the percentage of Z and increase in percentage of H animals, may be explained by considering their genetic backgrounds. If the Z animals shown in the genetic chart (page 171) as white circles are considered 100 per cent negative, and the H and L animals are considered convulsive to the degree of their shading, then we find that, for the mating of two L animals, the percentage of H in the genetic tree increases approximately 90 times in going from generation 1 to 6, whereas the percentage of Z animals in the genetic tree merely doubles itself.

A similar explanation may be employed to account for the positions of the individual generations relative to one another on the 0 per cent and 100 per cent convulsive scales.

We turn now to a consideration of the results obtained by the matings of H x L animals. Table 4, page 161 , indicates a slight increase in the percentage of H and Z animals going from generation 1 to 4 (columns 3 and 7), and conversely a decrease in the percentage of L animals, (column 5). Graph 4 (page 169) shows the same general results. The trend of the graphic lines for the individual generations approximates the straight line expected from 1:1 ratio resulting from the mating of H and L animals. However, as the graph indicates this ratio with its characteristic shape is only roughly approximated when individual generations are considered. The cause of variation from the expected shape may possibly be found in the genetic chart (page 171). In going from generation 1 to 4 it is found that the total percentage of convulsions in the genetic tree of the H x L matings is increasing; although there is a numerical increase of the Z animals, it is evidently insufficient to prevent the H scale of graph 4 from rising. For instance, it is evident that the increase in total percentage of convulsions is almost double the increase in the Z background (cf. genetic chart). This may account for the reversal in the positions of generations 1, 2, and 3 on the 100 per cent convulsive scale as compared with the 0 per cent scale of the graph.

Similar explanations may be given for the positions of the individual generations on the 0 per cent and 100 per cent scales of the graph. Thus F-1 contains less Z animals in its genetic background than is the case with F-2; hence F-2 stands above F-1 on the 0 per cent scale. Although the number of Z animals in the genetic background of the H x L matings of generation 3 is numerically superior to that of either F-1 or F-2, nevertheless the increase of this Z class is only about one fourth as great as the corresponding increase of Z in going from F-1 to F-2. Likewise the percentage totals of convulsions found in animals of the H and L groups present in the genetic backgrounds of generation 3 have together increased to an amount approximating the Z increase of F-3 over F-2. These factors taken together might explain the position of F-3 below both F-1 and F-2 on the 0 per cent scale and above them on the 100 per cent scale. The positions of the four generations on the 100 per cent scale may be explained in a manner similar to the one outlined above.

Table 5, page 162, shows the proportion of offspring exhibiting High, Low, and Zero percentage of convulsions, based on actual number of H x L matings in each generation. It is noted that each generation has a different ratio of convulsives to non-convulsives, and that only when the four generations are considered as a group is there a suggestion of the theoretical 1:1 ratio.

Table 6, page 163, shows the per cent of H, L, and Z animals produced by the mating of two animals in the H group in generations 1-6. Comparing the generations 1 and 6, columns 3 and 5, indicate that the percentage of H convulsive animals increases, while the percentage of L convulsive animals decreases. We likewise note that, within any given generation, with the exception of the first, the above statement holds true. However, the ratio of the difference between the groups of offspring is not constant, but varies for the different generations. If, in Table 6, columns 3, and 5, are totaled, and the totals of columns 3 and 5 are added to obtain a ratio of comparison between all convulsives and all non-convulsives, it is found that the first three generations have together a ratio of 2:1 in favor of the convulsives; generation 4 a ratio of 4:1 in the same direction; generation 5, 5:1; and generation 6, 9:1. If we total the figures in columns 3 and 5, and combine the totals for columns 3 and 5 to compare with column 7, we obtain the general ratio of 3:1 for the whole table.

Table 7, page 164, taking into account the actual number of matings of the H x L type, brings out substantially the same facts. Column 6 of this Table shows that, even if the relative number of H animals and L animals per litter are combined, for comparison with the relative number of Z animals, the former exceed the latter. Generation 1 appears as an exception to this general statement. Column 6 likewise indicates that there is no constant 3:1 ratio for individual generations but that the ratio of convulsives (H and L) to Z animals increases from generation 1 to 6. The 3:1 ratio may be obtained only by summating columns 3 and 4, and combining the sum of columns 3 and 4 for comparison with 6.

Consider now Graph 5, page 170. The general direction of the lines on this graph is from high left to lower right, the greater percentage of offspring from the H x H matings being themselves in the H class. Generation 1 is the only exception to this statement and here a reversal is noted. The marked difference between the first and second generations as to percentage of offspring of H and Z classification deserves comment. We note that the second generation produced the highest percentage of H type animals among the offspring of the H x H matings. A study of the genetic chart (page 171) shows this generation to be unique in having no background of Z animals in the genetic history of its H x H matings, so that the effect of the H animals in its genetic background is unchecked. This would lead us to suspect that, although generations 3, 4, 5, and 6, show more actual convulsions present in the backgrounds of their H x H matings, yet the effect of this genetic taint is held in check by the presence of Z type animals in their genetic backgrounds. And even though the first generation is like the second in not having its background of H animals held in check by the Z type, yet the percentage of convulsions in the H class animals is less than half that present in the second generation.

Generations 5 and 6 both have a greater percentage of H type animals in their genetic histories than do generations 3 and 4, and hence might be expected to lie higher on the 100 per cent scale of Graph 5 than the latter two generations. The exact positions of generations 5 and 6 cannot be predicted from the genetic chart, since actually generation 5 has a greater percentage of convulsions of the H type animal in its ancestral background than does generation 6.

Table 8, page 165, is concerned with a general summary of the entire breeding experiment and indicates the percentage of the three main types of animal produced by the three matings over six generations. Column 2 of this table shows that 258 animals, or 38 per cent of the total 762 rats used in the experiment, exhibited 50 per cent or more seizures. Columns 3, 4, and 5 indicate the percentage of these H animals produced by the three mating types. We note that the H x H matings produced the greatest proportion, while the L x L matings produced the smallest. Column 6 shows that, out of the total 762 animals, 177 produced by selective breeding were of the L class, that is responded convulsively less than 50 per cent of their trials. Columns 7, 8, and 9, show the percentage contribution, of each of the three types of matings to the total L animals produced. We note that the L x L matings have produced the greatest percentage of these animals. Similarly, column 10 shows that 39 per cent of the total population produced by selective breeding were animals which never succumbed to a seizure in any of their trials (Z class). Columns 11, 12, and 13, show the relative percentage of these Z animals contributed by the three mating types. As is evident, the largest percentage of Z animals is obtained from the mating of L x L. We likewise note that, in the strain of animals produced by six generations of breeding, the convulsives predominate over the non-convulsives, when both H and L type animals are considered as a general convulsive class for comparison with the Z group, considered non-convulsive. (Lower portion of Table 8, columns 2 and 3.)

Chronic Animals

Contrary to the result reported by Cole and Ibsen (7), for the interitance of congenital palsy in guinea pigs, we have noted throughout the breeding experiments definite behavior abnormalities on the part of our convulsive strain. For the most part we did not make a careful study of all the cases of abnormal behavior observed outside the stimulus situation. We have noted, however, that eating of the young is very common among the convulsive animals. Likewise a considerable number of animals susceptible to seizures have been born with rudimentary eyes.

We experienced no difficulty in breeding convulsive rats, and even succeeded in mating two "chronic" animals. The genetic chart indicates seven animals with white dots in the center of their circular representation. These rats were observed to have marked behavior abnormalities outside of the stimulus situation. There follows a brief resumé of the behavior peculiarities manifested by these animals (cf. genetic chart page 171):

Rat 1 - From the twenty-first day of its life this animal was observed to engage in circling activity without ever having been exposed to the convulsion-producing situation. The animal would wave its head in the air with a circular motion, and then turn its whole body first in one direction and then in the other, slowly at first and then more rapidly. Circles were executed in both directions, though they were not as energetic as those obtained in the auditory situation with other animals. The animal appeared to be able to refrain from the circling during the feeding and mating periods.

Rat 2 - Female animal, from the age of 32 days was observed to throw fits spontaneously in her cage. This rat had been subjected to auditory stimulation on ten occasions before this behavior was noted. No relation was found between time of onset of such behavior and time elapsing since last auditory test. Animal would tear blindly around its cage for 8 or 9 seconds and then remain motionless with rapid respiration. This rat appeared normal in other respects. The activity described above persisted throughout the life of the individual.

Rat 3 - This animal was observed to have a marked difficulty in coördination of its muscular reactions. When attempting to walk, it would fall over on its side. At other times, while sitting on its haunches washing its face, the animal would be seized with a spasmodic shuddering and shake from head to foot for varying periods of time. No sensory paralysis was observed. Attacks were variable, some thirty were observed while the animal was in its living cage. This abnormal behavior lasted throughout the lifetime of the animal.

Rat 4 - This animal seemed to have developed a type of nervous tic. Prior to its first test in the auditory situation, the animal was seized periodically with a violent scratching reflex. The head and nose were turned to the right side and the hind leg employed for scratching the nose. This scratching continued for periods as long as five or ten minutes. The animal would have ten or twelve such seizures in an hour's period. The damage to the nose and the obvious pain to the rat prompted us to kill this animal after we had recorded 102 such seizures in a period of two days.

Rat 5 - From the time of weaning, this animal was observed to lie on its side with all four feet moving in bicycle fashion. This behavior was alternated with spasmodic shuddering of the entire body. Following the appearance of this behavior the animal refused to eat and died of malnutrition. Twenty such seizures were recorded before death.

