ELECTROENCEPHALOGRAPHIC CORRELATES OF TEMPORALLY SPACED RESPONDING AND AVOIDANCE BEHAVIOR

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This study was undertaken to determine whether any EEG changes occurred during a multiple schedule of reinforcement consisting of repeated periods of avoidance behavior, a time-out (TO) period, and a period of differential reinforcement of low rates (DRL). The two monkeys were permanently implanted with bipolar electrodes in various subcortical areas. The EEG was recorded from these electrodes for several weeks before any behavioral training was undertaken. Training was then begun in the multiple schedule, and EEG recordings were taken frequently throughout the training period. When a stable performance level was achieved, drugs (*dl*-amphetamine and sodium pentobarbital) were introduced which disrupted the DRL performance but had little or no effect on avoidance behavior. The EEG recordings continued throughout these drug studies.

The data indicate that the marked behavioral differences noted in each component of the schedule were not reflected in the EEG. However, the EEG did correlate with the general level of alertness of the animals during the various components. The drugs which differentially affected the behavior in the components of the schedule did not differentially affect the EEG, but they did change the brain-wave activity equally in all components. Finally, EEG changes correlated with the complex motor response of lever pressing were not observed.

In recent years, many investigators (Rusinov & Rabinovich, 1958; Yoshii & Hockaday, 1958; John & Killam, 1959; Hearst, *et al.*, 1960; Chow, 1961) have studied the changes in the electroencephalogram (EEG) produced by repetitive visual or auditory stimuli during the acquisition of a conditioned response. John and Killam have called the repetitive stimulus a "tracer conditioned stimulus" because the responses can be identified in the midst of brain activity recorded from various loci in the brain.

The present investigation attempted to study the changes, if any, in this generalized brain activity itself, without using an external repetitive stimulus. The technique was to record from several brain areas during a multiple schedule of reinforcement consisting of repeated cycles of avoidance behavior without an exteroceptive stimulus (Sidman, 1953), a time-out (TO) period, and a period of differential reinforcement of low rates (DRL). Brady and Conrad (1960) characterized this latter behavior as follows: "The differential reinforcement of low rates (DRL) generates

a timing process which makes it possible for the organism to discriminate the duration of the interval elapsing since the last response. Since there is no exteroceptive stimulus in this situation, the event or events upon which reinforcement is contingent must be provided by the organism's own behavior" (p. 93). The present report analyzes the EEG correlates of this "self generated" behavior under control conditions and after it has been altered by pharmacological agents. Hodos, Ross, and Brady (1962) reported an analysis of complex response patterns which occurred during the DRL periods of this experiment.

Method

Two adult rhesus monkeys, M-49 and A-73, were studied. Surgery was performed under sodium pentobarbital anesthesia, at which time bipolar stainless steel electrodes were implanted. Each bipolar electrode consisted of two 0.010-in. wires twisted together and separated at their tips by 1-2 mm. The recording surface was the cross-sectioned diameter of the two twisted wires.

The electrodes were placed in the following structures in Monkey A-73: amygdaloid complex, globus pallidus, caudate nucleus, medial forebrain bundle, intralaminar nuclei of the

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thalamus, nucleus reticularis thalami, nucleus paraventricularis thalami, and the ventral tegmental nucleus. Figure 1 shows photomicrographs of the electrode locations. Because Monkey M-49 is presently a subject for another experiment, histological verification is not available at this time.

After implantation and attachment to the skull by dental cement, the electrodes were attached to a Sheatz (1961) pedestal. From this pedestal a connecting cable was led to a Grass Model 5 six-channel polygraph for recording the brain potentials. After surgery, the animals were allowed to recover for at least 1 week to 10 days before electrical recording was begun.

