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Schedules of Reinforcement With Intracranial Simulation

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Abstract

Mixed and multiple aperiodic and ratio schedules of reinforcement were maintained by rats which had stainless steel electrodes surgically implanted in specific areas of their midbrains. The "reinforcing" stimulus used was a 100-cycle, biphasic, square wave of a one-second duration. The voltage ranged from 1.0 to 2.0 volts and the current from .10 to .50 milliamperes.

Four subjects (S's) were used in the study. Three of the S's received electrical brain stimulation (EBS) and the fourth received food pellets as reinforcement. Only the latter "food control" animal was run on a 36-hour food deprivation schedule. All other subjects were not food-deprived.

Aperiodic (variable-interval) schedules of VI= 15 to 60 seconds and ratio (fixed-ratio) schedules of FR= 5 to 20 were maintained consistently for one hour sessions every 24 hours with all four animals.

At the time this paper was written, research was still in progress, therefore, final results were not then obtainable.

Introduction

The ideas of exploring the brain of concious animals with implanted electrodes is not new. In 1895 Golsinger used a single insulated needle with a plaque on the abdomen as the indifferent electrode to produce electrolytic lesions in the interior of the brain. Sellier and Verger, 1898, were apparently the first to make the lesions by bipolar electrolysis by using two needles bound together and insulated to their tips. This method is the one primarily in force at the present time. However, it was Ewald in 1898, who first used the method of electrical stimulation with freely moving animals. Our studies too, are concerned with behavioral correlates, and therefore, are directed toward the active, concious animal.

Ewald screwed an ivory cone to the skull of a dog and on the following day, inserted electrodes through it. A leash to the neck of the animal contained stimulating wires, and the power source, a small dry-cell battery, was carried by the observer. W.R. Hess (1932) did a great deal of work in this area and described his work in detail. He used sutures of the skull as his reference points to screw a metal frame and superstructure to the parietal bone.

A number of other research workers have been interested in exploration of the brain of unanesthetized animals, and different types of experimental procedures have been described in the literature. The implantation of electrodes in human beings and chronic animal preparations in psychological investigations have done much to increase the interest in such methods (Delgado, 1952).

Electrical stimulation of the brain has become an important tool in the study of complex phenomena in the central nervous system. This important tool came to be used in the investigation of complex integrative activity in animals and man; here, newer methods of implantation of electrodes allowed long-term studies to be made. In the fields of neuroanatomy, neurophysiology, psychology, and psychiatry, the technique has been applied to different portions of the brain, but the results that have been reported often appear to be inconsistent and are sometimes controversial.

James Olds (1958) has discovered and analyzed localized systems in regions of the brain where a primary reward effect is produced by electrical "self-stimulation". Here, the subject was able to press a bar to stimulate itself.

In terms of behavior, these experiments help to clarify the basic notions of reward and punishment which make up-to-the-present investigations of the "pain and pain-reduction theory" and the "drive reduction theory" more clear

themselves. The former theory holds that any increase in drive is essentially an increase in pain, and that reward is the decreasing of this "pain". The latter theory holds that the withdrawal of a strong stimulus to the brain might be rewarding, but the onset of a strong stimulus could only produce negative reinforcement. Subcortical structures in which electrical stimulation has a negatively reinforcing effect have been reported by Miller and his associates at Yale (1958). The work reported by Olds, however, indicated that there were large regions of the brain where electrical stimulation had the effect of a primary reward.

Olds' method of self-stimulation allowed animals to deliver shocks to specific points in their brains through chronically-implanted electrodes. A circuit was arranged whereby the animal (in this case a rat) could turn on the stimulus by depressing a lever. Under these new conditions, each lever-pressing response produced an electrical stimulation. At the point where the electrode tip resided in the brain, an electrical impulse was then delivered on a specified schedule. Olds used a 60-cycle sine wave, one volt r.m.s. through a total resistance of about 12,000 ohms. The current ranged from five to 150 microamperes. It was found that such an alternating current did not produce appreciable damage to the tissue as measured by the self-stimulation rates. In experiments with more than 200 electrodes implanted in different parts of the brain, thirty-five per cent of all electrodes placed were positively rewarding. Only five per cent were found to be negatively reinforcing and sixty per cent motivationally neutral.

