N73 24124

FINAL REPORT

INVESTIGATION OF THE NEUROLOGICAL CORRELATES OF INFORMATION RECEPTION

CASE FILE COPY

Report of Research Conducted by

Center for Neural Sciences

Indiana University

under contract with

National Aeronautics and Space Administration

Grant NGR 15-003-007

for period

1 January 1965 - 31 December 1971

SUMMARY AND CONCLUSIONS

Earlier experiments have shown that electrical stimulation of pathways or centers in the auditory nervous system of an unanesthetized experimental animal may elicit a behavioral response that the animal initially learned to make to an acoustical signal from a loud-speaker. With appropriate control experiments to rule out such possibilities as: the response can be elicited by electrical stimulation of non-auditory pathways or centers or the response may be elicited by any pattern of electrical stimulation of the auditory nervous system, it becomes reasonable to infer that the auditory sensation produced by the electrical stimulation of the auditory nervous system is the same or similar to the sensation produced by an acoustic signal from a loud-speaker.

The experiments described in this report represent an attempt to extend this general approach, namely, establishing the equivalence of two stimuli in terms of the behavioral response that they elicit.

The principal findings of the experiments are summarized briefly, below. Details are given in the main body of this report.

1. Animals trained to respond to a given pattern of electrical stimuli applied to pathways or centers of the auditory nervous system respond also to certain patterns of acoustic stimuli without additional training. Likewise, only certain electrical stimuli elicit responses after training to a given acoustic signal. For example, a train of clicks will most often give rise to a response that has been learned to an electrical stimulus consisting of a train of brief electrical pulses. A train of low frequency tone pulses will sometimes elicit a response but not as often as the clicks. High frequency tone pulses seldom elicit a response.

This specificity of the equivalent electrical and acoustic stimuli is important in considering possible future refinement of techniques of injecting information into the auditory system through electrical stimulation.

2. In most instances, if a response has been learned to a given electrical stimulus applied to one center of the auditory nervous system, the same stimulus applied to another auditory center at either a higher or lower level will also elicit the response. This kind of transfer of response does not take place when a stimulus is applied through electrodes implanted in neural tissue outside of the auditory system.

3. On the basis of a limited number of experiments done to date, it appears that animals cannot discriminate between electrical stimulation applied to one side of the system and similar stimulation applied at the corresponding level on the opposite side.

4. Sensitivity to electrical stimulation of an auditory center may be enhanced by simultaneous sound stimulation of the ears.

There are numerous experiments that can be done to develop further the methods and techniques of producing auditory sensations by electrical stimulation of the auditory nervous system. Most such experiments are time-consuming, require different kinds of technical skills, and require expensive instrumentation.

At present, the most rapid progress towards the development of knowledge and methods that may lead to at least a crude prosthetic device will probably be made through experiments with human patients. Although there are severe limitations in experimental procedures that may be used with human subjects, these limitations are outweighed by the advantage of working with a subject who can report verbally what he hears when different patterns of electrical stimuli are used to excite his auditory nervous system.

FINAL REPORT

Investigation of the Neurological Correlates of Information Reception, a Report of Research Conducted under NASA grant NGR - 15-003-007.

Introduction

Electrical stimulation of neural pathways or centers has been employed in a wide variety of experiments on central nervous system function. For example, it has been used: (a) to map motor and sensory areas of the cortex in anesthetized animals; (b) to explore sensory and motor cortex of man during surgery; (c) to elicit "emotional" responses through stimulation of subcortical centers via implanted electrodes in unanesthetized animals; (d) to serve as the unconditioned stimulus in learning experiments, stimulation again being given through implanted electrodes in unanesthetized animals. With the exception of a few preliminary experiments, use of the electrical stimulation technique as a means of injecting sensory information into experimental animals has been neglected.

In a series of experiments done during the period 1934-1938, Loucks (1) (2) (3) (4) showed the feasibility of using electrical stimulation of sensory neural structures as the conditioned stimulus in learning experiments. Although his stimulation technique did not permit study of complex waveforms, he was able to show differential effects of stimulating selected sites at both spinal cord and cortical levels of the central nervous system.

More recently Doty and co-workers (5) (6) (7) have also conditioned animals to respond to electrical stimulation of sensory areas of the cerebral cortex. The techniques which they developed to implant electrodes and to provide stimulation were an improvement on those first used by Loucks. Control experiments were done to make certain that information was being injected directly into the central nervous system rather than by way of sense organs in the meninges or skin. Some evidence was obtained bearing on the question, will a response conditioned to stimulation of one cortical locus be elicited by stimulation of other cortical loci?

In earlier experiments (8) (9) the principal investigator and associates were concerned with the problem of how information is coded in the auditory pathways and an attempt

was made to develop the method of direct electrical stimulation of the auditory system in unanesthetized animals as a means of gaining information about patterns of neural activity which may be equivalent to externally produced sounds. Patterns of neural activity produced by electrical stimulation are judged to be equivalent to patterns of neural activity produced by sounds presented to the ear when both elicit the same learned response in an experimental animal. A brief summary of the findings is given below:

1. Experimental animals (cats) may be conditioned to respond to direct electrical stimulation of the main afferent pathway of the auditory system at midbrain, thalamic, and cortical levels. There are no similar unconditioned responses elicited by stimulation of these sites.

2. Animals conditioned to respond to sound stimuli make the conditioned response when direct electrical stimulation is applied to the main afferent auditory pathway through electrodes implanted in the inferior colliculus or on the auditory cortex. Some evidence indicates that with a refinement of the stimulation technique the animals will respond to stimulation of the eighth nerve or primary cochlear nucleus, but stimulation at this level with present techniques produces unconditioned vestibular responses which conflict with performance of the learned response.

3. Animals trained to respond to stimulation of mesencephalic and thalamic centers of the main afferent auditory pathway make the conditioned response when presented with sound stimuli.

4. Animals conditioned to respond to direct stimulation of the thalamic nucleus of the main afferent auditory pathway do not make the conditioned response when the thalamic center of the visual system is stimulated. Similarly, animals trained to respond to direct stimulation of the thalamic nucleus of the visual system do not respond when the thalamic nucleus of the auditory system is stimulated.

5. Some animals trained to respond to one frequency of stimulation applied at the mesencephalic level of the main afferent pathway of the auditory system require further training before other frequencies of stimulation elicit the conditioned response. All animals stimulated at this level have been successfully trained to respond to a wide range of stimulation frequencies when generalization training was given.

In undertaking the research which is summarized below, it was planned to extend the findings of earlier experiments by:

1. Determination of spatio-temporal patterns of activity in the central nervous system which are equivalent in eliciting a response conditioned to a given restricted subset of possible stimulation patterns. This involves testing for the possible elicitation or transfer of the conditioned response to novel patterns of stimulation.

2. Tests of transfer of a response to specific spatio-temporal patterns of direct electrical stimulation within the central nervous system when the response has been conditioned to sound stimuli.

3. Tests of transfer of response to various sound stimuli when the response has been conditioned to restricted spatio-temporal patterns of direct electrical stimulation within the central nervous system.

The auditory system was chosen for study because reasonable hypotheses as to the possible nature of its central code have been formulated (see, for example, 10, 11, 12). These hypotheses are based upon extensive psycho-physical as well as electrophysiological data. Specifically, it is known that auditory information pertaining to frequency of a stimulus is transmitted centrally from the cochlea by means of a dual code which uses both place and periodicity information.

Methods and Procedure

Cats were used as experimental subjects in all experiments. Under anesthesia and with aseptic procedures bipolar or multiple electrodes, such that electrical stimuli could be applied between any two electrode tips, were implanted in centers or pathways of the auditory nervous system. In nearly all instances, stainless steel electrodes were used, teflon-insulated to within a millimeter or less of the tips. Leads from the electrodes were passed under the skin to an Amphenol subminiature connector that was attached to the skull by dental cement and stainless steel screws. A ground lead from the connector was attached to a stainless steel screw inserted in the skull.