The monkeys were maintained and studied in a primate restraining chair (Mason, 1958) located in an experimental booth lined with acoustical tile. Noise generated by a white-noise generator (Grason-Stadler) presented

through a speaker in the booth masked sounds from the programming and recording equipment which might have given discriminative clues to the monkey. The programming and recording apparatus was housed in an adjoining room. A telegraph-key lever, an automatic foot-pellet dispenser, and a visual stimulus panel with five differently colored lights were attached to the primate chair. Electric shocks of 0.5-sec duration and 5.0-ma intensity were given across the leg and seat of the animals.

The EEG's from the two animals were recorded over a 2-week period before any behavioral training was begun. Behavioral training was carried out in the following manner. A colored light was on continuously during the avoidance period, and a different-colored light was on continuously during DRL. The duration of each period of avoidance and DRL was 15 min, and each was always followed by a 15-min TO. Therefore, each hour

Fig. 1. A photograph of the electrode placements in Monkey A-73: A = amygdala; B = globus pallidus; C = caudate; D = medial forebrain bundle; E = intralaminar nuclei; F = Nucleus reticularis thalami; G = nucleus paraventricularis thalami; H = ventral tegmental nucleus.

consisted of an avoidance period, a TO, a DRL period, and another TO. The total session lasted 6 hr.

Figure 2 shows a sample of stable performance on the multiple schedule. During the avoidance period, a shock was delivered if the animal failed to press the lever for 20 sec. The S-S interval was also 20 sec. The shock was repeated every 20 sec until the animal pressed the lever. After several sessions of training,

Fig. 2. A cumulative record which demonstrates the sequence of the components of the multiple schedule and the appearance of a stable performance level.

the animals rarely received a shock. Because no reinforcement was delivered during the TO, there was little or no lever pressing. During the DRL period, a food pellet was delivered only if a lever response was separated by at least 21 sec from the preceding lever press. Food-pellet reinforcements are indicated in Fig. 2 by the downward strokes of the pen during the DRL periods. When a stable level of performance was reached, 25 to 30 reinforcements were received in each 15-min period. During the several months of this study, the animals received no food other than that which they acquired during DRL periods. There was free access to water, and vitamin supplements were administered daily.

Results

The data presented in this paper are from the records of Monkey A-73. Because the data from Monkey M-49 showed essentially the same results, they will not be presented.

The EEG records were analyzed by visual inspection, and direct measurements were made of both the frequency and amplitude of the waves. The data presented below represent the analysis of many hours of recording during the various components of the schedule throughout the several months of the experiment. The figures presented are only samples of typical recordings observed.

Figure 3 illustrates two phases of the electroencephalogram in the pretraining stage of the experiment. In Part A, the left half of the tracing shows, in all areas except the globus pallidus, a high-voltage (100-125 μ V), slow (3-5/sec) pattern mixed with 8-9/sec activity at 50 microvolts (μ V). The animal appeared asleep (eyes were closed) during this part of the record. In the right half of Part A, the monkey's eyes have opened and the EEG shows an alpha-like rhythm, predominantly from the intralaminar derivation. The frequency from this area is 9-11/sec at a voltage of 50-75 μ V. This section of the record is suggestive of a "relaxed" stage. In Part B of Fig. 3, a sleep pattern again appears for the first three-quarters of the record. During this period, the animal's eyes were closed. The arrows indicate the point at which a loud noise was made outside the monkey's booth. The animal was alerted, and a low-voltage (40-50 μ V), fast (8-12/sec) record appears in all leads.

Sleep patterns of the type shown in Fig. 3 were often recorded during the pretraining phase. However, once training had begun they were never observed again.

Fig. 3. The EEG records from the various electrode placements during the pretraining periods. They illustrate the frequency and amplitude patterns during the various stages of wakefulness.