Olds found the rewarding effect from a broad system of structures centered in the hypothalamus, rhinencephalon, thalamus, and parts of tegmentum. Self-stimulation rates were 5,000 per hour in the posterior hypothalamus, whereas rates in the anterior hypothalamus were slower, ranging from 400 to

1000 per hour. With electrodes in the preoptic, septal, and telencephalic areas, response rates ranged from 3,000 per hour in the preoptic area and posterior forebrain to about 200 per hour in the anterior forebrain. Satiation effects seemed to occur more rapidly in the forebrain areas than in the hypothalamic areas.

Hess discovered that stimulation in the hypothalamus produced a variety of apparently motivational effects such as rage, flight, and eating. He found that hypothalamic-stimulated rats gnawed at inedible objects upon electrical stimulation.

Neal Miller of Yale University trained rats, when hungry, to secure food by pressing a bar which delivered small pellets of food on a variable-interval (VI) schedule. He found that a food-satiated rat did relatively little work at the bar during the two-minute periods of non stimulation. During the two-minute periods when the stimulation was on, the rat worked at the bar which occasionally delivered food. Thus, we have further evidence that electrical stimulation in the areas that induce eating will also motivate the performance of learned instrumental responses that have been reinforced by food.

Miller also found that EBS can be used to (A) reinforce trial and error learning, (B) to establish a conditioned response, and (C) to serve as a punishment to make a hungry animal avoid food.

Brady (1955) has been exploring the relationship between the anatomical and functional correlation of the limbic system in experimental animals. This system includes the allocortical area which are surface structures (cortex) consisting of at least three layers, the juxta-allocortical portions which include cortical areas between the phylogenetically old allocortex and the new neocortex, and subcortical portions.

Brady found that lesion techniques were successful in exploring the limbic system, especially in the area of emotional correlates of behavior. The behavioral correlates of direct electrical stimulation of these limbic system areas has provided a new approach to experimental analysis of brain behavior in this area.

With an electrical stimulus generator to provide an electric stimulation "reward", stable "bar-pressing" rates have been sustained on both aperiodic and ratio reinforcement schedules. With permanent electrodes in the septal region of the rat, a bar-pressing response which is reinforced by electrical brain stimulation, only at irregular intervals (variable-interval schedule) or only after a fixed number of responses (fixed-ratio schedule) develops stable and durable properties similar to bar-pressing rates generated by the use of food or water reinforcement. This EBS behavior can be studied over a period of several months or more. In conjunction with Brady's work, it was found that as the average duration of the interval between electrical stimulation increased, the rate of bar-pressing decreased. Also on a fixed-ratio schedule (1:10), the rate of responding is very sensitive to EBS stimulus intensity.

It has also been found that higher rates of bar pressing to EBS stimulation are found with food and water deprived rats than with satiated animals.

A set of specifications for an ideal chronic-implanted electrode is not easy to devise. It involves consideration of (1) the properties of the embedded electrode itself, (2) the method of holding the electrodes so that they do not move, and (3) the way in which the free end of the electrode is connected to the stimulator and/or recorder.

The implanted electrode should produce no mechanical or chemical damage.

The electrodes must, of course, be mechanically fixed (to the skull) in a rigid permanent manner not likely to be disturbed or moved by the activity of the animal. All of this must be accomplished in as small a space as possible to prevent infection and tissue damage. There is also a requirement for small size and compactness of the electrode and itsholder unit, especially in work with small animals such as rats and guinea pigs. The system employed must be adaptable to the heads of various animals and must not impede the use of a stereotaxic instrument. Finally, the free ends of the electrode must be easily accessible to the stimulator and recorder.

As it stands at the present time, there exists a large variety of solutions to the many problems posed in maintaining functioning electrode contacts with the brain of an experimental animal (Sheatz, Vernier, and Galambos, 1955).

The present investigation studies and replicates some of the work previously done with EBS responding on single aperiodic and ratio reinforcement schedules. The study also investigates mixed and multiple variable-interval and fixed-ratio schedules. Techniques of chronic electrode implanting, electrical brain stimulation and food reinforcement correlations also are discussed in the present research.

Method

Subjects

The experiments were conducted with both Holtzman Sprague-Dawley and Long-Evans Hooded strains of rats. Both male and female subjects were used throughout the present research. Female Long-Evens Hooded rats were found to survive the electrode implant surgery very well and also were found to manifest high activity in the operant self-stimulation tasks. At the beginning of implant surgery, the subjects were approximately 90 days old and

weighed between 260 - 350 grams. None of the rats had prior experience with the apparatus.

Electrode-Implant Apparatus

The stereotaxic instrument used was a David Kopf instrument in which small animals such as the rat can be easily held. This instrument is shown in Fig. 1.