Electrodes were placed on auditory areas of the cortex after removal of over-lying skull and dura. Placement of electrodes in subcortical pathways was in some cases done by visual guidance and in other cases, by means of a Kopf stereotaxic instrument. Gelfoam was used to support electrodes and to cover exposed brain tissue. The electrodes were then attached to the skull by spreading dental cement over the gelfoam and over adjacent skull that had been carefully cleaned and made dry.

After placing of electrodes and connecting them to the Amphenol connector, muscles and skin were replaced and sutured, the skin being drawn snugly around the base of the connector. A cap was placed on the connector to keep contacts clean until time for use in an experiment.

A recovery period of ten to fourteen days was allowed before animals were used in an experiment.

Training of animals, whether to electrical stimulation through the implanted electrodes or to acoustic stimuli, was done in a double-grill box which was placed in a quiet room (double-walled, IAC type). A control panel, signal generators, Grass stimulator (S-8), timing circuits, and other equipment used in conditioning procedures were placed outside the quiet room. The experimenter operated the controls from a position in front of a one-way glass window through which he could observe the behavior of the experimental animal.

Animals were initially trained to respond to an acoustic stimulus from a loud speaker or to pulses of electrical current produced by the Grass stimulator and passed through an implanted electrode. Training procedure consisted of

presentation of the CS (acoustic or electrical stimulus) for approximately 10 seconds followed by electric shock delivered through stainless steel bars that formed the floor and sides of the double-grill box. A conditioned (or learned) response (CR) was movement of the animal from one compartment to the other of the double-grill box in response to the CS in order to avoid the unconditioned stimulus (US), shock to the feet. This conditioned avoidance response is usually learned quickly by the cat and is retained for long periods of time.

Transfer tests were given after a CR had been firmly established to a particular stimulus (a specific acoustic stimulus or eletrical shock to a given auditory center or pathway). On a test trial the CS was replaced by a different stimulus and the behavior of the animal noted. For example, if the CS that had been learned was 10 shocks per second applied to auditory cortex, a transfer test trial might be 10 clicks per second presented over the loudspeaker. Transfer is defined as making the CR (crossing in double-grill box) to the new stimulus without reinforcement by shock to the feet. When transfer occurs, it may be inferred that the shocks to the cortex and the clicks presented via speaker to the ear produce similar sensations -- sound alike to the animal.

During the experiments to be described, several kinds of transfer tests were given: acoustic signal -- electrical stimulus to auditory nervous system; electrical stimulus -- acoustic signal; electrical stimulus to one auditory center -- electrical stimulus to higher or lower auditory center; electrical stimulus to auditory center -- electrical stimulus to non-auditory center.

After postoperative tests had been completed, animals were anesthetized and perfused with saline and formalin. Brains were removed, sectioned and stained. Brain sections were examined to determine the paths of implanted electrodes and the locations of electrode tips.

Results

I. Equivalence of Electrical Stimulation of Auditory Nervous System and Acoustic Stimulation of the Ear.

The experiments here reported investigated the equivalence of (a) electrical stimulation of the inferior colliculus (IC) and (b) sound stimuli presented over a loudspeaker, by using the double-grill box shock avoidance response to produce discrimination behavior in cats. The experiments to be presented below differ from previous attempts to study equivalence between peripheral sensory stimuli and electrical of the central nervous system (CNS) in one or more of the following ways: 1. In the present work, a wider range of test stimuli were used. 2. Control animals were included to insure that stimulus equivalence and not a generalized set to respond was responsible for the results. 3. A strict criterion for original training was met before any transfer tests were conducted. 4. The animals were required to attend to a change in a continuously presented stimulus rather than to the sudden onset of a stimulus.
Subjects: Subjects were eight adult, healthy cats with normal appearing external and middle ears.
Procedure: (A general description of methods and procedure has been given above.) Seven animals were prepared in an aseptic operation with chronic bipolar electrodes located either in the left or right inferior colliculus. One cat also had electrodes implanted bilaterally in the superior colliculus (SC). The remaining animal had an electrode placed in the left SC only. The electrodes were constructed from .0016 in. stainless steel wire coated with Teflon except for 1 mm. at the tip. Electrode placement was done under visual guidance with the intent being to place the electrode tip in the apex of the colliculus.

Following recovery from surgery, 5 animals were trained to make an avoidance response in the double-grill box. The avoidance signal was a change from a continuous background stimulation rate of 1 electrical pulse per second (pps) to 10 pps. The pulses were delivered through the electrodes in th IC (or in the SC in one animal). The pulses were 3 to 6 ma. (peak current), .1 msec. square wave pulses produced by a Grass S8 electronic stimulator. After all animals had learned to perform the avoidance response to an increase in pulse rate, a series of test days followed. During the test days different sound stimuli were substituted for the

electrical stimulation. No shock punishment was used during test trials.

Two additional animals were first given avoidance training with acoustic stimuli, 1 vs 10 clicks per second and then were tested with electrical stimulation of the IC to see if the avoidance response would occur. The final animal was tested for transfer of the learned response when the electrical stimulation was delivered to the left or right SC.

Results: The data obtained from all 8 animals are shown in figures 1-8. Figures 1-4 show that all animals originally trained with electrical stimulation of the IC showed some degree of transfer to the acoustic test stimuli. The degree of transfer can be seen to differ for different test stimuli, with the greater percentage of transfer occurring for clicks and lower frequency tone pulses.

Figures 5 and 6 show the results obtained for two animals originally trained with clicks and later tested with electrical stimulation. Here again some sort of stimulus equivalence is suggested by the immediate (though incomplete) transfer demonstrated by both animals. The final two figures, 7 and 8, concern the animals with electrodes located in SC. Figure 7 shows that there was no transfer to test sounds when original training involved the SC. Figure 8 demonstrates that the animal originally trained with electrical stimulation of the IC showed no transfer or the avoidance response when tested with stimulation of either SC.

Implications and conclusions: Transfer of avoidance learning was observed in animals trained to respond to electrical stimulation of the IC and then tested with acoustic stimuli. Further, there appeared to be stimulus specificity involved in the elicitation of transfer. The control animals in the present study support the view that we are actually dealing with some kind of a stimulus similarity continuum and not merely with rapid learning of new stimulus-response associations.

II. Equivalence as Measured by Responses Made to New Sites in Auditory Nervous System after Training to Stimulation of a Single Site.

Methods and procedure: Forty-five adult male cats weighing between 4.5 and 7 pounds were used in the experiments to be described. Using sterile technique, twisted wire teflon-coated stainless steel electrodes (1 mm distance between the two tips) were implanted subcortically either by direct

visual inspection or by means of a Kopf stereotaxic apparatus in cats anesthetized with pentobarbital. Only the cross-sectional areas of the electrode tips were free of insulation. The electrodes were then fixed to the skull with dental cement and attached to an Amphenol subminiature connector which was grounded by means of a skull screw. Cortical electrodes (made by inserting a piece of teflon coated stainless steel wire through a hole drilled in a machined stainless steel screw) were implanted directly on the exposed surface after removal of the dura so that the lower of the bipolar electrodes extended 1 mm below the surface while the screw head rested on the surface. Exposed cortex was then covered with Gelfoam and the muscle and skin flaps sewn back together.

