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July 20, 2020

Mr. John Greenewald
27305 W Live Oak Rd
Suite 1203
Castaic, CA 91384

Dear Mr. Greenewald:

This is in response to your email dated July 7, 2020, requesting information under the Freedom of Information Act (FOIA) (enclosure 1). Under Department of Defense rules implementing the FOIA, published at 32 CFR 286, your request was categorized as "other".

The document that you have requested, AD0436460, entitled "Some Behavioral Correlates of Brain-Stimulation Reward: Part B", is approved for public release. It is enclosed.

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Sincerely,

Michael Hamilton

Michael Hamilton
FOIA Program Manager

2 Enclosures

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ANNUAL REPORT

1 January 1963 - 1 January 1964

Stanley S. Pliskoff and Roger W. McIntire
University of Maryland

Some Behavioral Correlates of
Brain-Stimulation Reward: Part B

Contract #DA-49-193-MD-2288

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ABSTRACT

1. Preparing institution: University of Maryland

2. Title of report: Some Behavioral Correlates of Brain-Stimulation Reward: Part B

3. Principal investigator: Stanley S. Pliskoff, Ph.D.

4. 23 pages, 5 figures, 1 January 1964

5. Contract number: DA-49-193-MD-2288

6. Supported by: U. S. Army Medical Research and Development Command, Department of the Army, Washington 25, D. C.

Part A of the present report was concerned with a detailed description of our brain-stimulation research with rats. Part B is concerned with our dog work, and the report discusses in detail several problems in generalizing our technology from rats to dogs. Solutions to those problems are discussed. Briefly, the report deals with:

1. The maintenance of behavior through brain-stimulation reward in the dog.
2. The design and construction of experimental equipment and electrode protective devices.
3. The search for a positively rewarding area in the dog's brain.
4. The future course of our research.

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ANNUAL REPORT

Part B

I. Aims

The research described in Part A of this report was supportive with respect to the accomplishment of our aims in Part B. We are concerned here with the extension of our findings to the distance control of dog behavior. More generally, we are concerned with the examination of the limitations and practicality of such behavioral control.

II. Some Problems

A. Perhaps the most significant problem was related to the practical question of whether or not substantial behavioral output could be maintained through the use of brain stimulation as a behavioral reward. Our work with rats indicated that it is theoretically possible. Whether or not procedures developed with rats can be applied successfully with dogs is another question; our guess is that there should be no problem in that respect. We are now in the process of evaluating the generality of our rat-developed techniques.

B. Problems arose regarding the anchoring of electrodes on the dog's skull. Our initial implants were quite unsuccessful in that respect, and we experienced two failures to maintain the electrode on the skull for more than several days. The "beating" which the electrodes take in the dogs' living quarters, coupled with the unavoidable difficulties of

B. (cont'd)

handling the dogs going into and out of the experimental situation, served to work the electrodes loose. Our anchoring procedure was identical in every respect to the technique employed with rats, and that may have been the problem. Seldom is electrode failure experienced with a rat. We discussed some basic modifications in technique, but decided to make another attempt with the old procedure. This time, however, the dog's skull was roughed up with the drill in order to provide "grips" for the dental cement. Another failure occurred, but this time we did not lose the electrode for over a week. The next attempt was successful. In addition to roughing up the skull, we drilled a number of small holes into, but not through, the skull and at an oblique angle with respect to the skull surface. The cement was applied at a somewhat looser consistency than ordinarily and, therefore, seeped into the many holes. Another coat of cement of normal consistency was then applied to the mounting. We have experienced no failures since the new technique was attempted.

C. Given that the electrode can be maintained securely in place with normal wear and tear, we experienced some problems with regard to cable connections to the electrode in the experimental situation.

1. The cable leading to the experimental box need not be heavier than that ordinarily used in rat research. The

1. (cont'd)

extension leading from the cable end to the dog was originally of the same durability as the connector cable used for rats. The first such cable lasted for about fifteen minutes before the dog tore it apart.

2. In addition, dogs tend to attack even the most durable cable attached to their head by sweeping their forepaw over the top of their head and hitting against the cable. Several such "swipes" is sufficient to break the electrode connection itself, regardless of how heavy or durable the cable is leading to the connector.