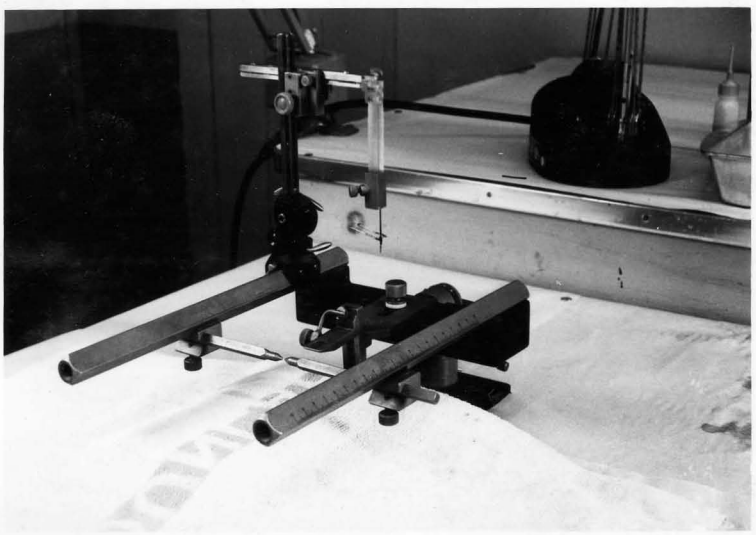

Fig. 1, David Kopf stereotaxic instrument

This model, which was very adaptable to use with rats, consisted of permanently-fixed anterior-posterior slide bars, mobile three-dimensional electrode carriage, external auditory meatus plugs, and a twin-adjustment incisor-nose holder. Both the L. Massopust and the J. de Groot atlases were used with this instrument. All animals used in the present study were implanted with the de Groot coordinate atlas. The use of this atlas enabled the experimenter to coordinate the stereotaxic instrument without having the animal fixed in the machine. This, however, was not possible with the Massopust atlas.

Within the electrode implant operation, the surgical instruments used were 1) an Emesco model #102, 12,000rpm dental drill unit, 2) a Bard-Parker #4 scalpel, 3) a Panaplastic grated tissue scraper, 4) an Aloe retractable separater, 5) Aloe skin suture tweezers, 6) an Adams wound-clamp clip tool, 7) an Ideal 2 c.c. glass-tip syringe, 8) Luer 25 gauge - 1/4" hypodermic needles, 9) Clay-Adams wound clips, 10) 3/16" stainless-steel skull screws, 11) Nu Weld prosthetic caulk liquid, 12) Caulk Cavity primer, 13) diluted Zephirian Chloride germicide, 14) Nembutal (pentobarbital sodium) and Chloral Hydrate anesthetics, 15) Ohaus 1000-gram balance, 16) Red Cross sterile swabs and pads, 17) an Burpee autoclave, and 18) other necessary equipment.