After a ten day recovery period, animals were placed in a double-grill box and trained to cross from one side to the other to avoid a shock delivered to the grill 10 seconds after the onset of the conditioned stimulus (CS). Ten trials of the CS were presented each day, interspersed with periods of a neutral signal. For most animals the neutral signal consisted of a one pulse/sec., 0.1 msec square wave delivered at 0.5- 3 mA/(measured peak to peak) from a Grass S-2 stimulator. During training the stimulus was continuously monitored on an oscilloscope. The CS consisted of a shift to a ten pulse/sec., 0.1 msec stimulus at the same milliamperage. Criterion was judged to be 9 correct responses in 10 trials on two out of three consecutive days. Originally, different parameters were used for cortical and subcortical stimulation (cortical stimulation being 50 pulses/sec in 50 msec trains delivered at 0.5 sec/pulse, 0.1-0.8 mA). Later a 1-10 discrimination was used for both cortical and subcortical loci.

After criterion was reached, two transfer trials were given daily, inserted at random among the training trials. Transfer trials consisted of 1 vs 10 electrical pulses delivered to other brain loci or 1 vs 10 sequences of tones, clicks or white noise. On transfer test trials, animals were given 10 seconds to respond and were not punished if they failed to do so. Ten transfer trials were given for each brain locus or for each peripheral acoustic stimulus during a total of five training days.

In one group of animals, an attempt was made to teach a right-left or left-right discrimination. A stimulus of 5 pulses/sec., 0.1 sec, 1-3 mA was delivered to an auditory center on either the right or left side. Test trials consisted of a shift to stimulation on the contralateral side.

Before training began and at the end of training (just before sacrifice) evoked potentials to sound were recorded through

the implanted electrodes using a Grass model 3 EEG machine. Clicks, white noise and tones of 800, 2000, 3000, and 4000 cps were used.

At sacrifice, the animals were anesthetized with pentobarbital, and perfused through the aorta with warm saline followed by 10% formalin. The brains were then removed, inspected grossly, embedded in celloidon, sectioned at 50 microns, and stained with thionin or Weil's.

Results:

1. Transfer after training at the level of the inferior colliculus (IC) (Table I).

Ten cats readily learned to respond to a change from 1 per sec. to 10 per sec. electrical stimulation of the right or left brachium of the inferior colliculus (BIC) or IC within 100-150 trials (given during a period of 10-15 days). All animals in which the electrodes were later found to have penetrated the IC bilaterally transferred without further training to stimulation (1 vs 10 electrical stimuli) of the contralateral IC. In three of the animals, the electrode to which transfer was attempted was situated just outside the IC, and in these cases (in which evoked potentials to sound could not be recorded) partial transfer occurred (20-60%). These animals could be trained to respond to 1 vs 10 stimulation through the second electrode.

After initial learning and transfer was complete, the response to stimulation through either the original or the second electrode pair was extinguished. It was then possible to show transfer of the extinction to the contralateral electrode pair. Subsequent retraining with the 1 vs 10 stimulus also transferred without further training to the opposite side.

Animals trained to respond to a 1 vs 10 pattern also responded readily to a 1 vs 5 or 1 vs 20 pattern, but not to less than 1 vs 5. Generally, as the frequency of stimulation increased (1 vs 20, 1 vs 100, etc) the interval between onset of the CS and the response of the animal diminished markedly. In six of the animals, transfer was also demonstrated to 1 vs 10 patterns of clicks or low tone pulses (800 cps, 1200 cps) but not to white noise bursts or tone pulses above 1200 cps. In a few animals (4 of 10), no transfer to sound occurred although evoked potentials to sound could be recorded through at least one electrode pair. These animals showed startle reactions when sound stimuli were turned on.

After training at the level of the IC, transfer also occurred to stimulation of either primary cochlear nucleus (PCN) in seven animals. In 3 of 5 animals the same strength of stimulation was used for both training and transfer. In the other two, a high strength (1 - 3 mA more) was needed to elicit responses to PCN stimulation. In these two animals evoked responses to sound recorded through the PCN electrodes were weak (20 uV). Generally, in animals that showed transfer readily, evoked potentials were in the range, 50-150 uV.

In three out of five animals with both cortical and IC electrodes, transfer to stimulation of auditory areas A_1 and A_2 occurred after training at the level of the IC. Transfer did not occur to stimulation through electrodes on the visual cortex or suprasylvian gyrus. In the other two cats, no transfer occurred to auditory cortex even at 1-2 mA.

2. Transfer after training at the level of the primary cochlear nucleus (PCN)

Learning readily occurred to PCN stimulation within 150 trials in 8 cats. Transfer without further training could be elicited by stimulation of the contralteral PCN or the ipsilateral or contralateral IC. In two cats, transfer did not occur. In these latter cases, at least one pair of electrodes was not in the auditory system. In one animal, the "PCN" electrode was within 1 mm of the superior olive. This animal learned rapidly and showed transfer to stimulation of the ipsilateral IC.

3. Stimulation of the medial geniculate (MG).

Five animals had electrodes implanted bilaterally in the medial geniculate. Evoked potentials to sound were recorded bilaterally in two of these animals and unilaterally in one. No evoked responses could be recorded in two cats. The two animals with bilateral evoked potentials learned to respond to MG stimulation and readily transferred to stimulation of the contralateral MG. The cat with unilateral responses was trained on that side with ease, but did not transfer to the opposite side. The two other cats did not reach criterion in 300 trials and behaved as if stimulation was disagreeable (loud vocalization and general excitation when stimulus changed from 1 pps to 10 pps).

4. Stimulation of auditory cortex.

Attempts to train animals to stimulation of the auditory

cortex failed in four cats. In two others, training was successful. One, trained to stimulation of A_1, transferred readily to A_2. The other, trained to stimulation of A_2, transferred to A_1. Neither showed transfer to stimulation of visual cortex.

III. Discrimination between Electrical Stimulation of Left and Right Sides of Auditory Nervous System.

Ten cats had electrodes implanted bilaterally in the inferior colliculi. Careful evoked potential records were made before training began. Stimuli were tones in the range from 800 cps to 4000 cps. It appeared that, in some animals, responses recorded from the two electrode pairs were not identical: one side gave better responses to higher tones, the other to lower tones. These differences were later found to have no effect on the ability of the animal to learn a right-left discrimination. Only 2 of 10 animals were able to learn to respond when stimulation was switched from one IC to the other. The other eight animals never reached criterion and often developed bizarre behavioral patterns such as sitting on the barrier between the two sides of the grill box or always responding to any detectable change such as a change in voltage or flicking of the stimulus to one IC off and then on again. These animals were trained for 350 trials and became very difficult to handle by the end of 150-200 trials. Even animals that reached 80% would also respond regularly to turning the stimulus off and then on again on the same side, suggesting that they had not learned to distinguish right from left. In one animal that learned the discrimination, evoked responses could not be recorded from the electrodes on one side; it was found later to have one electrode in the extreme posterior portion of the superior colliculus. The second animal that learned the right-left discrimination did have bilaterally placed IC electrodes. No noticable differences were present in the evoked potential patterns of the two sides in this animal.

IV. Interaction of Electrical and Peripheral Sensory Stimulation.

Electrophysiological experiments done in other laboratories have shown that the evoked response of cortical auditory or visual units to electrical stimulation of subcortical structures of the same sense modality is facilitated by constant retinal illumination. While these results suggest that the ability of animals to detect the electrical stimulation is being enhanced, there is no direct evidence for this conclusion. The animals were anesthetized and unable

to indicate by differential response whether or not their ability to detect the electrical stimulation was improved by continuous retinal stimulation.

The present study was conducted to answer two questions: (1) is the detection of electrical stimulation of a subcortical sensory structure facilitated in the unanesthetized cat by continuous background stimulation of the same sense modality, and (2) can a facilitation effect be shown to exist solely within the auditory system?

