

Learning and Cortically Evoked Movement during Propagated Hippocampal Afterdischarges

Abstract. Learned responses are absent during intense hippocampal discharges. Their absence is attributable not to a disruption of learning but to an effect upon the motor system.

The hippocampus and the cerebral structures related to it (the limbic system) have been implicated as the anatomical substrate of such behavior as emotion (1), memory and recall (2), and drive states (3). Hippocampal afterdischarges were used in this study to investigate the functions of this system. A hippocampal afterdischarge consists of high-amplitude electrical potentials that continue in the brain for as long as 90 seconds after the initiating electrical stimulus has ceased. Although a hippocampal afterdischarge begins in the hippocampus, it does not remain confined to it but propagates to other limbic structures, without ordinarily involving the neocortex. The immediately observable effects of a propagated hippocampal afterdischarge are few, despite the intense electrical activity of the brain. Learning techniques were therefore used to try to ascertain what was happening.

Conditioned cardiorespiratory responses and conditioned leg movement, learned prior to induction of afterdischarges, were absent during well propagated hippocampal seizures (4). However, if only one hippocampus was intensely involved, the responses were not markedly disrupted. One possible explanation of the disruption of the learned response during the afterdischarge is a deficit on the motor side. This appeared unlikely in view of the brisk leg movement, and the concomitant change in heart rate, evoked by an electric shock to a paw during the afterdischarge. On the other hand, the deficit did not appear to be sensory, since evoked potentials continued to appear at the auditory cortex during afterdischarges. It seemed reasonable therefore to hypothesize that it was the coupling of the sensory stimulus and the conditioned response that was disrupted. This view conforms with the assignment to the hippocampus of memory and other functions considered essential to learning. The hypothesis could be tested by determining whether or not animals could learn if their only learning trials took place during afterdischarges.

Seven cats were trained exclusively during hippocampal afterdischarges to lift a paw to avoid a shock. The animals had electrodes implanted aseptically in both hippocampi, in the neocortex, and

in various relevant subcortical structures. The sites of the electrode tips were determined histologically. The afterdischarges were customarily elicited by a train of 62.5-pulse/sec, 2-ms biphasic square waves lasting 10 seconds or less, whose peak-to-peak current was usually about 0.3 ma. The duration of the afterdischarges varied from 10 to 90 seconds, and one to four learning trials were given during a single afterdischarge depending upon its duration. Each trial consisted of a 2.5 second, 62.5-pulse/sec auditory sawtooth wave whose intensity was approximately 93 db relative to 0.0002 dyne/cm², followed by a 0.5 second shock to the foot which was terminated or avoided by the cat's raising his right hind paw. The cat was suspended in a holder that restrained its movements. This restriction permitted electroencephalography with few movement artifacts. Bipolar electrical recordings were obtained throughout training and testing for learning.

Prior to the actual learning sessions, the auditory signal alone was tested for its effectiveness in eliciting a discrete leg response. No such responses occurred to the sound alone, either in the presence or absence of afterdischarges. During the actual period of training, which took place only during the afterdischarges, three of the cats (1, 2, and 3 in Fig. 1) seldom avoided the shock, although a few discrete

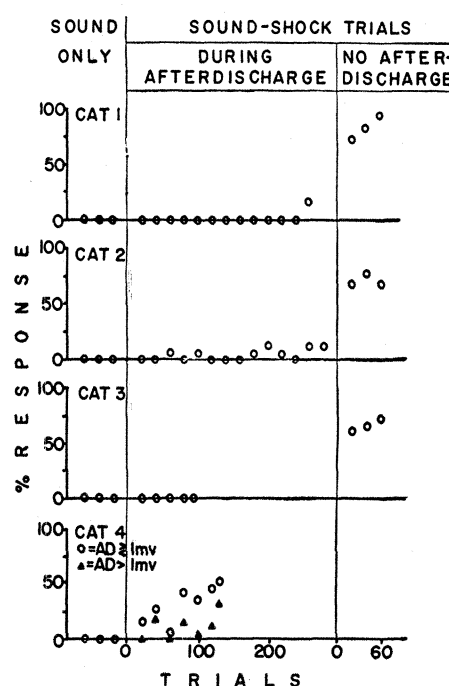


Fig. 1. Learning during afterdischarges in the relative absence of performance (cats 1, 2, and 3). Performance may also take place if afterdischarges are not intense, and occasionally even during intense afterdischarges (cat 4).