The solution to both problems took several weeks to work out. In fact, we occasionally still have a dog who can tear our cable apart. When that happens, we rebuild it and attempt to make it impervious to further attack with additional shielding. On the whole, the solution has been quite satisfactory and will serve us well as a device for the protection of the electrodes in the field. The dog is equipped with a standard harness which fits snugly but not too tightly. The cable from the stimulator is fastened to the harness. A connector cable runs from the harness to a terminal strip at the back of a plastic helmet worn by the dog. The helmet is securely fastened to the top of the dog's head by a set of chin straps. It serves to protect the implanted electrode in addition to the relatively delicate connection (under the helmet)

C. (cont'd)

from the electrode to the inside of the terminal strip. After the helmet was designed and constructed in our shop, we have never had a dog tear a connector from the implanted electrode. In addition, paw sweeps across the top of the head do no damage since the cable runs flat along the back of the dog's neck to the harness. Figures 1 and 2 show the helmet in place on an implanted Beagle. The saddle arrangement on the dog is for the portable stimulator and power pack. Note, also, the connector in the technician's hand (Figure 2).

D. The dog has not been a popular organism in the behavioral laboratory. Our experience with the species indicates that size and the inconvenience in maintaining the species are not the only factors. Our work with the dog dates primarily from our entry into the new laboratory building, the summer of 1963. The problems we have experienced with the species to date and our solutions, where possible, will now be discussed.

1. The dog is a rather social animal. I have reference not so much to the dogs' response to other dogs, but to man. Dependencies and preferences are easily established and can interfere with the experimental procedure and even the experimental atmosphere in the laboratory. We have found it necessary to prohibit unnecessary interaction between the dogs and the

1. (cont'd)

   personnel.

2. The breed that we began our work with is the Beagle. The stereotaxic atlas by Lim, Liu and Moffitt was constructed on the basis of Mongrel and Beagle data. In addition, Beagles were easy to obtain. The breed, however, does not respond well to punishment. Our experience was that the dog shows a tendency to freeze and to develop "incapacitating fear" when subjected to even mild punishment.

We obtained the advice of professional dog trainers regarding their training techniques. The results of that inquiry were revealing. Almost unanimous was the advice that punishment is a valuable technique in the control of dog behavior, and that the Beagle is a poor breed for punishment training. The Terrior family was recommended, particularly the Wire Haired Terrier. We have purchased two of them and have compared their experimental food-rewarded performance with that of our Beagles. No simple conclusion was possible, but our strong impression was that the Terriers, particularly the one named "Rocky", were not easily intimidated. By comparison, our Beagles are much more easily intimidated. We are continuing to work with both species, however, since our initial work on electrode placement had been done with Beagles.

Figure 1 A test dog wearing the protective helmet and saddle for the distance stimulator.

Figure 1

Figure 2 The test dog. The technician is holding the connector (fastened to the dog's harness) which receives the stimulator cable.

Figure 2

Figure 3 and Figure 4 The experimental cage. The paw-press lever is on the right with a food hopper on the left. The cable can be seen in the cage in Figure 4. The cable suspension system can be seen in Figure 3.