A chronic bipolar electrode was implanted in either the left or right inferior colliculus of six cats. Surgery was accomplished under nembutal anesthesia and under aseptic conditions. The electrodes were constructed by twisting together two pieces of teflon-coated stainless steel wire. The last 1 mm. tip of each electrode was bared of the teflon insulation, and a 1 mm. tip separation was used. Electrodes were implanted under visual guidance. The electrode wires were soldered to a miniature connector, which was fastened to the cat's skull with acrylic cement.

Following recovery from surgery, all cats were given avoidance conditioning training in a double-grill box. The double grill box was located in a sound-shielded room.

Throughout a training session, each animal experienced a continuous background of electrical stimulation: .1 msec pulses at a rate of one per second. The current for different animals ranged from 3 to 6 ma. Current was delivered to the inferior colliculus by means of a flexible overhead cable coming from a Grass electronic stimulator (model S8B) and attached to the connector on the cat's head.

The avoidance signal was an increase in the rate of electrical stimulation from 1 pulse per second to 10 pulses per second. The faster train of pulses was presented for 10 seconds or until the cat made the avoidance response of crossing from one compartment to the other of the double-grill box. If at the end of 10 seconds the animal had not made the respone, electrical current was passed through the bars of the box until an escape response occurred. All cats were given ten trials a day, with intertrial intervals ranging from 1 to 3 minutes. Avoidance learning was usually complete in less than 100 trials.

When each cat had reached a criterion of at least 9 avoidance responses out of 10 trials for 3 successive days, a series of trials was presented in which the stimulation current was gradually reduced until a value was found

where the avoidance response was no longer performed. As all failures to avoid were punished with shock, it is assumed that a failure to make an avoidance response denotes a failure to detect the change in rate of electrical stimulation.

At this point, a series of test days was begun where white noise at 70 db SPL was present on half the trials. The white noise trials were haphazardly intermixed with no-noise trials, and an additonal minute was added to the inter-trial intervals to allow any startle effects of the noise onset or offset to habituate. Current values of electrical stimulation in the range of those previously found to be undetectable for each cat were used. For all six cats it was possible to find a current value of electrical stimulation at the inferior colliculus that was highly likely to be detected in the presence of the white noise but that had a low probability of being detected in the absence of the white noise. (Table 1).

Summarizing the data for all six animals, correct responses were made on 90.3% of the trials in the presence of the white noise, while only 10.6% correct responses were observed to the same current values in the absence of the white noise. A t-test for matched groups was performed on the proportion of correct responses for each cat in the presence and absence of white noise. The results indicated that the detection of the electrical stimulation was significantly better under the white noise condition ($p < .001$).

Beginning with the first day of avoidance training, a record of spontaneous responses (crossing from one compartment to the other in the absence of the avoidance signal) was maintained. These responses, when they occurred, were immediately punished with shock. This procedure soon resulted in the elimination of all spontaneous responses. As there was no recurrence of spontaneous responses during the trials accompanied by white noise, it seems reasonable to believe that the relevant variable was still the increase in rate of electrical stimulation and that the animals were not making spontaneous responses that were mistaken for avoidance responses.

The similarity between the present data and those of electrophysiological studies is fairly evident. Facilitated detection of a centrally applied stimulus occurred as a result of the simultaneous presence of a peripheral background stimulus. The facilitation manifested itself in the form of increased number and frequency of unit discharges in the electrophysiological studies, and in a greater probability of making an avoidance response in the present behavioral study.

Table 1. Avoidance responses for each cat made in the presence and absence of white noise.

Cat No.	Current (ma.)	Total Trials (no.)	White Noise Trials Number Correct	White Noise Trials Number Incorrect	No White Noise Trials Number Correct	No White Noise Trials Number Incorrect
97	2.0	6	3	0	0	3
127	1.2	12	5	1	1	5
137	2.1	14	6	1	1	6
145	3.0	22	10	1	0	11
187	1.2	22	9	2	2	9
242	1.9	14	7	0	1	6

Fig. 1

I-Co-97

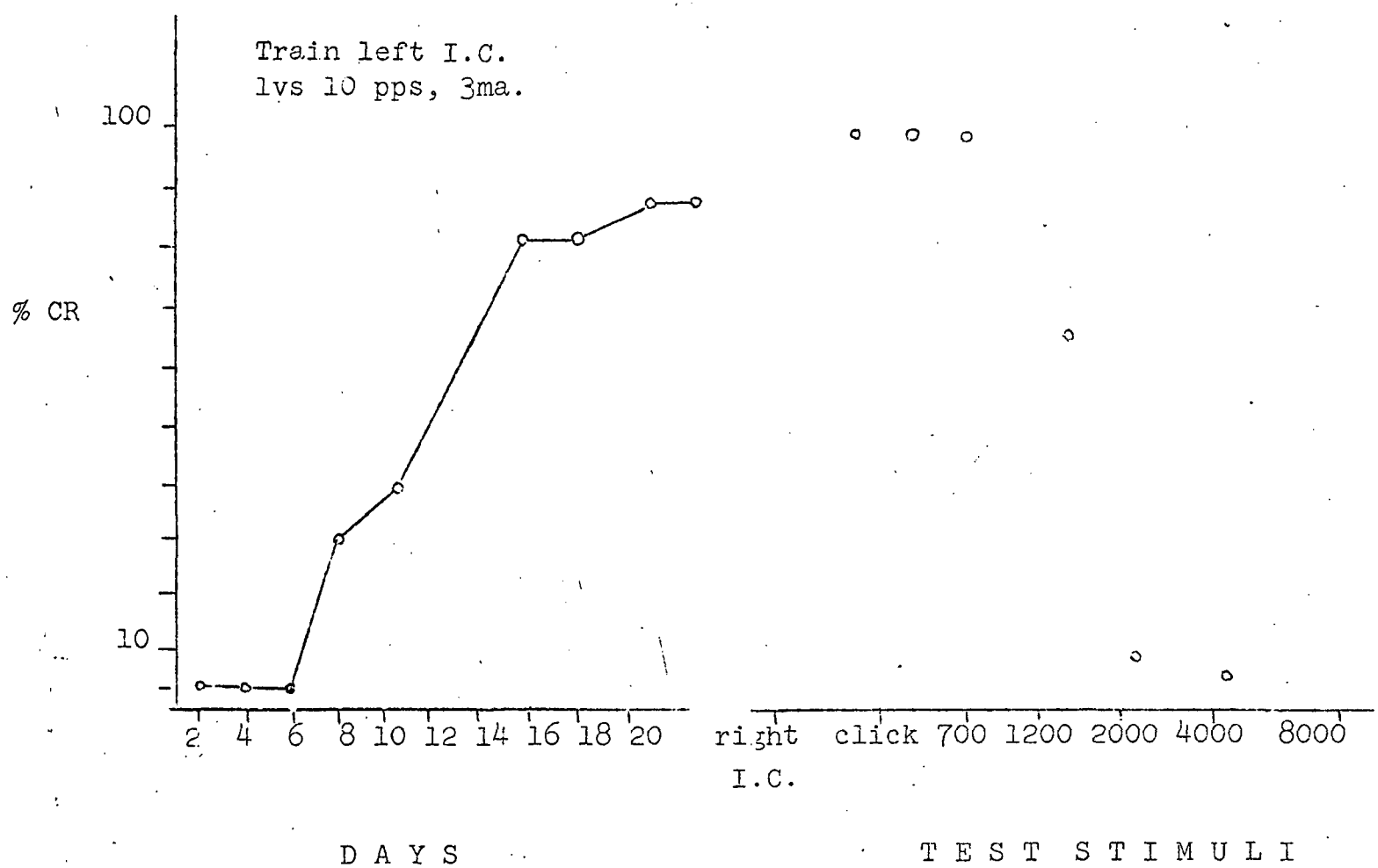

Train left I.C.
1vs 10 pps, 3ma.
100
10
% CR
2 4 6 8 10 12 14 16 18 20
right I.C.
click 700 1200 2000 4000 8000
DAYS
TEST STIMULI