Early in the training procedure, the alpha-like rhythm again appeared during the TO, as the upper half of Fig. 4 shows. During TO, the intralaminar electrode record shows 8-10/sec rhythm at 100 μ V, which switches to an irregular 5-6/sec frequency when the DRL

Fig. 4. The EEG recording of the components of the schedule early in the training period. The arrow indicates the point of transition from a TO to a DRL period.

period begins. This is indicated by arrows in the upper half of the figure. The recording from the nucleus paraventricularis thalami changes in time out from 5-6/sec frequency at 70 to 80 μ V to 30 to 40 μ V amplitude at the same frequency during the DRL period. The EEG during the avoidance component revealed an irregular frequency of 4-6/sec intermixed with fast activity at 9-12/sec. This is most prominent in the intralaminar placement.

Figure 5 shows EEG recordings made after Monkey A-73 had achieved the stable level of performance shown in Fig. 2. During TO, the tracing on the upper channel (intrala-

Fig. 5. The EEG recording from three components of the schedule after a stable level of performance was achieved.

minar) has an amplitude of 65 to 75 μ V at a frequency of 4-6/sec, with some superimposed fast activity. The activity in the nucleus paraventricularis and ventral tegmental nuclei are of the same frequency at 30 to 40 μ V amplitude. During the DRL period, the amplitude decreases slightly, and a suggestion of increased superimposed fast activity appears in the upper two channels. The recording during the avoidance period reveals more fast activity in all channels, superimposed on the 4-6/sec rhythm.

The "sharp spikes" seen predominantly in the lowermost channel are artifacts due to a poor spark-suppressed circuit. These artifacts occurred at the instant of a lever press.

DRUG STUDIES

Drugs were administered which have been reported to affect differentially the components of this schedule (Sidman, 1955, 1956). Fig 6 presents the effects of sodium pentobar-

Fig. 6. The effect of sodium pentobarbital (10 mgm/kg I.P.) on the EEG during the various components of the schedule, 120 min after drug administration.

bital, 10 mgm/kg intraperitoneally. Under the influence of this drug, DRL responding was completely disrupted whereas avoidance behavior declined somewhat in rate. The EEG revealed an increase in frequency in all leads (10-11/sec). The amplitude in the intralaminar derivation also increased slightly. In Fig. 6, the sharp waves in the third channel of the DRL and the avoidance components of the control period are artifacts correlated with chewing. The drug therefore appeared to change the EEG equally in all components

of the schedule, whereas behaviorally there was a marked differential effect.

Figure 7 illustrates the EEG under the influence of *dl*-amphetamine, 2.0 mgm/kg intraperitoneally. The control periods for all components are on the left. Under the influence of the drug, the DRL behavior was again disrupted, whereas the avoidance rate declined only slightly. The EEG revealed an increase in frequency, predominantly in the intralaminar placement. This increase to 10-11/sec appeared as a superimposed rhythm

Fig. 7. The effect of *dl*-amphetamine 2.0 mgm/kg I.P. on the EEG during the various components of the schedule.

on the basic 4-6/sec frequency. In contrast to the pentobarbital-induced fast activity, the amphetamine effect did not appear in the recording from the ventral tegmental electrode. As with pentobarbital, the EEG changes due to *dl*-amphetamine were manifested equally in all components of the schedule.

Thus, although the two drugs affected both the behavior and the EEG of the animals, they differentially affected only the behavior in the components of the schedule, not the EEG.

DISCUSSION

The evidence presented in this paper suggests that the brain activity recorded during temporally spaced responding (DRL) and avoidance behavior reflects the state of "alertness" of the animal. In the pretraining period, the EEG reflects various levels of the wakefulness continuum, *i.e.*, sleep patterns, relaxed-awake and alert-awake patterns. Direct observation of the animals correlated well with the EEG analysis. As training progressed

and a stable level of performance was achieved, these stages were no longer observed. The records showed predominantly fast activity similar to that seen in periods of alertness during the pretraining session. (See Fig. 2.) A small but definite increase in frequency was noted during the DRL and avoidance components of the schedule compared with that in the TO. This increase suggests that the animals were more "alert" during these components. Further study of this small EEG frequency change with electronic frequency analysis would appear to be warranted.