The implanted electrode used is shown in Fig. 2. It consisted of two

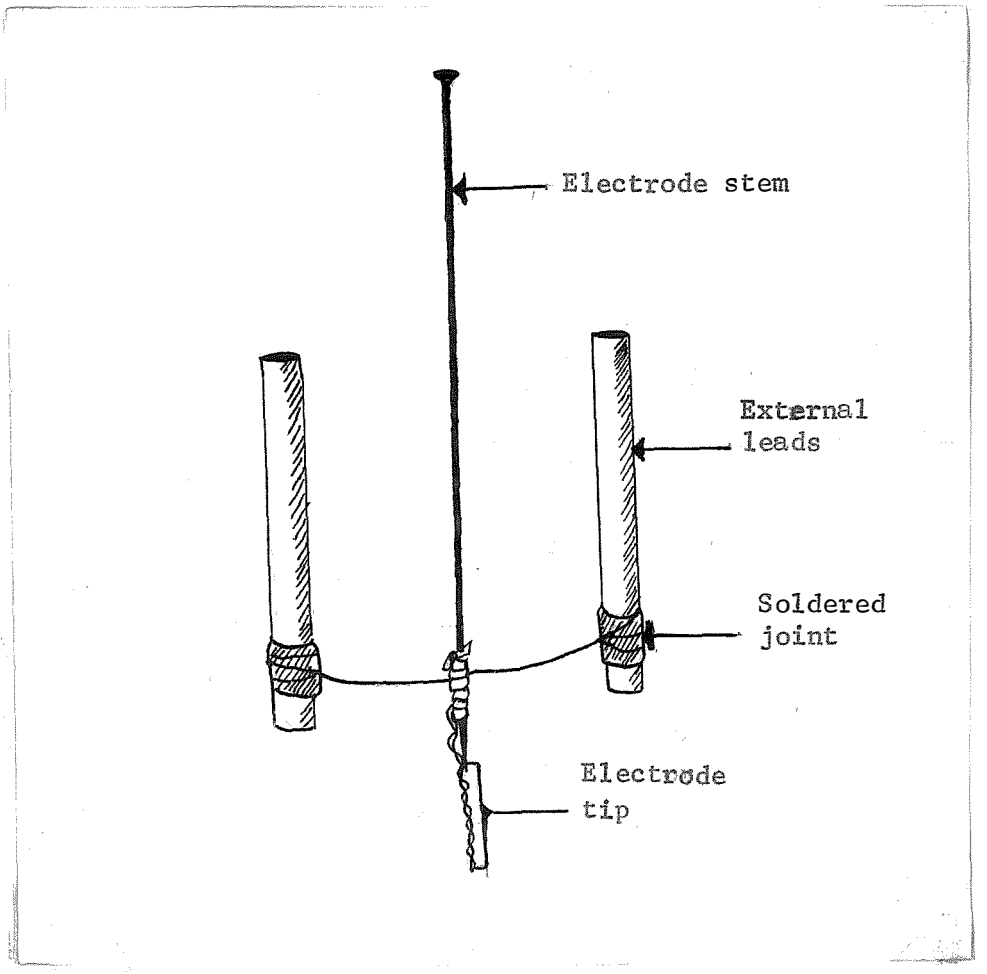

Fig. 2, Schematic of electrode assembly

twisted stainless-steel wires which were insulated except at their tip. Tiny leads from each of the two wires were soldered to larger copper leads which protruded from the top of the subject's head.

Behavioral Apparatus

The experimental chamber, in which the bar-pressing behavior took place, was a compartment measuring 11 1/2" X 12" X 17", three sides of which were constructed of clear plastic and the back side of sheet aluminum. The floor consisted of steel rods, 3/32" in diameter and .5" apart. The experimental chamber was located within a sound-proofed chest, the door of which had a one-way viewing window, thereby permitting a clear view of the animals. The inside of the outer chest was completely covered with grounded copper screen in order to decrease extraneous electrical influences.

A 60-watt bulb in the roof of the shielded chest provided illumination for the duration of the experimental session. An exhaust fan provided ventilation. The various aperiodic and ratio reinforcement schedules used in the experiment were programmed by electrical apparatus located in a room separate from that which contained the experimental chamber. A cumulative recorder, counters, and timers provided a record of the responses. Electrical impulses were delivered to the animal by a multiple stimulus generator. A swivel in the top of the experimental chamber allowed free movement of the animal without entanglement of the input wires to the implanted-electrode leads.

A rotary food dispenser delivered uniform size pellets to the "food control" animals according to the appropriate fixed-ratio or variable-interval sessions.

Definition of the Shock Stimulus

The stimulus was a 100-cycle, biphasic, square wave. In general, for

the series of experiments, the current ranged from .10 to .50 milliamperes, and the voltage ranged from 1.0 to 12.0 volts. Everything except voltage (and of course amperage) was kept constant throughout the study. Resistance qualities of the electrode were tested immediately after implantation. This variation in threshold intensity was mainly due to fluctuation in body resistances of each rat. The "train" duration of the one millisecond impulses was one second.

Procedure

Electrode-Implant Technique

The animal was weighed in order to determine the proper quantity of Nembutal (pentobarbital sodium) and Chloral Hydrate, which were used together as anesthetics. Injection of Nembutal preceded that of Chloral Hyrate by approximately 15 minutes. After the head of the rat was shaven, the rat was "zeroed" in the ear bars and bite plate, which was previously adjusted to five millimeters above the interaural zero line according to the J. de Groot stereotaxic atlas (1952). A 2-4 cm. longitudinal incision was made and was widened by means of screw and spring-type retractors. The skull was then scraped in order to remove overlying muscle and tissue. Next, the electrode placement was determined and an entry hole was drilled in the skull with a dental burr unit. Three smaller holes were drilled lateral to the entry hole. Very small stainless-steel screws were set in these holes to serve as foundations for the acrylic cement which held the electrode in place (shown in Fig. 3). After the electrode had been lowered into place (shown in Fig. 4), an adhesive acrylic cement was built up around the screws and the electrode stem. A sealer-primer served to prepare the skull so that the acrylic would tightly adher to it. After the "building up" process had been completed, the electrode stem was snipped off as is