Figure 3

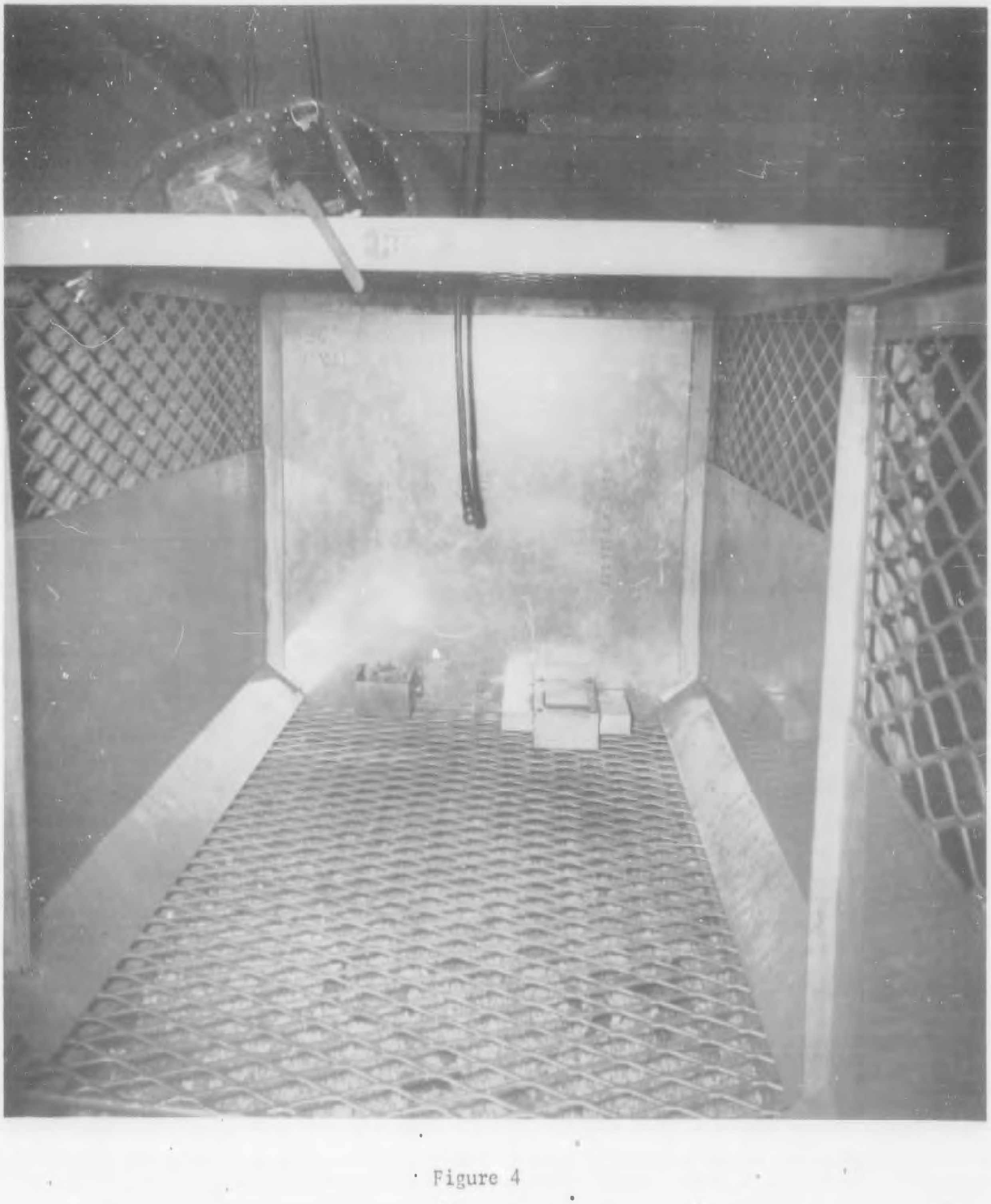

Figure 4

Figure 5 A dog working for brain-stimulation reward.

Figure 5

III. The Electrode Placement

The control of behavior through brain-stimulation reward supposes our ability to place an electrode in a rewarding area of the brain. Data from the rat and monkey offer the best starting points in a search for the rewarding area (s) in question. Our first attempts, implanting several electrodes in each dog, were aimed at the septum, posterior hypothalamus, the region of the red nucleus (a placement which provided some of our most successful "hot" positive rats) were rather discouraging. Substantiating a finding at Walter Reed with one dog, those placements were weakly positive. Typical performance in a paw-press situation was characterized by a very low rate of pressing (each press producing stimulation) interrupted by rather long periods of no responding. Responding, when it occurred, was frequently executed with the chin from a prone position in the box.

As stated above, stimulation in the septum, posterior hypothalamus and in the region of the red nucleus gave poor behavioral results on every occasion. Two hypotheses, each suggesting a course of experimental action, were entertained.