Despite the frequency changes just discussed, however, the EEG as recorded from several brain loci in this study did not reflect the gross differences in behavior produced by the multiple schedule. Pentobarbital and *dl*-amphetamine, which differentially affected behavior in each component of the schedule, changed the EEG equally in all components. Under pentobarbital, the animal appeared drowsy in all components (but continued its avoidance behavior), and the EEG reflected this level of wakefulness. With *dl*-amphetamine, the animal appeared fully awake with eyes wide open; but, again, the behavior was very different in the components of the schedule, whereas the EEG reflected only the state of alertness of the animal.

In his study of brain electropotentials during visual discrimination learning, Chow (1961) states the following: "It is also possible that the electrographic waves could be incidental, indicating a state of the animal during learning, but not a reflection of the process itself." (p. 387) The data presented in this paper would tend to support this idea.

Finally, many authors (Hearst *et al.*, 1960; Yoshii & Hockaday, 1958; Rusinov & Rabonovich, 1958; John & Killam, 1959) describe variation in evoked response amplitude during the conditioning process. The present investigation, which did not use a repetitive external stimulus, did not uncover any such localized brain changes. In an attempt to explain similar negative results in his study, Chow (1961) lists the following possibilities: "First, the electrodes may not be placed in the structures where crucial neural events take place. Second, the EEG records obtained are too gross to reveal subtle neuronal alterations. Third, the tracing may contain significant EEG trends which are not detected by

visual inspection. Fourth, . . . there still remains the task of ascertaining that the EEG alterations are indeed reflections of neural events of the acquisition processes and not incidental by-products." (p. 388) A similar analysis is certainly applicable to this study.

In conclusion, it is interesting to note that the complex motor response of lever pressing did not evoke any specific brain-wave pattern from the various areas monitored.

REFERENCES

- Brady, J. V., and Conrad, D. G. Some effects of brain stimulation on timing behavior. *J. exp. Anal. Behav.*, 1960, **3**, 93-106.
- Chow, K. L. Changes of brain electropotentials during visual discrimination learning in monkey. *J. Neurophysiol.*, 1961, **24**, 377-390.
- Hearst, E., Beer, B. S., Sheatz, G., and Galambos, R. Some electrophysiological correlates of conditioning in the monkey. *EEG Clin. Neurophysiol.*, 1960, **12**, 137-152.
- Hodos, W., Ross, G. S., and Brady, J. V. Complex response patterns during temporally spaced responding. *J. exp. Anal. Behav.*, 1962, **5**.
- John, E. R., and Killam, K. F. Electrophysiological correlates of avoidance conditioning in the cat. *J. pharmacol. exptl. Therap.*, 1959, **125**, 252-274.
- Mason, J. Restraining chair for the experimental study of primates. *J. appl. Physiol.*, 1958, **12**, 130-133.
- Rusinov, V. S., and Rabinovich, M. Y. Electroencephalographic researches in the laboratories and clinics of the Soviet Union. *EEG Clin. Neurophysiol.*, 1958, Suppl. No. 8, 3-36.
- Sheatz, G. Multilead technique for large and small animals. In Daniel Sheer (Ed.), *Electrical stimulation of the brain*. Austin, Texas: University of Texas Press, 1961, Pp. 45-50.
- Sidman, M. Avoidance conditioning with brief shock and no exteroceptive warning signal. *Science*, 1953, **118**, 157-158.
- Sidman, M. Technique for assessing the effects of drugs on timing behavior. *Science*, 1955, **122**, p. 95.
- Sidman, M. Drug-behavior interaction. *Ann. N.Y. Acad. Sci.*, 1956, **165**, 282-302.
- Yoshii, N., and Hockaday, W. J. Conditioning of frequency-characteristic repetitive electroencephalographic response with intermittent photic stimulation. *EEG Clin. Neurophysiol.*, 1958, **10**, 487-502.

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