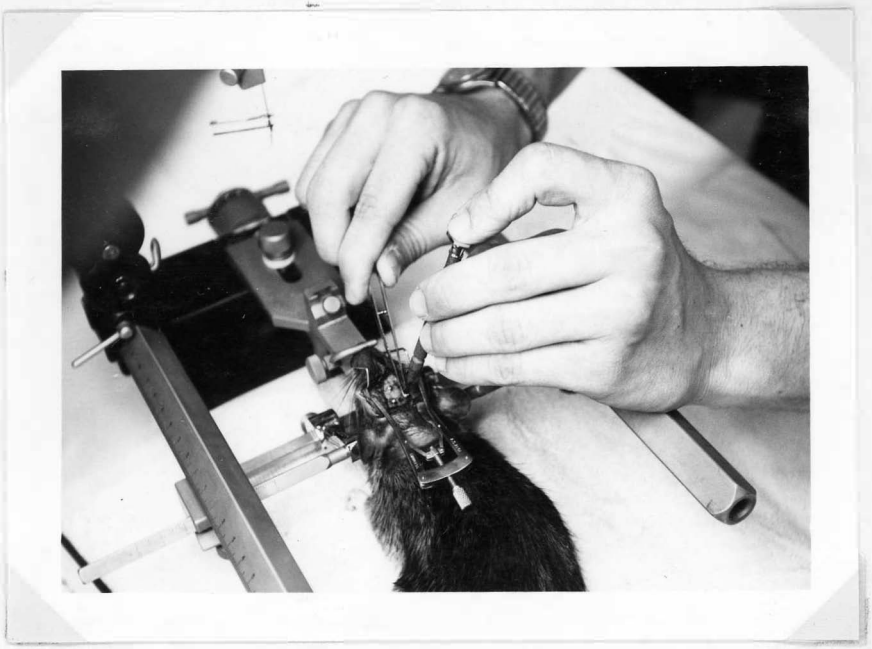

Fig. 3, Insertion of stainless steel screws

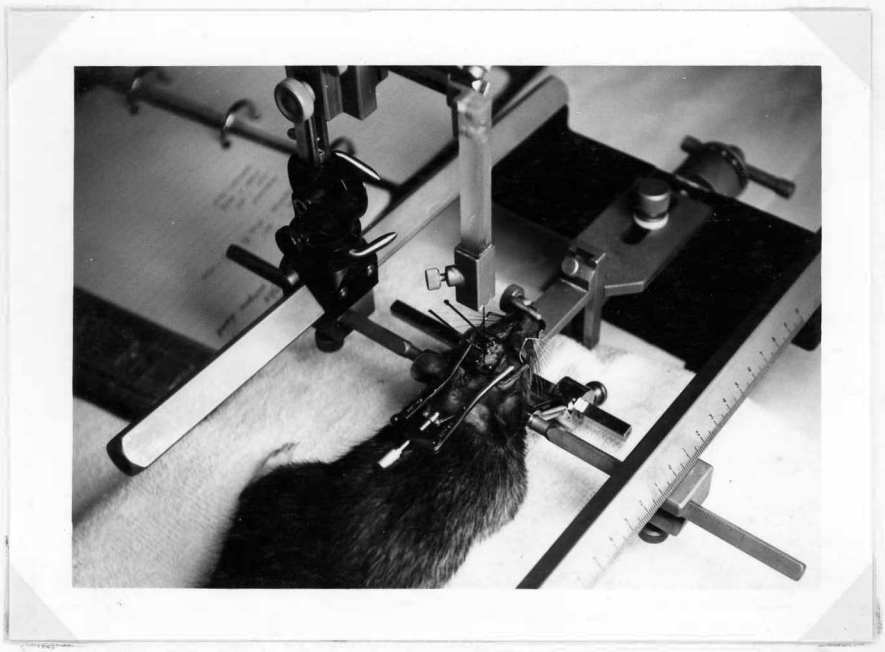

Fig. 4, Electrode lowered into place

shown in Fig. 5 flush with the top of the acrylic. The incision was closed by means of stainless-steel wound clips applied at close intervals (shown in Fig. 6). Finally, the resistance of the implanted electrode was tested by means of a multi-meter.