Rat 6 - Similar behavior to that reported for rat 2. Spontaneous fits were observed in the living cage. Animal had no previous experience with auditory stimulation. Fits were periodic and on other occasions the animal appeared perfectly normal.

Rat 7 - Animal had spasms from the time of birth. The entire body was involved. A violent shaking was followed by a rigid comatose state. Conditions became progressively worse causing death at the age of fourteen days.

Some of the above abnormal reactions observed in animals outside the stimulus situation seem similar to the type of behavior reported by Stockard (42) in guinea pigs, and mentioned by us in another section of this paper.

TABLE I.

Percent of Convulsive and Normal Animals, Generations 1 - 6, Produced by All Mating Combinations

Generation	100 per cent convulsive	H	L	Z	Difference		D/σDp*
					F-1	F-6	
F-1	.07	.13	.30	.49	.18±	.060	3.00
F-2	.05	.20	.18	.56	.07±	.062	1.12
F-3	.08	.26	.25	.40	.07±	.062	1.01
F-4	.15	.25	.23	.37	.19±	.069	3.06
F-5	.20	.33	.20	.26			
F-6	.25	.20	.23	.30			

*Based on standard error

TABLE II.

Number of H, L, and Z Animals Produced by L x L Matings, Generations 1 - 6.

Generation	Number of H	Percent H	Number of L	Percent L	Number of Z	Percent Z	Percent difference in H, L, Z, generations 1 - 6	D/6Dp*
1	2	.06± .04	7	.20± .068	25	.74± .074	.13± .085	1.52
2	21	.16	28	.21	80	.62	.06± .275	.219
3	12	.18	19	.18	33	.52	.19± .121	1.57
4	6	.15	13	.33	20	.51		
5	9	.31	7	.24	13	.45		
6	5	.19± .075	7	.26± .266	15	.55± .095		

*Based on standard error

TABLE LII.

Proportion of "H", "L" and "Z" Animals Produced in Generations 1 - 6, by Mating of L x L, Considering Number of L x L Matings in Each Generation.

Generation	Number of LxL matings	Relative number of H per litter.	Relative number of L per litter.	Relative number of Z per litter.	Ratio
F-1	3	.6	2	8	1:13 or 1:3
F-2	18	1	1	4	1:4 or 1:2
F-3	7	1	2	4	1:4 or 3:4
F-4	4	1	3	5	1:5 or 4:5
F-5	3	3	2	4	3:4 or 5:4
F-6	3	1	2	5	1:5 or 3:5

TABLE IV.

Number of H, L, and Z Animals Produced by Mating of H x L Animals.

Generation	Number of H	Percent of H	Number of L	Percent of L	Number of Z	Percent of Z	Percent difference of H, L & Z comparing gen. 1 & 4	$D/\sigma D_p$*
F-1	10	.30± .079	9	.27± .076	14	.42± .085	.08±.13	.61
F-2	22	.28	15	.19	41	.52	.16±.10	1.60
F-3	25	.43	17	.29	16	.27	.09±.14	.61
F-4	7	.38± .114	2	.11± .073	9	.51± .127		

*Based on standard error

TABLE V.

Proportion of H, L, and Z Animals Produced in Generations 1 - 4 by Mating of H x L Animals Considering Number of H x L Mating in Each Generation.

Generation	Number of H x L matings.	Relative number of H per litter.	Relative number of L per litter.	Relative number of Z per litter.	Ratio
F-1	3	3	3	4	3:4 or 3:2
F-2	2	2	1	4	2:4 or 3:4
F-3	6	4	3	3	4:3 or 7:3
F-4	2	3	1	4	3:4 or 1:1

TABLE VI.

Number of H, L, and Z Animals Produced by Mating H x H in Generations 1 - 6.

Generation	Number of H	Percent of H	Number of L	Percent of L	Number of Z	Percent of Z	D F-1, F-6.	$D/\sigma D_p$*
F-1	12	.24	19	.38	19	.38	.26±.102	4.5
F-2	17	.80	0	0	4	.19	.19±.098	1.8
F-3	20	.51	6	.15	13	.33	.29±.074	3.9
F-4	31	.57	11	.20	12	.22		
F-5	37	.63	11	.18	10	.17		
F-6	22	.70	6	.19	3	.09		

*Based on standard error

TABLE VII.

Proportion of H, L, and Z Animals Produced in Generations 1 - 6 by Mating of H x H, Considering number of H x H Matings.

Generation	Number of HxH matings.	Relative number of H per litter	Relative number of L per litter	Relative number of Z per litter	Ratio
1	4	3	4	4	3:4 or 7:4
2	3	5	0	1	5:1
3	5	4	1	3	4:3 or 5:3
4	6	6	2	2	3:1 or 4:1
5	6	6	2	2	3:1 or 4:1
6	3	7	2	1	7:1 or 9:1

Table VIII

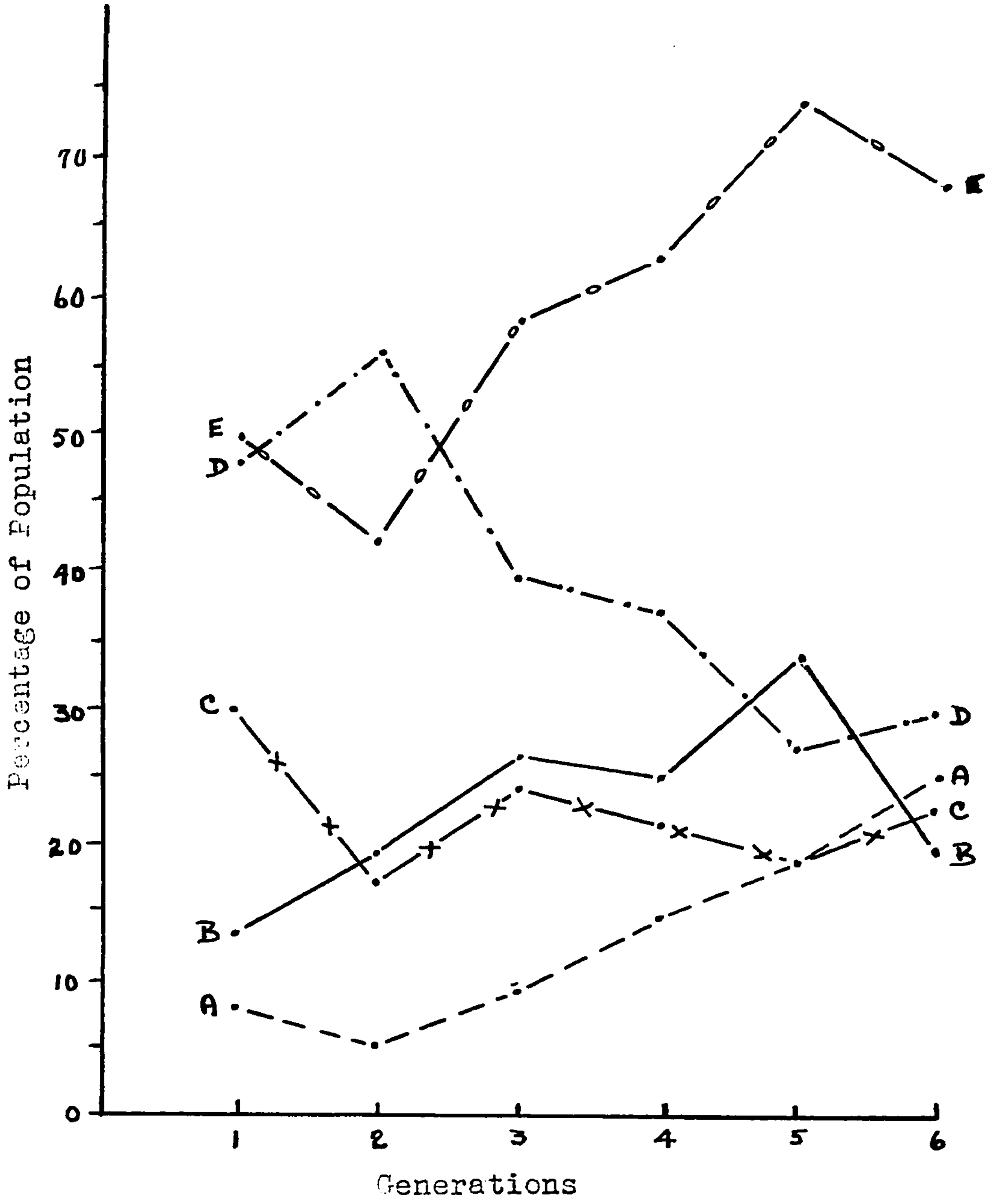
Percent of H, L, and Z Animals Produced by the Three Types of Matings

Generation	H	HxH	HxL	LxL	L	HxH	HxL	LxL	Z	HxH	HxL	LxL
1-6	258	139	64	55	177	53	43	81	327	61	80	186
	38%	53%	24%	21%	23%	29%	24%	45%	39%	18%	24%	56%