Fig. 2

I-Co-137

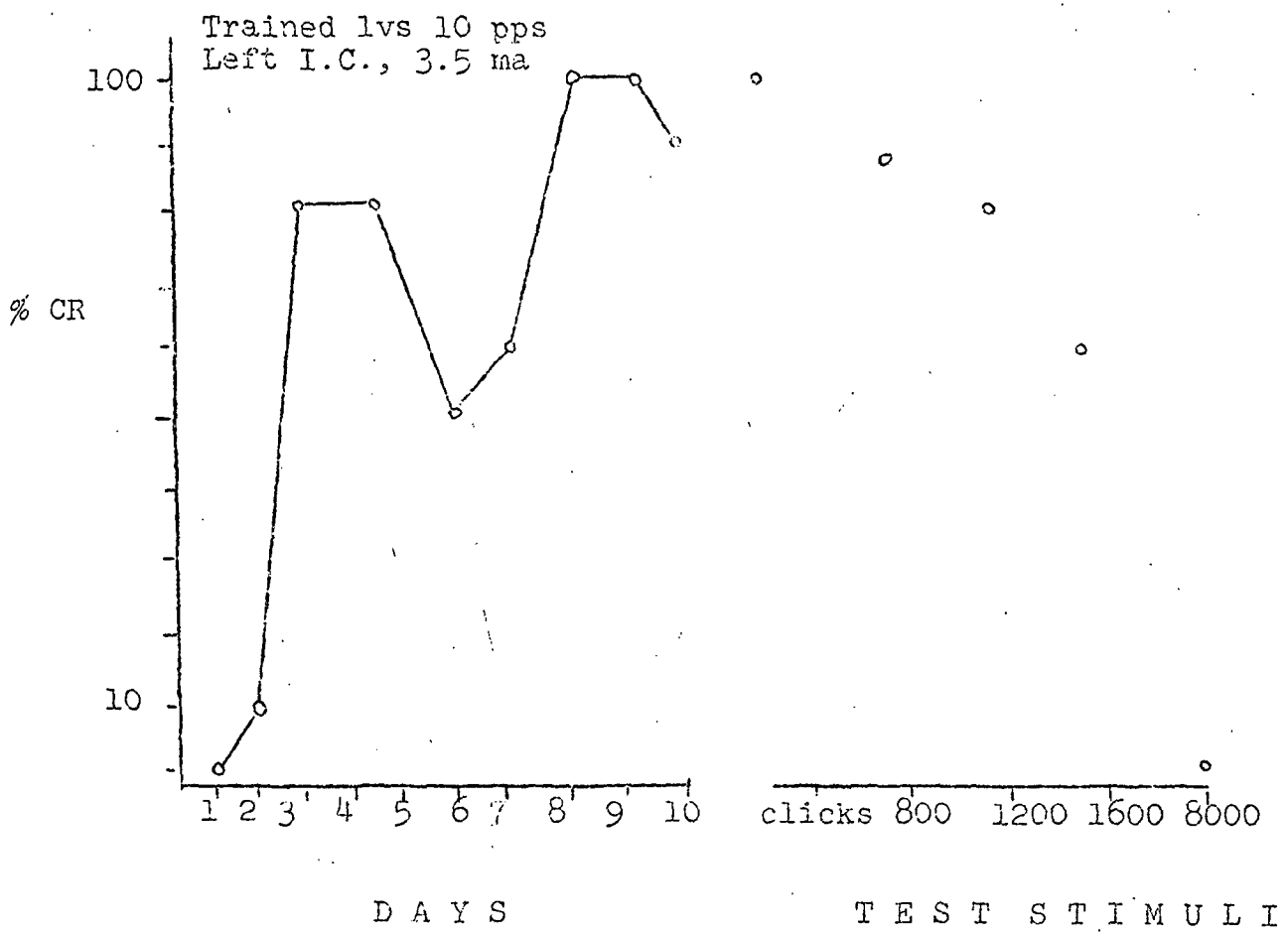

Trained 1vs 10 pps
Left I.C., 3.5 ma
100
% CR
10
1 2 3 4 5 6 7 8 9 10
DAYS
clicks 800 1200 1600 8000
TEST STIMULI

Fig. 3

I-Co-147

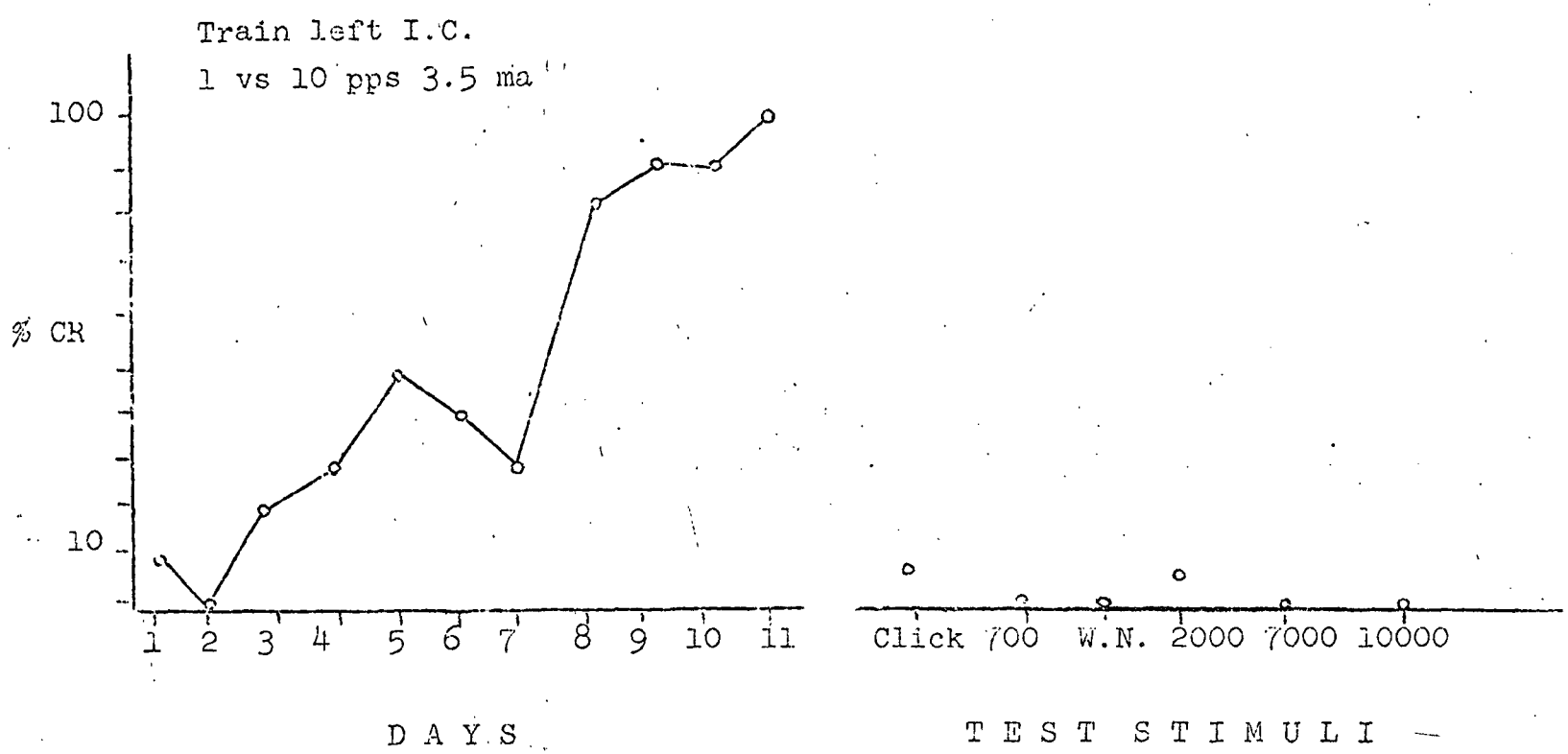

Train left I.C.
1 vs 10 pps 3.5 ma
100
% CR
10
1 2 3 4 5 6 7 8 9 10 11
DAYS
Click 700 W.N. 2000 7000 10000
TEST STIMULI