A. The electrodes employed in these dogs were the same as those used in the rat with regard to all dimensions except length. The wire (iridium platinum) is 10 mils in diameter with a 2-mil coating of insulation. Two such wires are twisted so as to form a bipolar pair, with the insulation removed only at the very tips of the wires. The electrical field produced by

A. (cont'd)

such a bipolar tip is considerable in size relative to the structures stimulated in the rat brain, but it is much smaller relative to the size of the structures stimulated in the dog brain. Perhaps our failures were due to insufficient stimulation. An argument against this hypothesis can be strengthened on the basis of monkey data; rat-sized electrodes are quite adequate to produce strong behavioral effects with stimulation of the appropriate brain sites in monkeys.

B. There is always the possibility that the accuracy of our implanting technique leaves something to be desired. Certainly there is enough variability in the sizes of our dogs to give pause for thoughton this possibility. We decided, therefore, to pay closer attention to the variable of dog size and to reject dogs that deviated outrageously from the limits specified in the stereotaxic atlas.

As an attempt to evaluate the first hypothesis, we employed one of our dogs implanted with three electrodes: septum, posterior hypothalamus and red nucleus. Stimulation at each of those placements alone gave unsatisfactory results. We stimulated across placements, i.e., an entire electrode (twisted pair of wires) was used as a single pole and another electrode was used as the other pole. Stimulation

III. The Electrode Placement (cont'd)

across about 10 mm. of tissue from the tip of the posterior hypothalamus placement to the tip of the red nucleus placement provided our first glimpse of satisfactory lever-pressing performance. The dog pressed at a fairly high rate, with short breaks. The voltage required, however, was in the neighborhood of about 80-90V. Our usual stimulator, a 100 cps sine-wave audio generator, had to be abandoned in favor of a variable transformer device capable of delivering the required voltage with a 60 cps sine-wave. We next attempted, with the same dog, to stimulate across the red nucleus and septal electrodes. After about 2000 "fast" responses, convulsions developed of sufficient severity to kill the dog.

Consistent with the above observations, we felt that the best placement might turn out to be somewhere between the posterior hypothalamus and red nucleus. Another dog (Einse, by name) was implanted in accordance with that deduction, but no success was obtained.

While considering the details of the next attempt in the posterior hypothalamus-red nucleus area, we implanted still another dog in an area we had not explored previously. In order to produce a larger field at the electrode tip, we spread the two wires of the bipolar pair so that the tips of the two wires were about 2 to 3 mm. apart. With the plane

III. The Electrode Placement (cont'd)

of the spread wires oriented in the anterior-posterior direction, the electrode was implanted in the region of the medial forebrain bundle. The stereotaxic coordinates, with reference to instrument zero as described by Lim, Liu, and Moffitt, were anterior-posterior, 20; lateral, 2.5; vertical 7.0. The dog was by far the most satisfactory preparation yet. He was named Eureka I. Sustained lever pressing could be obtained using 100 cps sine-wave stimulation without excessive voltage levels. Our working voltage is about 12-15V, peak to peak. The dog was tested for several days with no deterioration in performance. A question arose: should we continue to work with Eureka I or should we sacrifice him for histological analysis? We decided on the latter course in order to obtain information as soon as possible with regard to the exact location of the electrode tip. Histology has just been completed on that dog, and our judgement is that the electrode tip was in the median forebrain area, perhaps in the Campi Foreli. At the same time, another dog, Eureka II was implanted with the same coordinates and electrode configuration. That another success was obtained was immediately apparent. The dog was easy to train with moderate levels of stimulation. In addition, his lever-pressing performance was characterized by high, sustained rates with very small pauses. Following a pause, the dog would return to work with no priming (i.e., free stimulation). Priming was almost

III. The Electrode Placement (cont'd)

always necessary with the less positive placements used prior to Eureka I. Eureka II was given an endurance test: he was kept in an experimental box for a continuous eight hours. During that test, he emitted 50,000 lever presses, each rewarded with stimulation. That response rate compares very favorably with the best performances obtainable with rats. Eureka II was then placed on fixed-ratio schedules in which the response requirement per stimulation was raised over about one week of testing. The maximum obtained was about 60 to 1, but that performance became difficult to maintain, although we later determined that stimulation after each response (a return to continuous reinforcement) continued to maintain high rates of response. The latter observation indicated that the poor performance developed at FR60 was not due to tissue destruction at the electrode tip, but rather to the schedule requirement. Eureka II is still alive and healthy and we are continuing to work with him. We will attempt to produce better schedule performance by employing some of our techniques developed with rats.