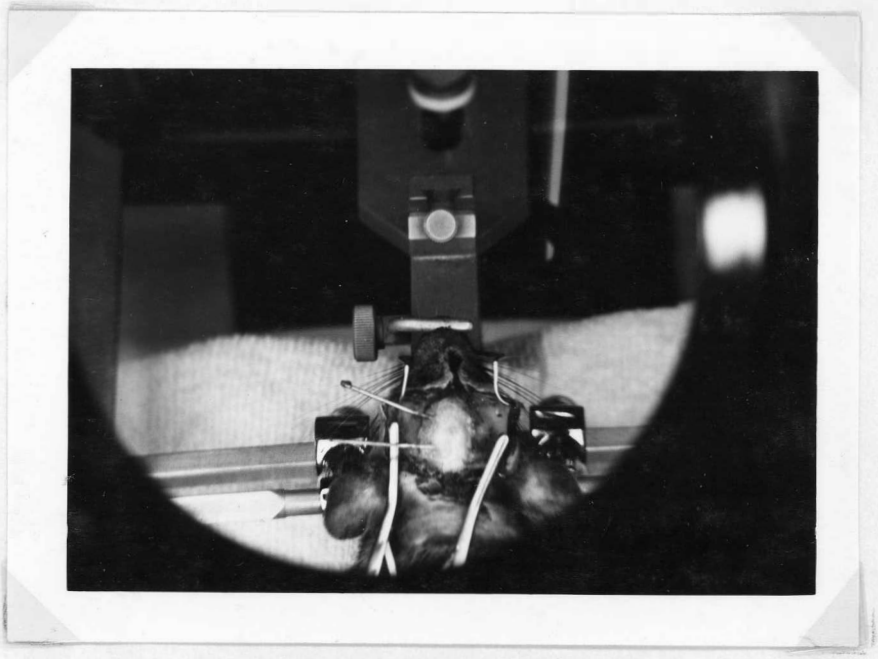

Fig. 5, Completed electrode implant

Fig. 6, Closing of incision with wound clips

Behavioral Techniques

Initially the implanted rats were placed in the EBS chamber and were stimulated at random by the experimenter to determine their behavioral reactions. The current and voltage thresholds were also noted at this time. Those animals which displayed at least faint bar-pressing activity to the electric stimulation were then shaped to press the bar in order to receive an electrical impulse stimulus. Two EBS animals (#54 and #55) and one food control animal (#35) were initially shaped by successive approximation to respond on aperiodic VI schedules ranging from 5 to 60 seconds. An additional EBS (#67) was initially shaped on an FR schedule of reinforcement. This animal was successively shaped from FR = 2 up to FR = 15.

Next, a mixed variable-interval and fixed-ratio schedule of reinforcement was used with animals #54, #55, #67 (EBS reinforcement) and #35 (food reinforcement). With such a mixed schedule, no discriminative stimulus (S^d) of any kind was given with either of the two successive schedules. Thus the animal had no external sensory cues telling him that he had been switched from the aperiodic to the ratio schedule of reinforcement or vice versa. On day #1, the fixed-ratio session preceded the variable-interval session. On day #2, the variable-interval session preceded the fixed-ratio session. This alternation was continued throughout the experiment.

Finally, #54, #55, and #67 were run on a multiple schedule whereby the fixed-ratio schedule segment of the session was accompanied by a red feedback light (S^d), and the variable-interval segment was not accompanied by a red feedback light. As in the mixed schedule, all animals were run for one hour on FR and one hour on VI in alternate succession for two-hour sessions.

All EBS animals were fed on an ad. lib. basis and were watered regularly. The food control animal was run on a 36-hour deprivation schedule.

Results

The final results of this research were incomplete at the time this report was written. A number of facts, however, have been gathered concerning work done to date.

Mixed Schedule

Animal #54 was built up to a mixed schedule of FR = 10, VI = 30 seconds; animal #55 to an FR = 15, VI = 60 seconds; animal #35 (food control) to an FR = 10, VI = 60 seconds, and animal #67 to an FR = 5, VI = 15 seconds.

Table I summarizes the rate of response obtained with the mixed schedules; in all cases, the average rate of responses was used for the FR-VI data:

Table I

Animal's Number	Number of Sessions	Average FR Rate	Average # of Reinforcements	Average VI Rate	Average # of Reinforcements
#54	(FR = 10 4(VI = 30"	837	84	984	111
#55	(FR = 10 5(VI = 60"	504	53	608	51
	(FR = 15 4(VI = 60"	276	18	448	51
#35	(FR = 10 1(VI = 60"	1989	199	1081	55
#67	(FR = 5 1(VI = 15"	121	71	497	96

Long delays of responding toward the end of the session provided strong evidence for satiation effects with the food control animal. From the food control data obtained, rates for EBS and food reinforcement were nearly identical for comparable schedules. Thus, the satiated EBS animals responded as much for brain stimulation as the 36-hour deprived food control animal did for food on an identical schedule.