fig.4

I-Co-208

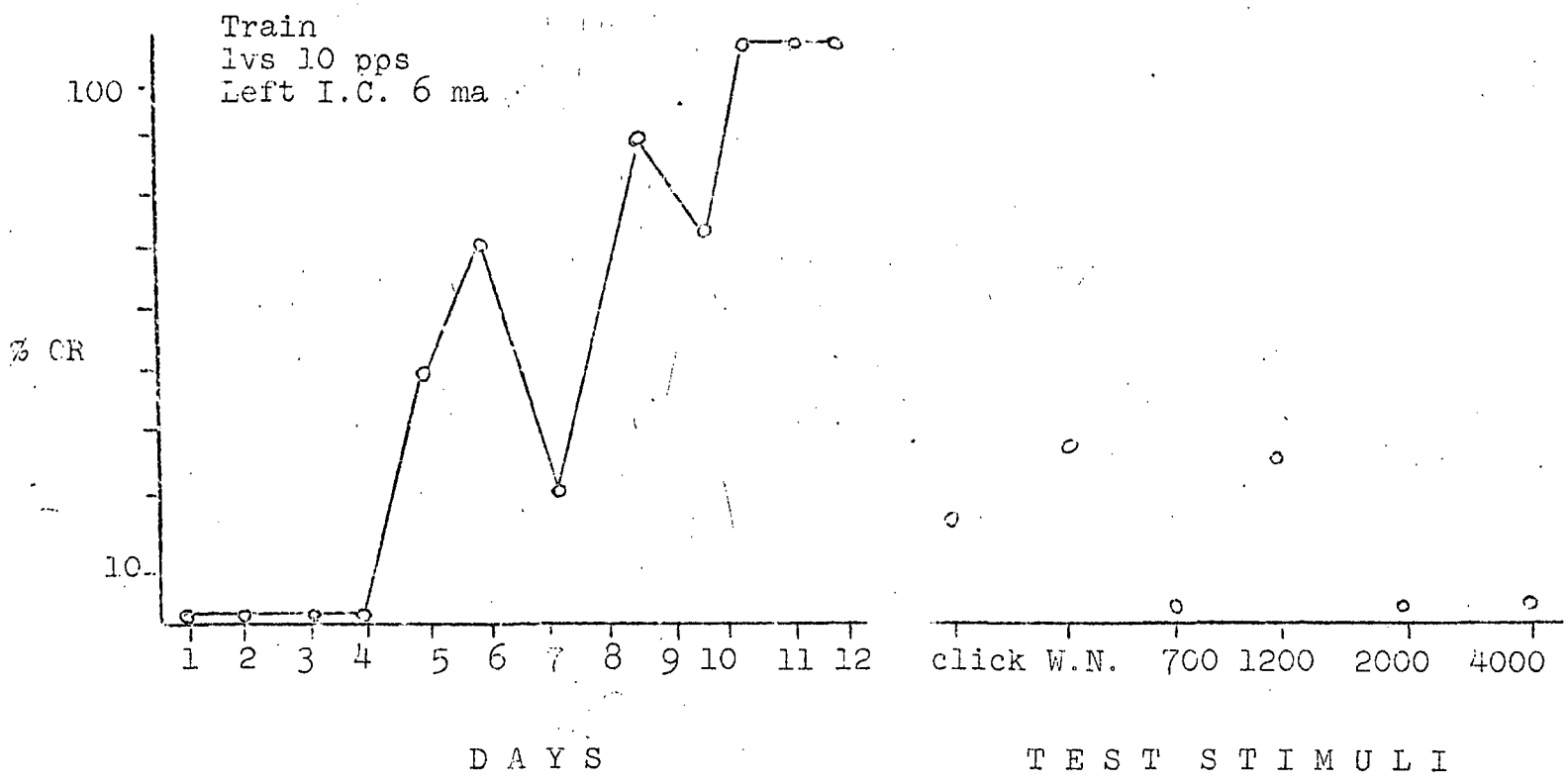

Train
1vs 10 pps
Left I.C. 6 ma
100
10
% CR
1 2 3 4 5 6 7 8 9 10 11 12
DAYS
click W.N. 700 1200 2000 4000
TEST STIMULI

Fig. 5

I-Co-32

Electrode in left I.C.