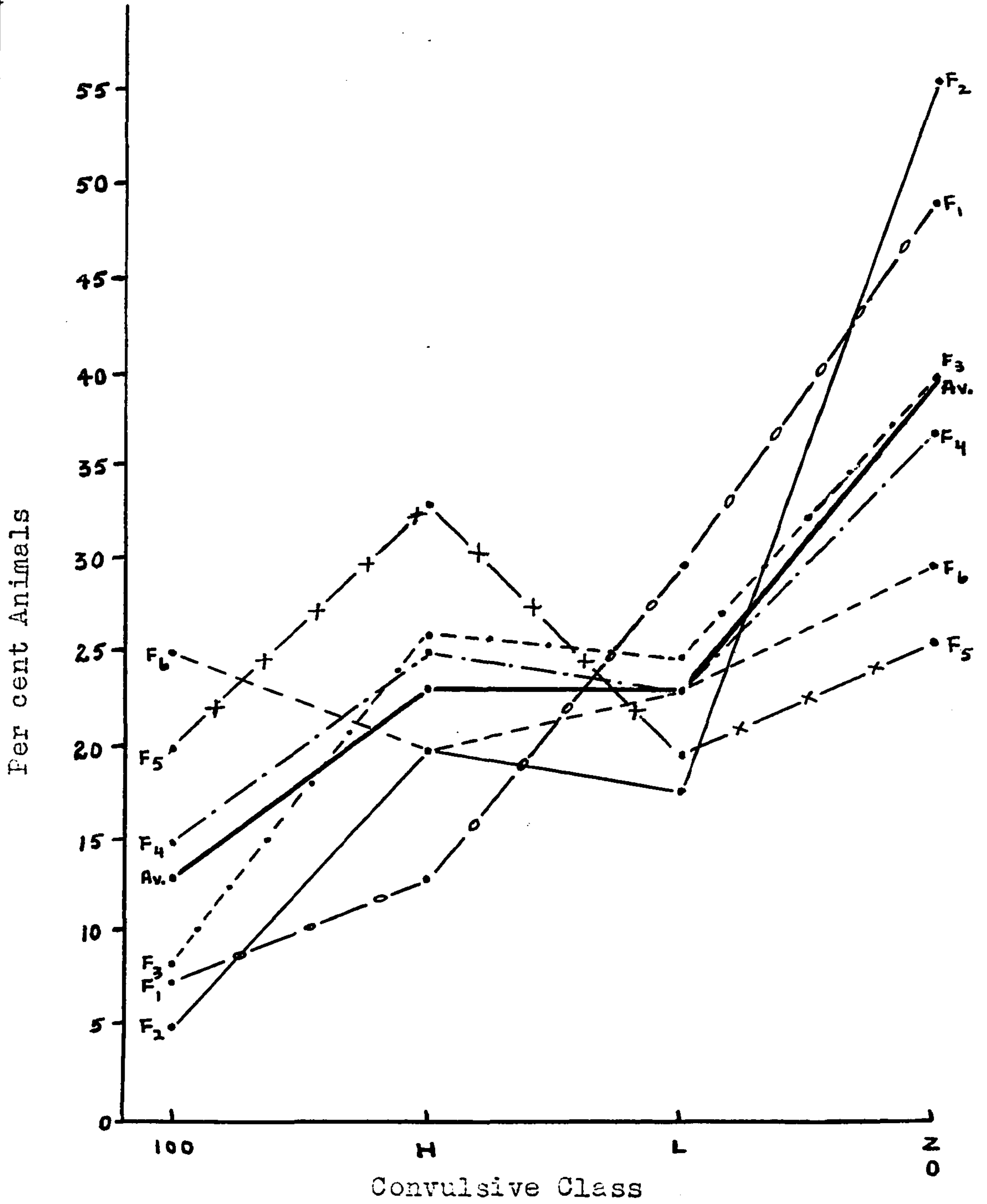
Original Stock	H+L	Z	D		D/ Dp*
	45%	55%	.16±	.124	1.29
Gen.6	61%	39%	.16±	.124	1.29

*Based on standard error

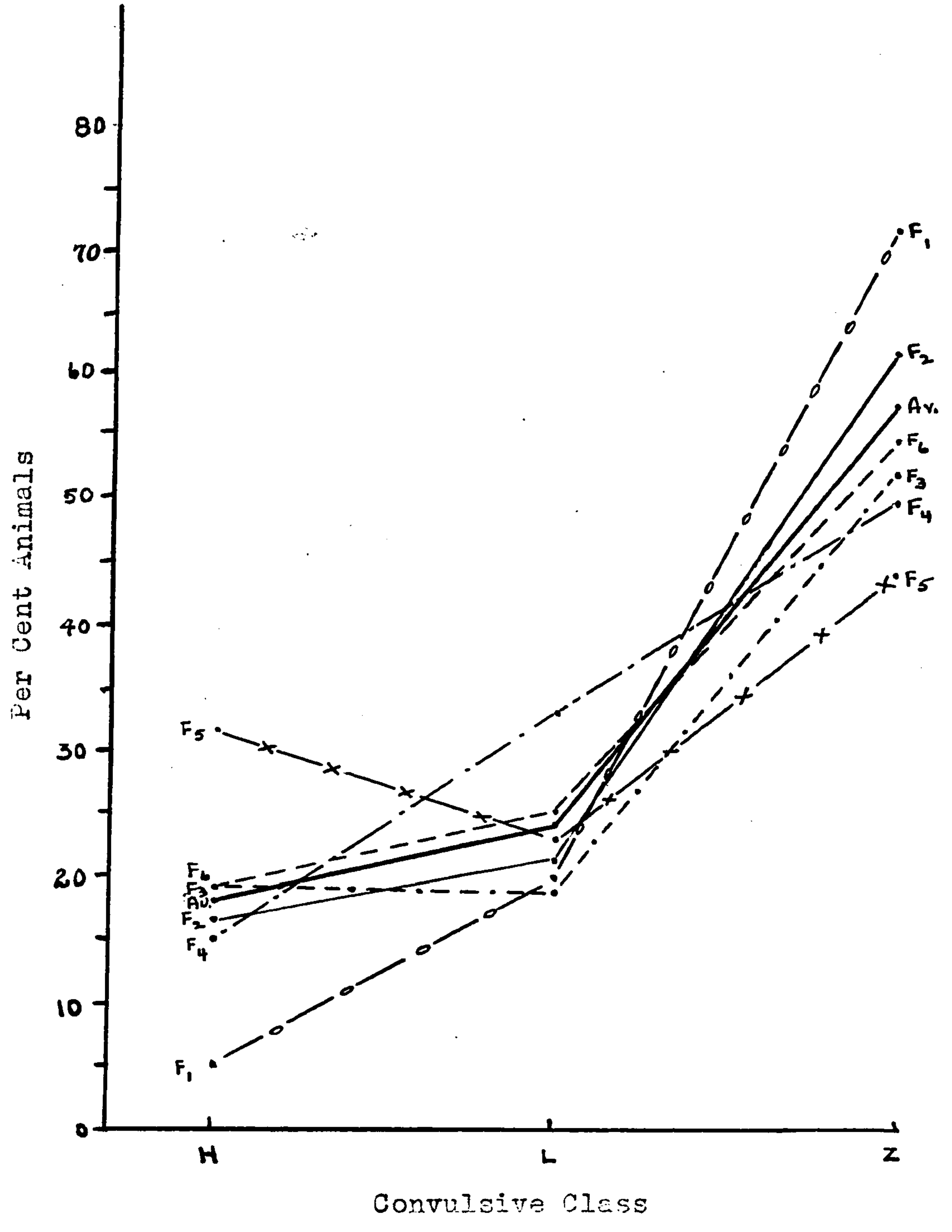
Graph 1
Relative Distribution of the Convulsive Classes
in the Six Generations



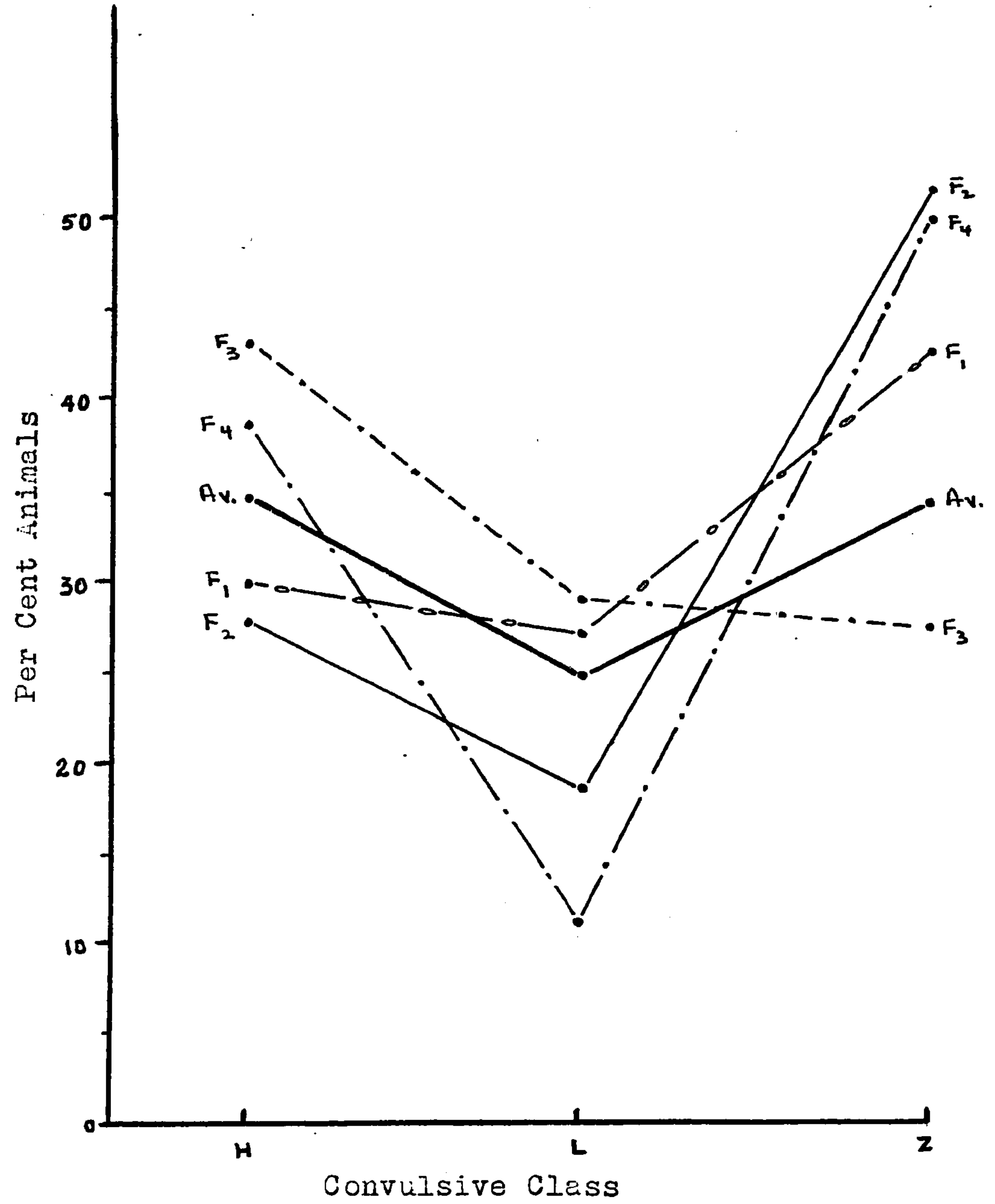
Graph 2
Relative Distribution of Percent of H, L, and Z
Class Animals in the Six Generations