Multiple Schedules

Animal #54 was built up to a multiple schedule of FR = 15, VI = 30 seconds; animal #55 to an FR = 15, VI = 60 seconds and animal #67 to an FR = 15, VI = 15 seconds. Animal #35 had not yet been programmed on a multiple schedule.

Table II presents the average rate of response during the multiple FR-VI schedules:

Table II

Animal's Number	Number of Sessions	Average FR Rate	Average # of Reinforcements	Average VI Rate	Average # of Reinforcements.
#54	4(FR-10 (VI-30"	691	69	925	107
	6(FR-5 (VI-30"	732	49	1099	108
#55	4(FR-10 (VI-60"	589	58	524	46
	7(FR-15 (VI-60"	623	41	739	55
#67	1(FR-10 (VI-15"	1371	136	1702	210
	3(FR-15 (VI-15"	1218	81	1589	208

Apparatus Results

The implanted electrodes and acrylic plugs remained permanently secured throughout the entire study. In initial attempts, two of the animals lost their electrode plugs, the reason for which was probably an inadequate bond between plug and skull.

The fastener clips used to connect the input leads to the electrode prongs held securely for most of the sessions. In some instances, either the snap leads slipped off the electrode prongs or the snap leads broke off at their soldered connection to the input wires. Apparatus failures were

not included in the results.

Cumulative Records

Fig. 7 illustrates characteristic response patterns of the cumulative records for EBS #55 and EBS #67 on multiple schedules. All of the EBS animals demonstrated typical rates of response of VI schedules in which the animals respond at a steady rate dependent upon the number of reinforcements given over a period of time. The animals also demonstrated typical FR segments in which they showed a pause after the reinforcement followed by a very high rate of response. These results are simular to those demonstrated by other investigators using food and water reinforcement in subjects such as pigeons, rats, cats, monkeys, and man.

Although under a similar mixed schedule, EBS #55 responded slower than #35 (food control), the characteristic steady response rate under VI and the characteristic pause under FR was obtained in both animals. EBS #67 on a multiple schedule of FR-VI demonstrated a high rate of response similar to the food control animal.

Under the higher FR schedules, all of the EBS animals demonstrated longer pauses after the obtainment of reinforcement. This results compare to similar findings with food and water reinforcement on FR schedules.

There was an interaction between the VI and the FR rates of responses. For example, the animals run under a low VI (VI = 15") demonstrated a high rate of response during both the VI and the FR segments, while the animal run under VI = 60" demonstrated a low rate of response on both the VI segment and FR segment. (See Fig. 7).

Discussion

Brady (1955) obtained simple FR and simple VI schedules using EBS. In the present study, as Fig. 7 demonstrates, multiple and mixed FR and VI schedules within the same sessions were obtained through the use of intra-