Train with clicks,
1 vs 10 cps

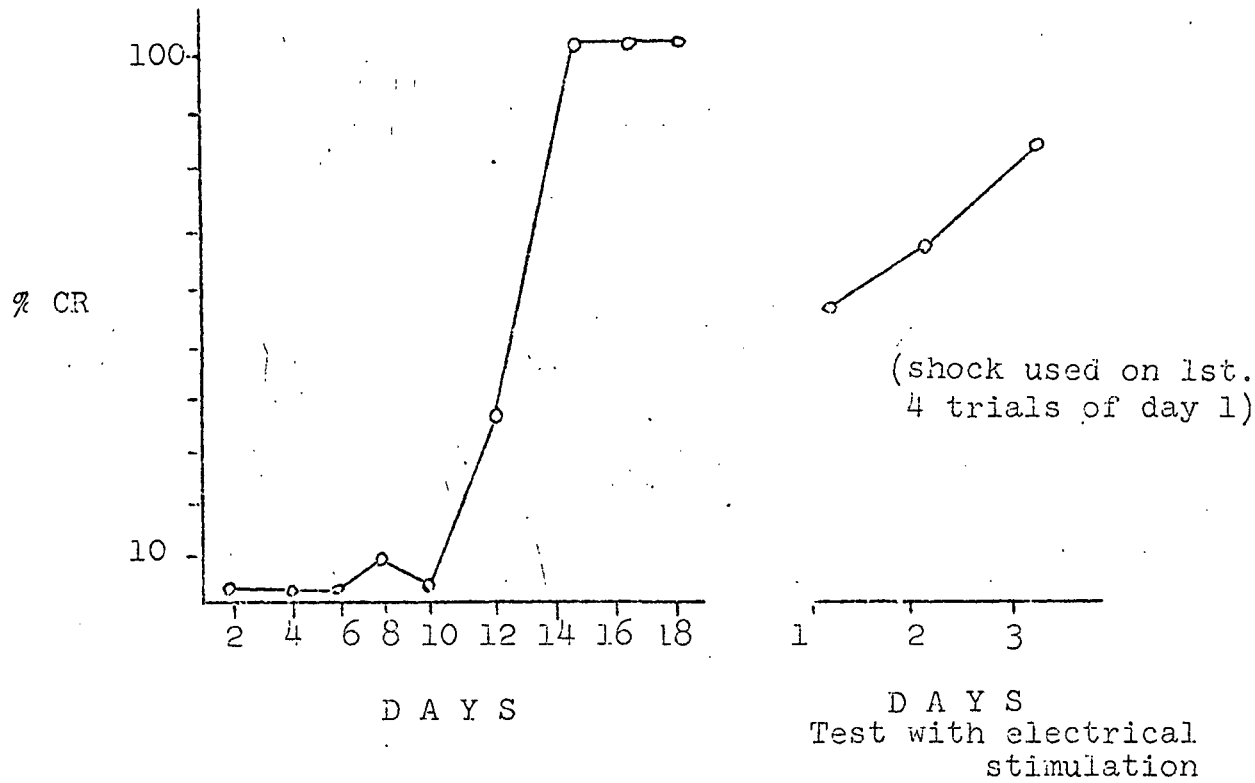


Fig. 6

I-Co-145

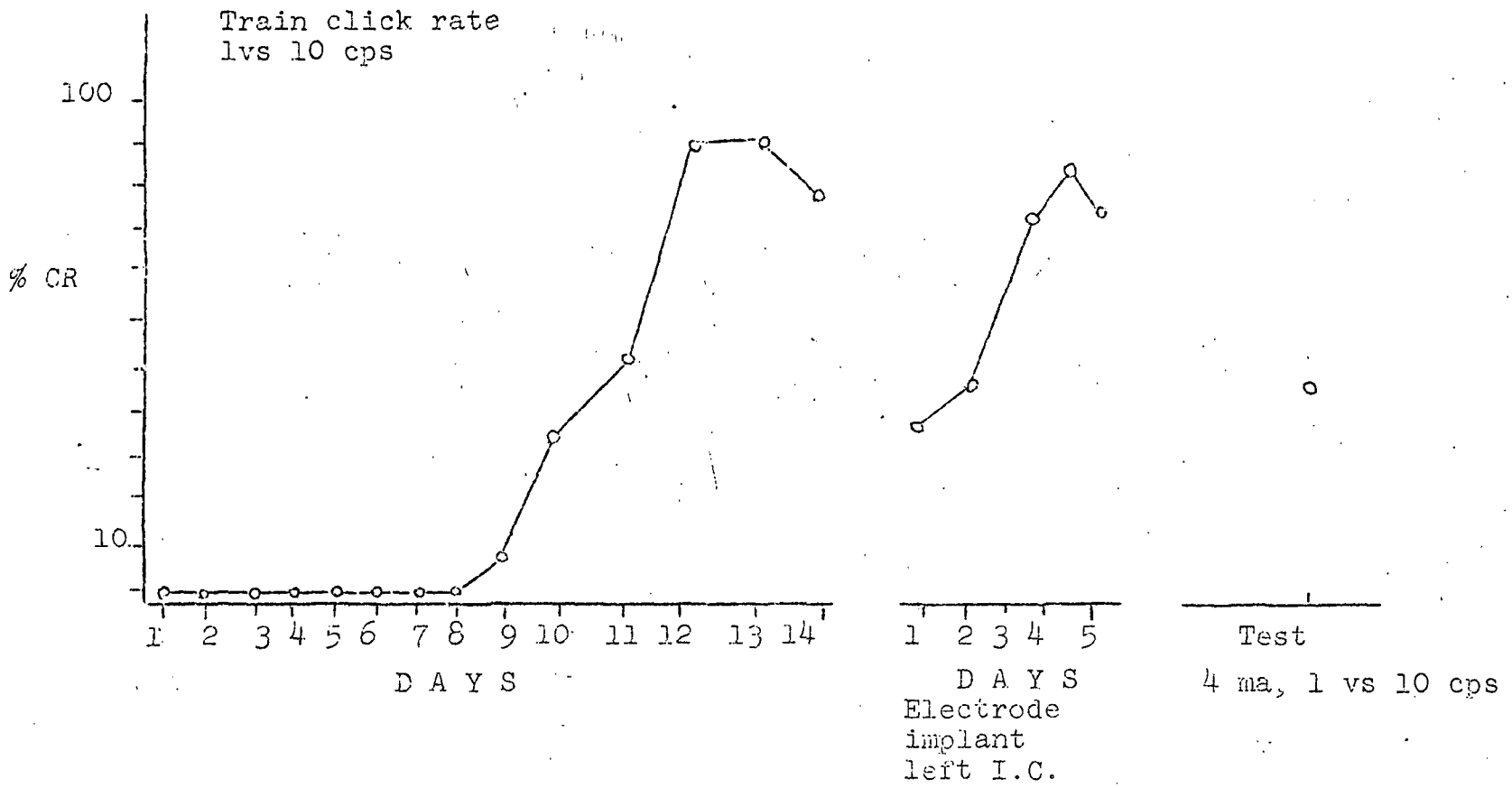

Train click rate
1vs 10 cps
100
% CR
10
1 2 3 4 5 6 7 8 9 10 11 12 13 14
DAYS
1 2 3 4 5
DAYS
Electrode
implant
left I.C.
Test
4 ma, 1 vs 10 cps