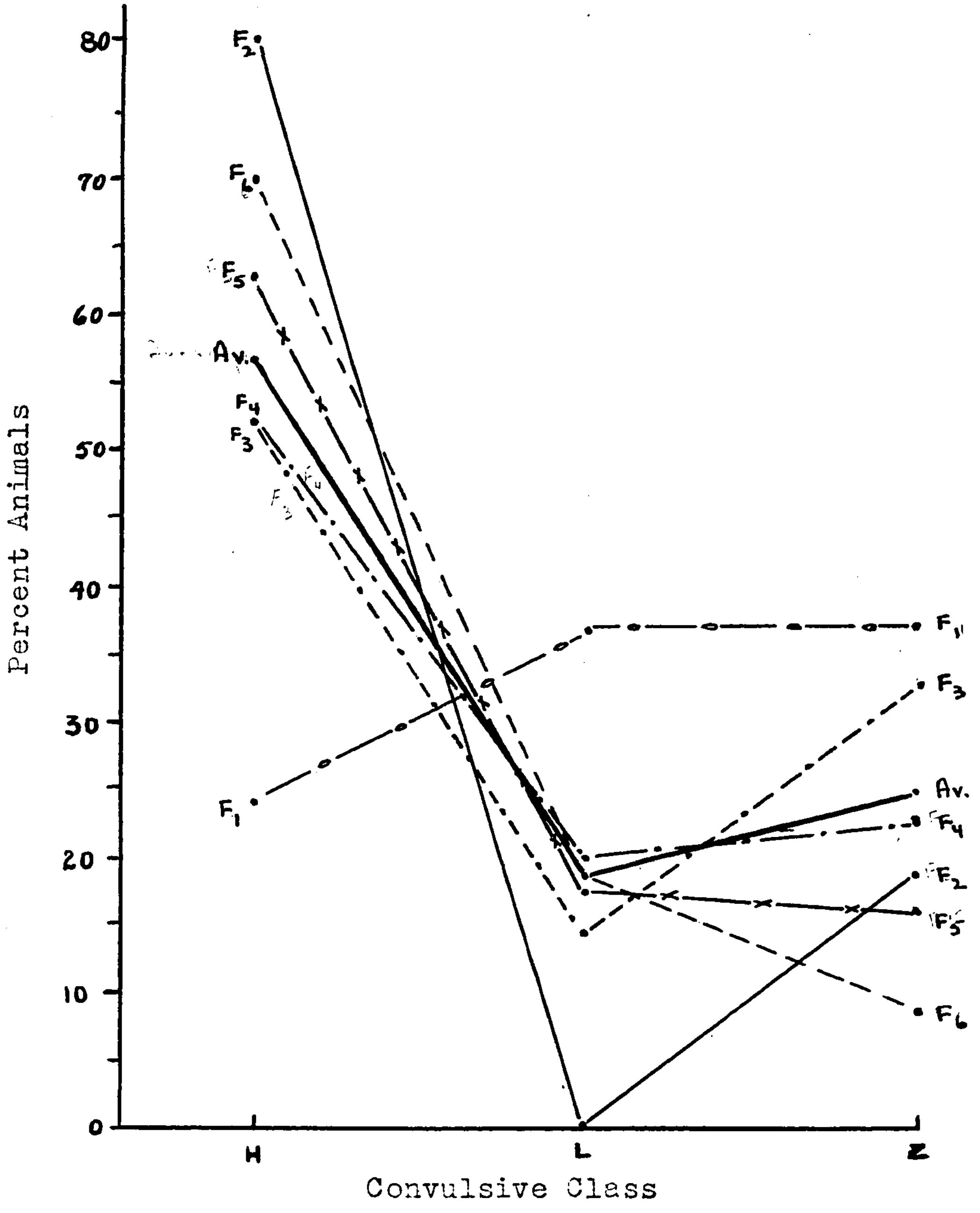
Graph 3
Percent of Animals in the Three Convulsive Classes in Six Generations of LxL Matings

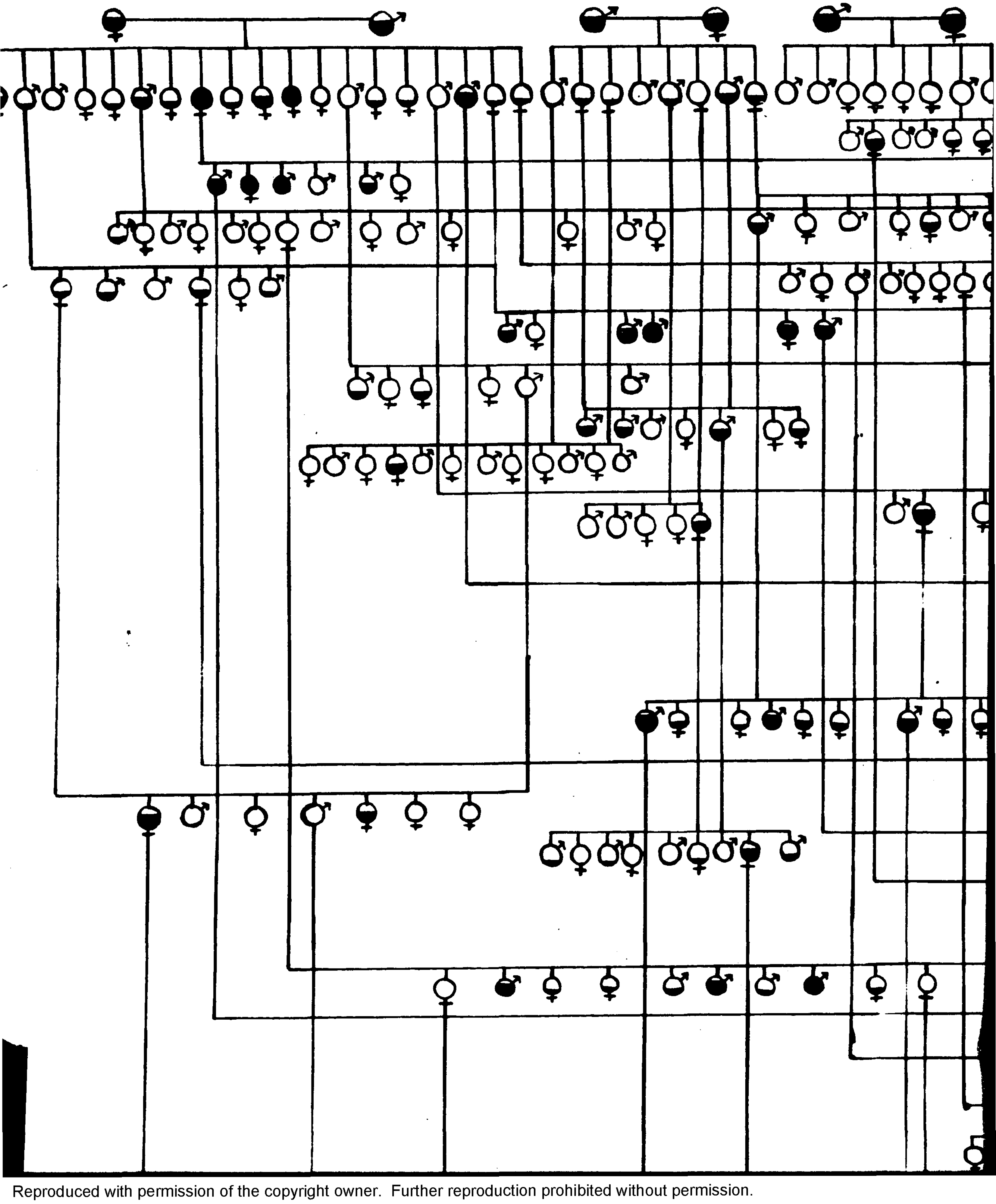


Graph 4
Percent of Animals in the Three Convulsive Classes in Four Generations of LxL Matings