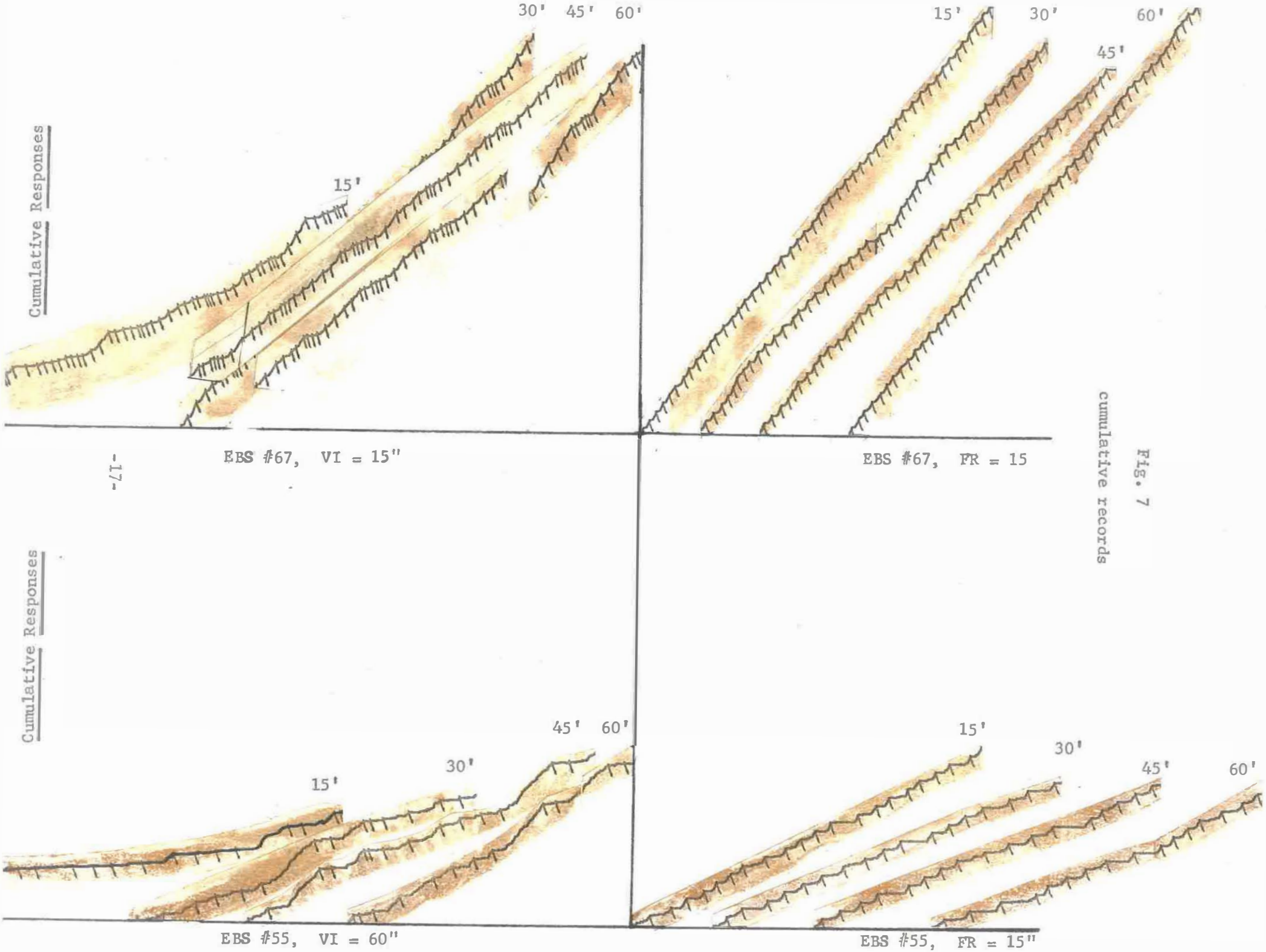

Fig. 7 cumulative records

cranial self stimulation. Theis indicates that EBS might be a more efficient reinforcement technique than previously reported.

In many cases, the EBS animals would run from the bar and manifest a type of chewing movement and hovering behavior which was more typical for FR than for VI schedules of EBS.

The interaction between the two schedules for multiple sessions are typical during the early development of such early schedules.

The fact that VI affects FR is not atypical for multiple schedules of this type during the early stages of development. Later on, in multiple schedules, there is less effect of one segment on the other. With continued data, we would expect the VI segment to have less effect upon the FR schedules.

The following conclusions were reached:

We have generated more complex behavior than previously demonstrated as manifested by multiple schedules.

During the FR segments, the animal demonstrated more pausing than with conventional reinforcement.

There were some interactions between the length of the VI schedule and the rates of response manifested during the FR segment. This interaction might drop out if the S's were run over a long period of time on this type of multiple schedule.

Such conclusions were based upon the data recorded. Although the animals manifested more differentiated behavior on the multiple schedules than on the mixed schedules, such an effect may have been due to the fact that the mixed schedule preceded the multiple schedule. Because of this sequential effect, the mixed and multiple schedules were not compared.

To simply assume that the electrode is residing exactly at the place dictated by the atlas coordinates is not experimentally valid. The experimenter may have made an error in his coordinate measurements , the electrode

may have deflected from its course due to some obstruction in its path, or the brain of the subject concerned may have differed anatomically from the atlas used. Therefore, histological verification is a neccessity in order to validate the exact position of the implanted electrode. Such a verification was impossible at the time this paper was written since the research animals were still being run.

Due to the fact that the study was one of successively increasing the aperiodic and ratio schedules of reinforcement, the number of sessions needed for an animal to manifest stable bar-pressing behavioral depended upon that particular animal as well as his schedule. Thus, one animal might produce consistent operant behavior on the first session whereas other animals might need as many as fifteen sessions to reach the same level of performenace. This might be due to the area of the brain stimulated.

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