Fig. 7

I-Co-187

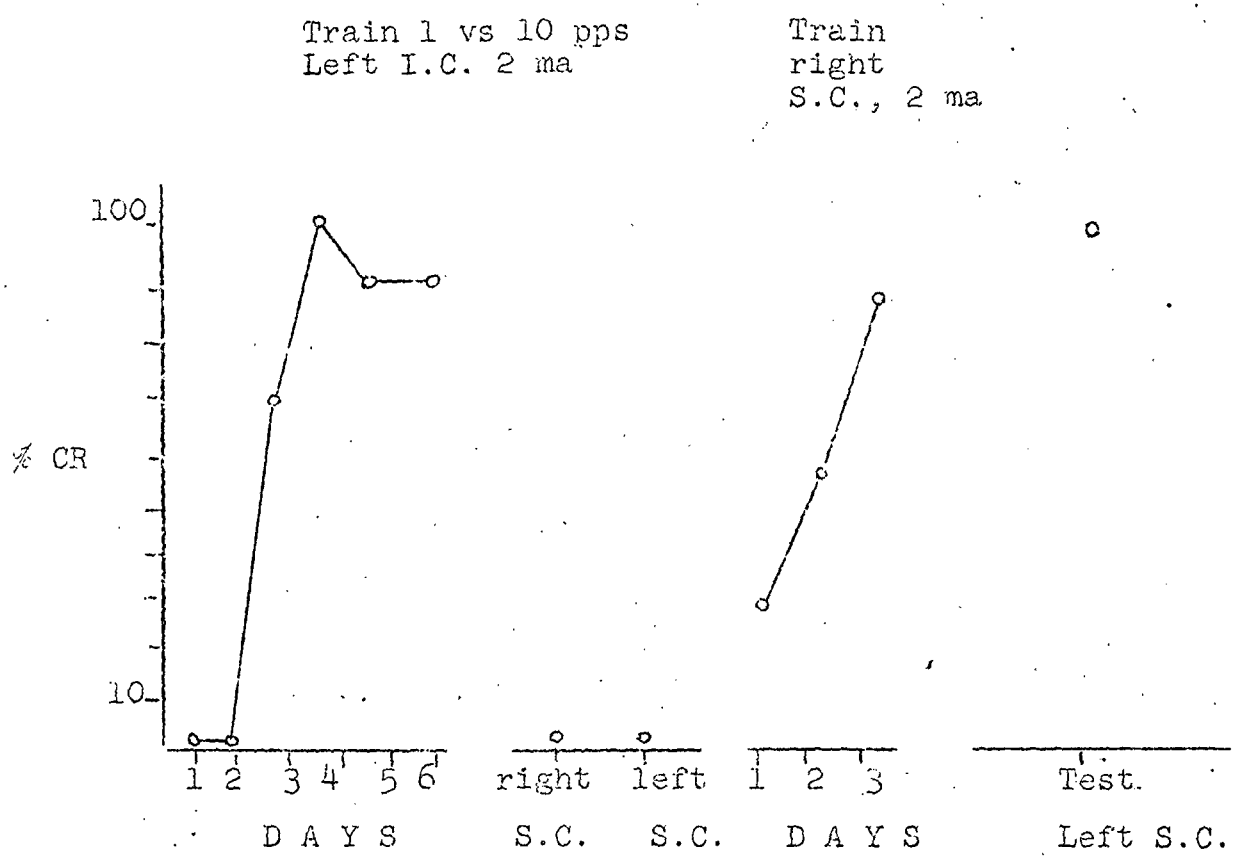
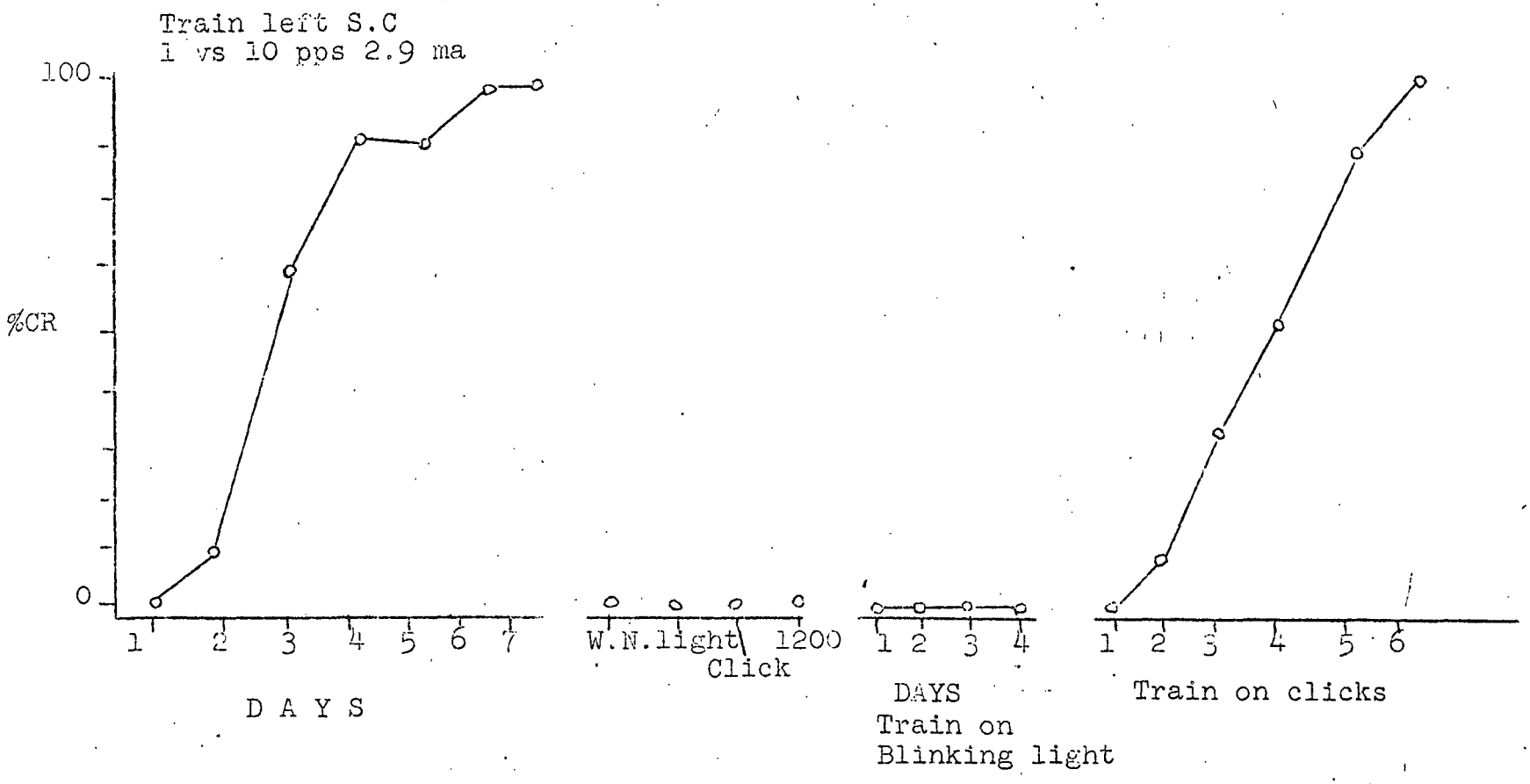

Train 1 vs 10 pps
Left I.C. 2 ma
Train
right
S.C., 2 ma
100
% CR
10
1 2 3 4 5 6
DAYS
right
S.C.
left
S.C.
1 2 3
DAYS
Test.
Left S.C.

Fig. 8

I-Co-192


Train left S.C
1 vs 10 pps 2.9 ma
100
%CR
0
1 2 3 4 5 6 7
DAYS
W.N.light
Click
1200
1 2 3 4
DAYS
Train on
Blinking light
1 2 3 4 5 6
Train on clicks

APPENDIX A

Personnel who participated in the research project:

W.D. Neff, Ph.D.	Research Professor and Director, Center for Neural Sciences
F.B. Colavita, Ph.D.	Postdoctoral Fellow
T.R. Dolan, Ph.D.	Research Associate
T.L. Langford, Ph.D.	Research Associate
J.A. Ramaley, Ph.D.	Research Associate
J.H. Casseday	Research Assistant
R.J. Adair	Laboratory Technician
W.S. Soell	Laboratory Technician
A. Tzankoff	Laboratory Technician
M. Gater	Electronics Technician
C. Hicks	Secretary
M.E. Horin	Secretary
M.R. Chambers	Animal Caretaker
M. Oberholtzer	Animal Caretaker

REFERENCES

1. Loucks, R.B., "A technique for Faradic Stimulation of Tissues Beneath the Integument in the Absence of Conductors Penetrating the Skin", J. Comp. Psychol., 18, 305-313, 1934.

2. Loucks, R.B., "The Experimental Delimitation of Neural Structures Essential for Learning: the Attempts to Condition Striped Muscle Responses with Faradization of the Sigmoid Gyri", J. Psychol., 1, 5-44, 1935.

3. Loucks, R.B., "Studies of Neural Structures Essential for Learning. II. The Conditioning of Salivary and Striped Muscle Responses to Faradization of Cortical Sensory Elements and the Action of Sleep on Such Mechanisms", J. Comp. Psychol., 25, 415-426, 1938.

4. Loucks, R.B., and Gantt, W.H., "The Conditioning of Striped Muscle Responses Based upon Faradic Stimulation of Dorsal Roots and Dorsal Columns of the Spinal Cord", J. Comp. Psychol., 25, 415-426, 1938.

5. Doty, R.W., Rutledge, L.T., and Larsen, R.M., "Conditioned Reflexes Established to Electrical Stimulation of Cat Cerebral Cortex", J. Neurophysiol., 19, 401-415, 1956.

6. Doty, R.W. and Giurgea, C., "Conditioned Reflexes Established by Coupling Visual and Motor Cortex Stimulation", The Physiologist, 1, No. 4, 17, 1958.

7. Doty, R.W., and Rutledge, L.T., "'Generalization' between Cortically and Peripherally Applied Stimuli Eliciting Conditioned Reflexes", J. Neurophysiol., 22, 428-435, 1959.

8. Neff, W.D., Nieder, P.C., and Oesterreich, R.E., "Learned Responses Elicited by Electrical Stimulation of Auditory Pathways", Fed. Proc., 18, 112, 1959.

9. Nieder, P.C., and Neff, W.D., "Auditory Information from Subcortical Electrical Stimulation in Cats", Science, 133, 1010-1011, 1961.

10. Licklider, J.C.R., "Three Auditory Theories", PSYCHOLOGY: A Study of a Science, Koch, S., (ED.) McGraw Hill, New York, 41-144, 1959.

11. Neff, W.D., "Sensory Discrimination", pp. 1447-1470 in: Field, J., Magoun, H.W., and Hall, V.E. (EDS.), Handbook of Physiology: Neurophysiology III. Washington, D.C., American Physiological Society; Baltimore, Williams and Wilkins, 1960.

12. Licklider, J.C.R., "Periodicity Pitch and Related Auditory Process Models", International Auditology, 1, #1, 1-26, 1962.