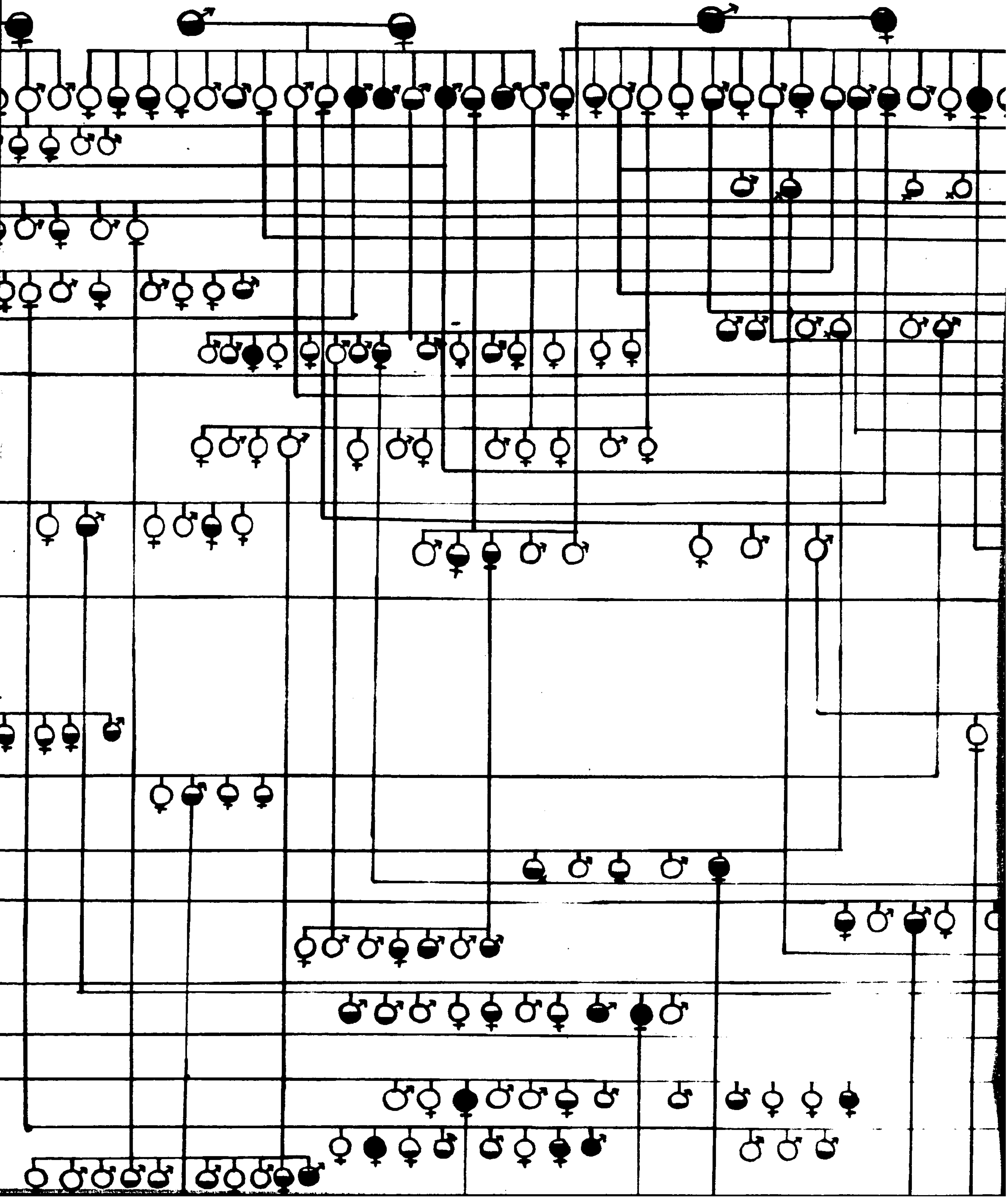


Graph 5
Percent Animals in the Three Convulsive Classes in Six Generations of HxH Matings

