Electrical activity of the entorhinal cortex during conditioned behavior

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Holmes, J. E. AND W. R. Adey. Electrical activity of the entorhinal cortex during conditioned behavior. Am. J. Physiol. 199(5): 741-744. 1960.—A 4-6-cps wave form was observed in the entorhinal cortex of 8 out of 10 cats studied with the implanted electrode technique. When the animals were trained to approach a concealed food reward, the slow waves always accompanied the act of walking to the goal, and the rhythm stabilized in the range of 5-6 cps. When the habit was subjected to extinction, the rhythm gradually dropped out, to return promptly with retraining. Stimulation of the entorhinal area had no effect on behavior as long as seizures were avoided. A similar 4-6-cps rhythm was observed in the hippocampus during the early stages of training in two animals. It is suggested that the entorhinal slow waves are a correlate of an alert state of readiness to act.

Recent studies of intact animals with implanted electrodes have revealed interesting correlations of behavior with the activity of rhinencephalic structures. Specifically, a slow 4-6-cycle rhythm has been observed in the hippocampus and the adjacent entorhinal cortex. This has been correlated with arousal (1), with the Pavlovian orienting reflex (2), the stabilization of temporary connections (3), and with planned motor performance (4, 5).

The present study deals with recordings from the entorhinal cortex of cats during the learning and performance of a delayed response test involving approach to a food-containing goal box.

Materials and Methods

Bipolar stainless steel electrodes with exposed recording tips 1.5 mm apart were stereotaxically implanted in 10 cats. A small plug on each animal’s head permitted connection to a Grass paper-writing electroencephalograph but allowed relatively unrestricted behavior. Electrode implantations were verified by gross and microscopic examinations of the brains.

FIG. 1. Training apparatus for delayed response test. Cat is placed on starting platform with the bridge walkways raised as shown. The animal’s attention is then drawn to a food container and tests placed in 1 of the 2 pans on the right. Choice of pans is randomized. After a 5-10 sec. delay the bridge is lowered, and the animal walks to 1 of the goal boxes. Boxes are placed so that the animal cannot see the reward until he reaches it.

The animals were trained in a delayed response situation involving a choice between two pathways to identical pans, one containing a concealed food reward (fig. 1). The animal is placed on the starting platform with the bridge pathways up as shown. Food is placed in one of the two pans and there is a 5-10-second delay. The bridge is lowered by hand, and the animal allowed to walk to one of the two pans. Extinction trials were identical except for the absence of the reward. Extinction was carried out until approximately half the trials in any day’s run did not produce walking to the goal box. For stimulation a Grass stimulator with 1-msec. square wave

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FIG. 2. Selected EEG tracings from 1 animal. Left entorhinal area above, right below. First record shows animal untrained, slow waves during spontaneous walking (underlined). Next record shows the time food was shown to animal (1st arrow), bridge lowered (2nd arrow) and animal reached goal box (3rd arrow). In third record the slow rhythm is largely confined to the approach phase after the bridge is lowered. Subsequent tracings show the gradual decrease in slow rhythm with extinction and its return with retraining. Standardization—50 μV, 1 sec.

RESULTS

In 8 of the 10 animals studied a slow 4-6-cps rhythm occurred spontaneously in the entorhinal cortex (fig. 2). It seemed associated with alertness and attention to stimuli, extraneous noises, insects in the room, etc. It always accompanied walking from platform to platform in the training apparatus.

Changes in entorhinal activity with training. Slow waves occurred during the act of walking to the goal box whether the choice was correct or not. These bursts were at the faster end of the spontaneous range of frequencies (i.e. at 5-6/sec.). Training past the point where the animal was getting many runs 100% correct did not alter the duration or frequency of the entorhinal activity during walking. After training, however, the 4-6-cps rhythm tended to occupy less of the delay period before the actual walking.

The slow waves continued to occur both spontaneously and with other directed walking, such as walking from goal box back to starting platform. It did not necessarily accompany less purposeful movement, i.e. walking back and forth on the starting platform between tests.

Extinction was carried out in four cats. The animals continued to walk to the goal box on some trials of each day’s run. Typical slow waves accompanied such behavior. After several days there would occur a few trials in which the animal remained at the starting platform (‘no go’). Initially, these were accompanied by slow wave trains nearly as long as those occurring with walking. With more training, however, the slow wave response on no go trials became shorter and less obvious. On the same day a ‘go’ trial would exhibit slow wave patterns of short duration. Retraining these animals produced electrical patterns indistinguishable from those of earlier training (fig. 2).

Effects of electrical stimulation. Electrical stimulation of the entorhinal area was attempted in four animals. Both unilateral and bilateral stimulation were used at frequencies of 6 and 100 cps and varying voltages of a 1-msec. biphasic square-wave pulse. There was no altera-
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The animals performed as well during or immediately following stimulation as without it. Seizures were identical electrically and behaviorally at either stimulation frequency. They were always propagated to other brain structures (globus pallidus, hippocampus, reticular formation, opposite cortex). The behavioral changes were similar to those described by others (6) for the hippocampus. The animals stood still and seemed unaware of the environment. Sometimes there was facial twitching or urination. When the discharge stopped, the animal proceeded to walk to a goal box as usual, although activity in the entorhinal cortex was usually depressed. Under these circumstances the animals made poor scores.

Simultaneous recordings from the entorhinal cortex and the hippocampus were made in two animals (CA4 in one animal, fimbria near CA3 in another). During the initial stages of training there was slow wave activity in both areas. It did not appear to be synchronous. The relationship of the two rhythms has been analyzed in detail by Adey, Dunlop and Hendrix (5). As training continued and the habit became established the 4-6-cps pattern dropped out of the hippocampal tracing but persisted in the entorhinal record (fig. 3).

DISCUSSION

The entorhinal area has extensive interconnections with the brain stem (7), and it is interesting to speculate on its role in attention and arousal. Some of the records from our animals during early training show a 4-6-cps pattern in the reticular formation at the level of the superior colliculus. Grastyan has published similar findings (2).

Certainly there is not enough data available at present to define accurately the behavioral correlate of the 4-6-cps rhythm. We favor the view that it accompanies an alert state found in goal-directed motor activity. Since it appears without gross movement, both spontaneously and during extinction of the approach habit, we suggest that it indicates a readiness to act.

The relationship between the slow waves and the propagation of impulses to such structures as hippocampus...
campus and brain stem is not clear. Grastyan and co-workers (3) have suggested that the slow waves may be the electrical signature of a cortex that is inhibited or 'turned off.' This does not provide any satisfactory explanation for the change in frequency with training observed here. Adey, Dunlop and Hendrix (5) have concluded that the changing slow wave patterns in entorhinal and hippocampal areas actively subserve the integration of information.

Since a massive seizure discharge from this area produces a striking behavioral arrest, it is not unreasonable to suppose that its rhythmic activity produces a modulation of behavior. This modulation could be achieved through influence on sensory input (recognition of the conditioned stimuli) or motor output (approach behavior). The correlations observed in this study would seem consistent with either view.

It would appear that despite their resemblance, the slow wave rhythms in the entorhinal area and the hippocampus are not identical in phase and distribution. One may, of course, represent propagated activity from the other. This relationship of the two structures may also play a major role in the conditioning process (4).

REFERENCES