Eureka III has been implanted; the coordinates were the same as those used with Eureka I and II. We have had some problems with Eureka III in that the skin incision has not healed properly. The area around the electrode remains wet and shorting of the electrodes is a continuing problem with him.

III. The Electrode Placement (cont'd)

In the absence of shorting his performance is very much like that of the first two dogs in his series. Figure 3 is a photo of the dog test cage. The cable suspension system can be seen above the cage. Figure 4 shows the interior of the test cage. The paw-press panel is on the right, and the food hopper is on the left. The cable can be seen as well as the helmet and harness assembly. Figure 5 is a photo of one of the test dogs actually working. The fact that the presence of the photographer did not distract the dog attests to the potency of brain-stimulation reward.

Our next task will be to obtain a reliable aversive placement in the dog. The control of behavior in the field, particularly the development of such control during training, will very likely require some degree of punishment for unwanted behavior. The actual degree to which punishment is required, if at all, remains to be seen. Our feeling is that it would be better to determine the aversive placement now, while we are thinking about placements, rather than to return to the placement problem later when we are primarily engaged in later aspects of the work.

IV. The Distance Stimulator

A crucial aspect of our work involves the use of a portable stimulator, capable of being carried by a dog, and triggered by a radio frequency signal. The design and construction of

IV. The Distance Stimulator

that stimulator unit was assigned to the then Diamond Ordnance Fuse Laboratory, now the Harry Diamond Laboratory or HDL. The unit as designed was capable of delivering 100 cps sine-wave stimulation at levels useful with a dog. The unit had two independent channels so that either or both of two electrodes could be stimulated. Delivery date was scheduled as 1 July 1963. Contact between our laboratory and HDL was maintained by our electronics consultant, Mr. Irwin Schpok. His familiarity with our requirements and his ability to evaluate their progress was a major factor in obtaining the unit. A number of difficulties were experienced on the technical end-they were evaluated and where necessary, design changes were made to expedite the work. The unit was delivered along with the transmitter about October, 1963.

When Eureka II proved to be a dog capable of good performance, it seemed natural to subject the HDL stimulator to an extensive, indoor test by placing the dog in the experimental box with the stimulator on his back and the transmitter so arranged as to fire the stimulator on a lever press. In setting up the test, it became apparent to Mr. Schpok that the stimulator unit was not functioning properly. It has been returned to HDL for the appropriate modifications, and we are awaiting its return.

We had prepared a "backup" unit to cover just such a contingency. The unit consists of a model airplane, radio control

IV. The Distance Stimulator

transmitter and receiver. The receiver is built into a small, portable capacitor-discharge stimulator. The indoor test with Eureka II will be conducted with our unit so that procedural details can be worked out prior to the return of the HDL unit. If the HDL unit continues to be unreliable, some other arrangement will have to be made in order to obtain a distance stimulator capable of meeting our requirements. We do not anticipate that our home-made unit will have the durability or versatility for field work.

V. The Next Steps

As indicated above, our next step is to obtain a reliable aversive placement in the Beagle. In addition, we are attempting to locate our positive placement in another breed, i.e., the Terrier.

In general, we are in a position to pursue several lines of research simultaneously. Up until the positive placement was located, our work was restricted to a search for it, paralleled by our rat work regarding the maintenance of behavior. Now, however, we can proceed with detailed investigations into the properties of brain-stimulation maintained behavior in the dog. In order to expand our work in that direction, we are cutting back on the amount of rat work in the laboratory. Some will continue in order to provide for the discovery of new information and the development of new

V. The Next Steps (cont'd)

techniques.

The questions that we will pursue in the near future are:

A. Are the techniques developed to maintain substantial performances with the rat adequate with the dog? We are now attacking this question with Eureka II.

B. What are the coordinates of a reliable aversive placement in the dog?

C. Since the control of behavior can be resolved in large measure to the problem of stimulus control, we are undertaking a series of stimulus generalization and discrimination studies, ranging from simple light on-light off designs employing brain-stimulation reward and/or punishment to more complex matching-to-sample studies.

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