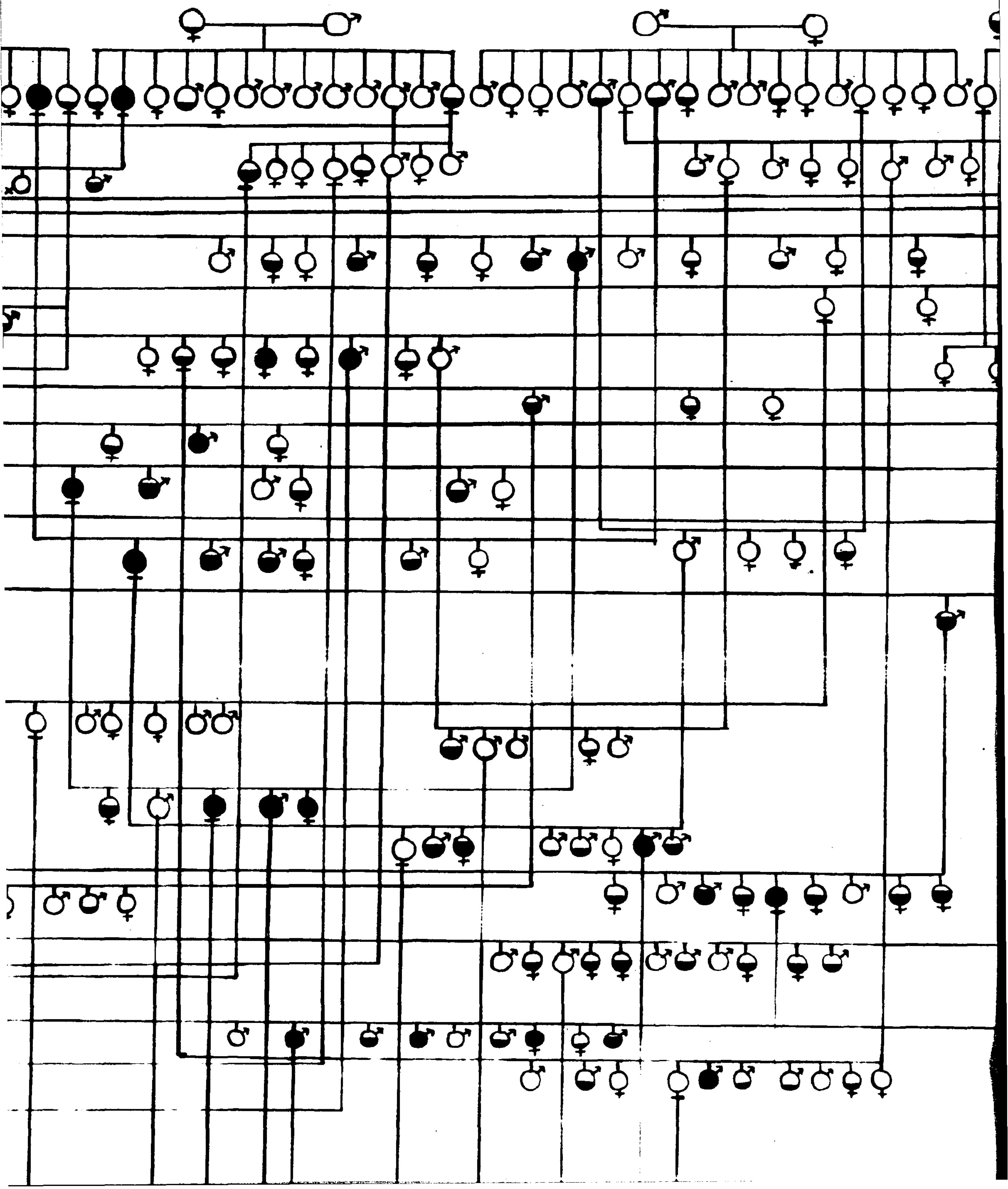


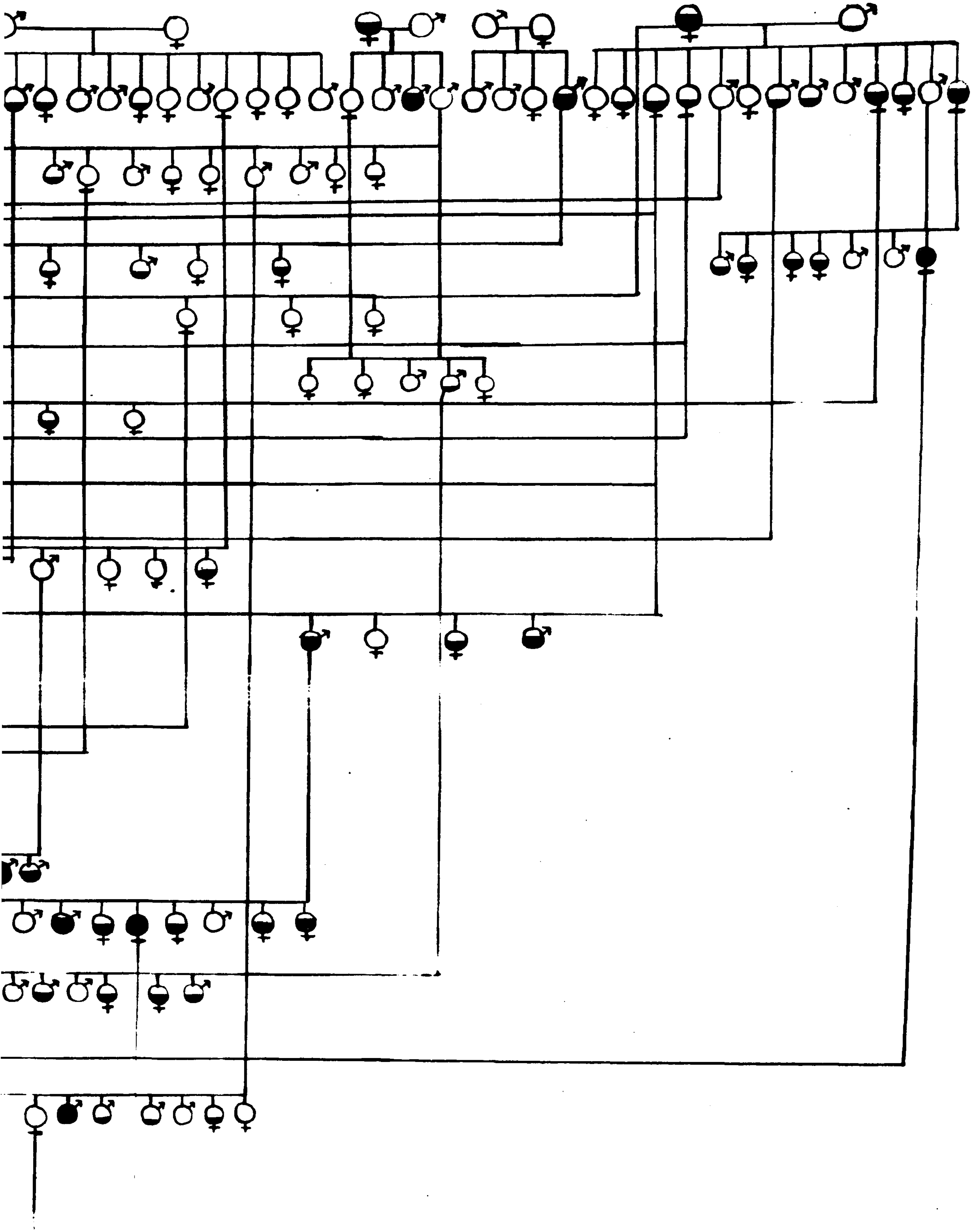


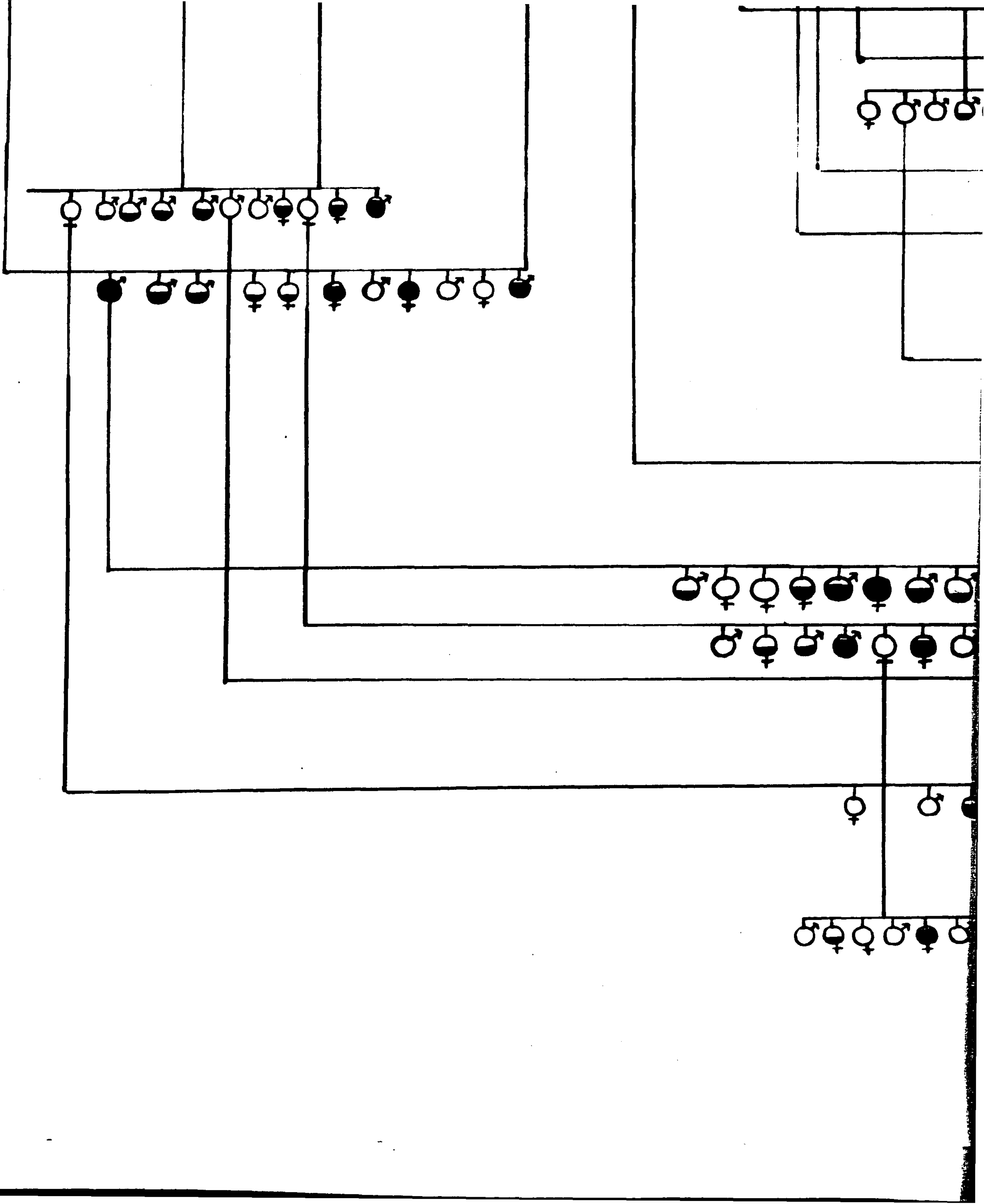
GENETIC CHAR

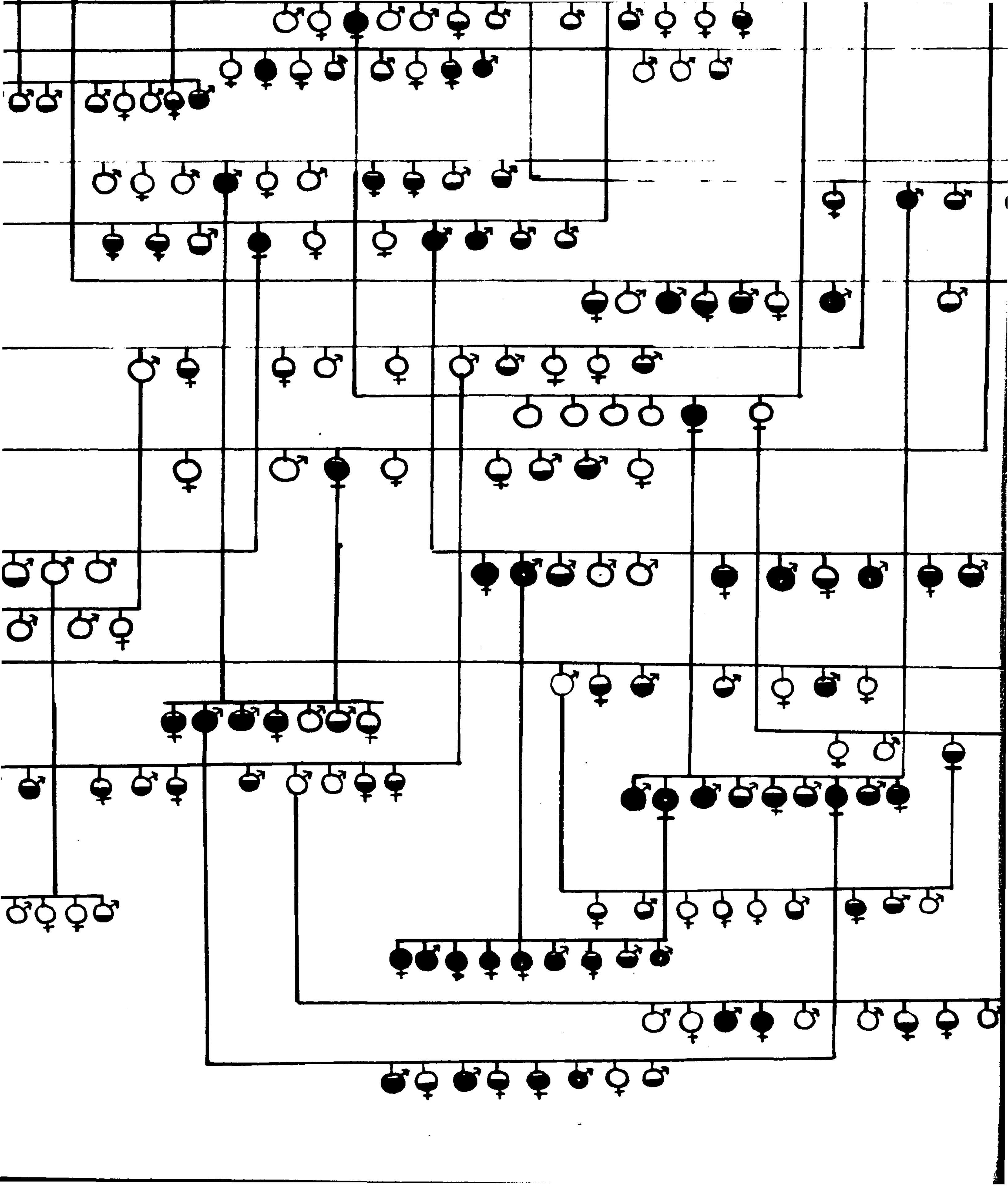


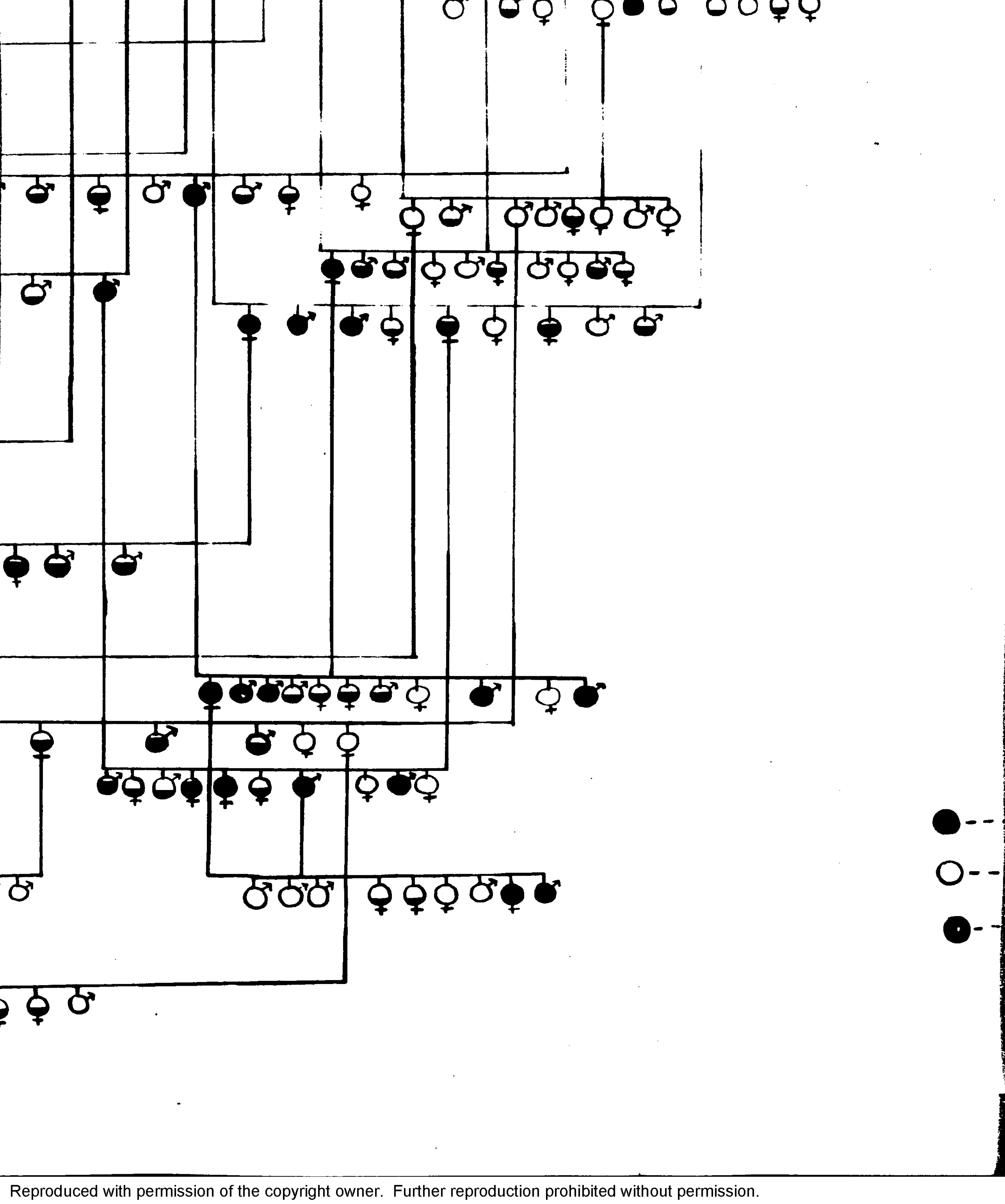
ART

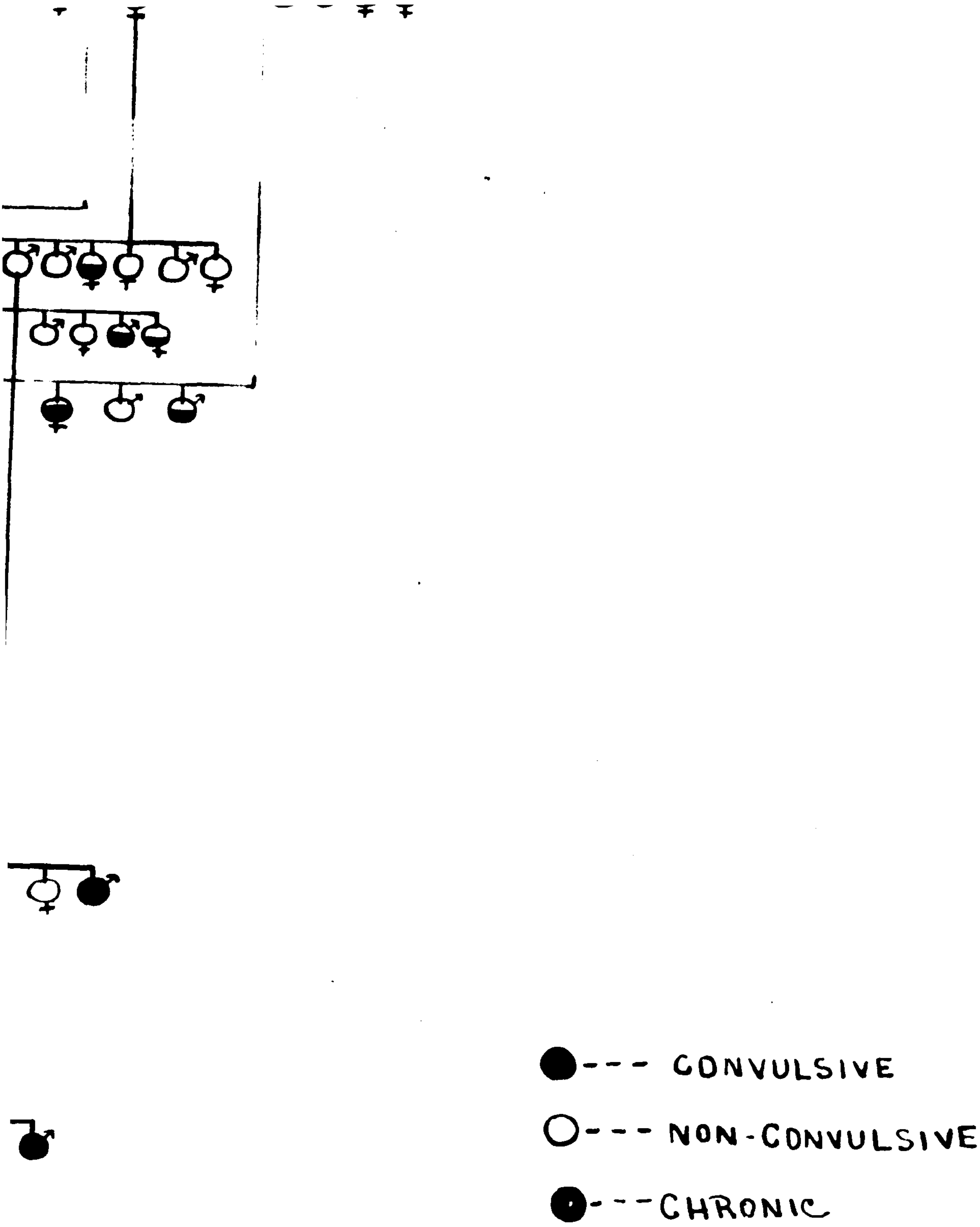











● --- CONVULSIVE
○ --- NON-CONVULSIVE
◉ --- CHRONIC

Discussion

Generally speaking the results of our breeding experiments over six generations are satisfactory in that they have indicated that it is possible, by an elective breeding, to produce a strain of animals in which the percentage exhibiting convulsive seizures exceeds those not succumbing to the seizures. The results are not satisfactory in so far as genetic laws are concerned.

As we have had occasion to note in a previous section, Maier has attempted to establish that experimentally induced convulsions in the rat are subject to the laws of Mendelian inheritance; specifically, that the convulsions are inherited as a Mendelian dominant. Maier has himself pointed out that his experiments have been carried out on too few animals to warrant definite conclusions as to the genetic laws to which the trait might conform. We emphasize this deficiency. We further point out that our genetic chart indicates, with one exception, no case in which the mating of two Z animals has produced 100 per cent Z in the offspring. Similarly, matings of two H animals have failed to give any indication of conforming to the expected 3:1 ratio, when individual generations are considered. Likewise, matings of H x L animals have not shown that a 1:1 ratio is adhered to in each generation.

From the results we have reported there is a suggestion that there is some genetic law, to date undetected, in operation. The general picture presented by the graphic representations of the results of the three mating types is suggestive of such a law. We have noted that the results of mating two H animals can be pictured by a graph whose general direction is from high on the convulsive scale to low on the Z scale. Matings of two L animals have yielded results which, when plotted graphically for the generations, indicate a high percentage of offspring on the Z scale and a low percentage on the 100 per cent scale. The plotted results for the offspring of H x L matings yield approximations to the expected 1:1 ratio.

The 9:7 ratio of convulsive to non-convulsive obtained on the entire population studied and expressed in Table 8, is also indicative of the presence of a definite genetic pattern.

Of greater significance, from our point of view, is the influence of the convulsive history of the parents on the offspring. Two years' study of the problem of transmission of convulsions, employing 762 animals, has definitely indicated that the actual percentage of convulsions in the genetic background of the offspring, regardless of the type of mating, is influential in determining the degree to which the offspring themselves are susceptible. We cannot see how Maier has succeeded in producing animals by selective breeding which conform so closely to the Mendelian ratios, when to our knowledge he has never made sufficient tests on the parents to determine their "convulsivity" in terms of the per cent of times that they react positively. Our arbitrary division of convulsives into H and L types has seemed justified on studying the graphs of the foregoing section. Animals whose histories indicate less than 50 per cent seizures are noted to closely follow the trend of the Z group, rather than that of the H group. It is only when we add this group in with the H animals that we are able to get ratios approximating Mendelian expectations. As we have previously pointed out we do not feel that such a combination is justified, although for theoretical purposes we have ourselves, at times, combined the groups.

The fact that each mating through the generations has presented different ratios, when the generations are considered individually, indicates that the convulsive backgrounds and the genetic histories in general cannot be ignored and are probably responsible for the lack of a constant ratio for any mating type in all the six generations.

Summary and Conclusions of Section 3

Twenty rats, aged twenty-one days, were selected from the colony of the University of Cincinnati, and tested by auditory stimulation for the presence or absence of convulsive reactions. These animals were divided into an H group, consisting of rats reacting with convulsive seizures 50 per cent or more of their 60 standard preliminary tests, an L group consisting of animals reacting positively less than 50 per cent of their trials, and a Z group of animals not succumbing to seizures in any of their 60 trials. Offspring from the three types of mating resulting from the above classification, namely, H x H, H x L, and L x L, were studied over 6 generations. Each animal was given a standard test of 60 trials under auditory stimulation in order to determine its classification before being mated. The following conclusions have been formulated from this study:

1. Under the condition of the study, it is possible by selective breeding of a known proportion of convulsive and non-convulsive rats, to produce, at the end of 6 generations, a strain having a higher percentage of convulsions than the original group.
2. Similarly it is possible to produce a strain having a lower percentage of non-convulsives than the original group.

3. By selective breeding it is possible to produce so-called "chronic" cases in which the abnormal behavior pattern occurs outside of the usual stimulus situation.
4. There appears to be a definite influence of the entire genetic history of the parents on the susceptibility of the offspring to convulsive seizures.
5. The above finding makes doubtful the Maier hypothesis that convulsive behavior in the white rat is inherited as a single Mendelian dominant.
6. The general picture of the graphic results presented for the different matings in the various generations, as well as certain combinations of the data, suggests the presence of a genetic law governing the transmission of convulsive tendencies.
7. The total distribution of 9 convulsive animals to 7 non-convulsive suggests a possible dyhibrid factor.

Part V.

General Summary and Conclusions from the Entire Study

General Summary and Conclusions

In the foregoing studies we have developed and supported the theory that the convulsive seizures obtained in the white rat, under the conditions outlined in Part II, Section 1, are functional, due to the stimulation of the emotional centers. Certain psychological, mechanical, and physiological methods of alleviating the convulsive seizures are likewise discussed in this section, which lend support to our theory.

We have found that the effect of convulsions on a previously learned maze habit varies with the type of apparatus on which animals are trained and re-tested (Part III, Section 2). No essential difference between the learning ability of convulsive and non-convulsive rats, as measured by the time taken to learn a maze to a critera of three errorless runs, was noted.

It is possible by selective breeding to produce at the end of six generations a strain having a higher percentage of convulsions than the original stock. We were unable, however, to find evidence that the convulsions were transmitted according to Mendelian ratio.

BIBLIOGRAPHY

(1) Anderson, O. D., and Liddell, H. S., Observations on experimental neurosis in sheep. Arch. Neural. Psychiat., 1935, 34, 330-354

(2) Bajandurow, B., Zur physiologie des sehenanysators bei vogelin. Z. Vergl. Physiol., 1932, 18, 288-306

(3) Bayroff, A. G., Air blasts as substitutes for electric shock in discrimination learning in white rats. J. Comp. Psychol., 1940, 30, 413-418

(4) Bonhote, L. J., Waltzing character in Mus rattus. Proc. Zool. Soc., London, 1912, 6, 7-8

(5) Britt, S. H., and James, S. Q., Criteria of frustration. Psychol. Rev., 1940, 47, 451-470

(6) Clark, L. P., Frustration and epilepsy. Psychoanal. Rev., 1922, 9, 367-401

(7) Cole, L. J., and Isben, H., Inheritance of congenital palsy in guinea pigs. Amer. Nat., 1920, 54, 130-151

(8) Cook, S. W., Experimental neurosis, survey of methods used to produce. Amer. J. Psychiat., 1939, 95, No. 6

(9) ________ The production of experimental neurosis in the white rat. Psychosamatic Med., 1939, 1, No. 2

(10) Curtis, Q. F., Experimental neurosis in the pig. Psychol. Bull., 1937, 34, 723

(11) ________ Frustration as an experimental problem. Character and Pers., 1938, 7, 140-144

(12) Darrow, C. W., Emotion as relative functional decortication: the role of conflict. Psychol. Rev., 1935, 42, 566-578

(13) Dice, L. R., Inheritance of waltzing and epilepsy in mice. Jour. Mammal., 1935, 16, 25-35

(14) Erickson, T. C., Spread of epileptic discharge. Arch. Neural. Psychiat., 1940, 43, 429-452

(15) Fortuyn, Von, A. B. D., Uber den systematischen Wert der japanischen Tanzmaus. Zool. Anz., 39, 177-190

(16) Freeman, G. L., A method of inducing frustration in human subjects and its influence on palmar skin resistance. Amer. J. Psychol., 1940, 53, 117

(17) Griffiths, W. J., The effect of dilantin on convulsive seizures in the white rat. J. Comp. Psychol., 1942, 33, 291-296

(18) Hall, C. S., and Martin, R. F., A standard experimental situation for the study of abnormal behavior in the rat. J. Psychol., 1940, 10, 207-210

(19) Hampton, P., Review of Maier's studies of abnormal behavior in the rat. New York: Harper, 1939

(20) Heron, W. T., Inheritance of brightness and dullness in maze learning ability in the rat. J. Gen. Psychol., 1941, 59, 41-49

(21) Heron, W. T., Inheritance of maze learning ability in rats. J. Comp. Psychol., 1935, 19, 77-89

(22) Hooper, J. J., A peculiar breed of goats. Science, 1916, 43, 571

(23) Humphrey, G., and Marcuse, F., New methods of obtaining neurotic behavior in rats. Amer. J. Psychol., 1939, 52, 616-619

(24) Hunter, W. S., The discrimination method. Journ. An. Behav., 1912, 2, 138

(25) Jacobsen, C. F., Wolfe, J. B., and Jackson, T. A., An experimental analysis of the functions of the frontal association areas in primates. J. Nerv. Ment. Dis., 1935, 82, 1-14

(26) Karn, H. W., A case of experimentally induced neurosis in the cat. J. Exp. Psychol., 1938, 22, 589-593

(27) Laones, T., and MacDowell, E. C., Circling of two gene traits in the mouse. Amer. Nat., 1935, 69, 720-768

(28) Liddell, H. S., The experimental neuroses and the problem of mental disorder. Amer. J. Psychiat., 1938, 94, 1035-1043

(29) ________, Anderson, O. D., Katyuka, C. Y., and Hartman, L. A., Use of adrenal cortical hormone with neurotic sheep. Amer. J. Physiol., 1938, 30, 341-342

(30) Lindsley, D. B., and Finger, F. W., Electroencephlographic and other physiological aspects of androgenic seizures in rats. Psychol. Bull., 1941, 38, 579

(31) Lord, E., and Gates, W. H., Shaker, a new mutation of the house mouse. Amer. Nat., 1929, 63, 435-442

(32) Lush, J. L., Nervous goats. J. Hered., 1930, 21, 242-247

(33) Maier, N. R. F., Studies of abnormal behavior in the rat. Abortive behavior and its relation to the neurotic attack. J. Exp. Psychol., 1940, 4, 369-393

(34) ________, and Glaser, N. M., Inheritance of neurotic pattern. J. Comp. Psychol., 1940, 30, 413-418

(35) ________, and Glaser, N. M., Studies of abnormal behavior in the rat; comparison of some convulsive producing situations. Comp. Psychol. Monogr., 1940, 16, No. 1

(36) ________, Glaser, N. M., and Sacks, J., Influence of metrazol on seizures occurring during auditory stimulations. J. Comp. Psychol., 1941, 32, 379-388

(37) Morgan, C. T., and Morgan, J. D., Auditory induction of an abnormal pattern of behavior in rats. J. Comp. Psychol., 1939, 25, 505-508

(38) Notkin, J., Is there an epileptic personality make-up? Arch. Neur. Psychiat., 1929, 26, 799-803

(39) Page, J. D., Studies in electrically induced convulsions in animals. J. Comp. Psychol., 1941, 31, No. 1

(40) Pavlov, I. P., Conditioned reflexes. (Tr. G. V. Anrep.) London: Oxford Univ. Press. 1927

(41) Riddle, O., A case of heredity ataxia in pigeons. Proc. Soc. Exp. Biol. and Med., 1918, 15, 56-58

(42) Stockard, C. R., Experimental modification of the germ plasm and its bearing on the inheritance of acquired characteristics. Amer. Philos. Soc., 1923, 62, 311-325

(43) Watson, M. L., The inheritance of epilepsy and the waltzing of mice. Contr. Lab. of Vert. Gen., Univ. of Michigan, 1939, No. 11, 24

(44) Wortis, S. B., Experimental convulsive seizures. J. Nerv. Ment. Dis., 1933, 77, 233-245