Table 1. Increase in latency and decrease in magnitude of cortically elicited movements during afterdischarges as compared to movements elicited in their absence. All differences significant at $P < .001$.

Cat	Mean $\pm$ S.D.*	N
	<i>Increase in latency (sec)</i>	
A	0.37 $\pm$ 0.07	24
B	0.18 $\pm$ 0.04	23
C	2.16 $\pm$ 0.25	29
	<i>Decrease in magnitude (mm)†</i>	
A	6.06 $\pm$ 0.49	24
B	1.77 $\pm$ 0.19	26
C	3.30 $\pm$ 0.45	38

* S.D., standard deviation of the mean. † 1 mm re-recorded response = 12.5 mm actual movement.

avoidance responses appeared. In these cats the afterdischarges were well propagated to both hippocampi. In trials after the hippocampal afterdischarges were discontinued, these animals all responded at levels so high as to indicate that learning had already taken place. Five additional cats were trained in a fashion identical to that of the experimental animals except that the training took place without afterdischarges being induced. In the first 100 trials none of them showed a level of learning comparable to that of the experimental animals when no longer given afterdischarges. When one computes the percentage response for each block of 20 trials for each cat, the maximum response achieved by any cat does not exceed 35 percent in any block up to the 100th trial. The maxima for the other cats are 15, 5, and 0 percent. Had the experimental animals learned only during the trials following the discontinuance of the afterdischarge, their percentage avoidance response should have been no higher than that of these controls. The data thus indicate that learning took place during the afterdischarges.

In two of the cats the afterdischarges were not well propagated to both hemispheres, and these animals showed discrete anticipatory leg responses during the afterdischarges. The graph at the bottom of Fig. 1 shows the anticipatory responses made by one of these cats. The data are plotted irrespective of the magnitude of the afterdischarge, and also when only afterdischarges in excess of 1 mv are present. The relative number of responses during intense afterdischarges is small, in agreement with the results in the other animals.

In two of the animals no evidence of learning was obtained. In both these cats grand mal seizures were regularly precipitated. This may account for their failure to learn. The tendency to develop grand mal seizures increased in the course of inducing hippocampal afterdischarges in all the animals. In

the two just mentioned grand mal seizures were particularly common.

Since it was evident from the data of the experiment just described that the failure to elicit a conditioned response during a well propagated hippocampal afterdischarge was not due to the actual disruption of the coupling between the conditioned stimulus and the conditioned response, the motor side of the phenomenon was subjected to closer scrutiny. Electrodes were implanted in the motor cortex so that electrical stimulation would elicit a movement of the forepaw. Electrodes were also placed in both hippocampi. After the animals had fully recovered from the effects of the operation, the magnitude and latency of cortically evoked movement were determined in the presence and absence of propagated hippocampal afterdischarges. The results of this study are shown in Table 1. The latency of the cortically evoked movement increases during hippocampal afterdischarge, and correspondingly the magnitude of the movement decreases. Although all the cats show differences in the same directions, the magnitudes of the differences are not the same. In order to record the movements in the chronic preparation it was necessary to use a weight to bring the forepaw to a consistent starting point. This, together with other differences such as the strength of the cat, the placement of the electrodes, and threshold values, probably accounts for the observed differences between animals.

The occurrence of learning during hippocampal afterdischarges renders unlikely the thesis that the hippocampus is the main recording system of experience. It also makes improbable the supposition that hippocampal afterdischarges are responsible for the amnesia of epilepsy or shock treatments. The decrease in the cortically evoked motor response during hippocampal afterdischarges provides an explanation, at least in part, of the disruption of the learned response during such seizures (5).

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Scintillation Counting of Beta

Activity on Filter Paper

Abstract. Scintillation counting of beta activity on filter paper, with monoisopropylbiphenyl as a solvent of low volatility, was investigated. The method is attractive since no sample preparation is involved, and the activities are measured directly on the filter paper wetted with the scintillator solution. A linear dependence of counting rate on total activity was found for iodine-131, phosphorus-32, sodium-22, and carbon-14, and counting efficiencies were determined.

Radioactive samples are frequently collected on filter paper during the processes of separation or purification of labeled material. Direct scintillation counting of the sample on filter paper is feasible (1). Such a procedure circumvents difficulties arising from insolubility of the sample in aromatic liquid scintillation solvents. Although it is usually possible to synthesize the sample into a form soluble in a liquid scintillator (2), or to incorporate small amounts of aqueous solution in a liquid scintillator (3), these methods are indirect and time consuming, and they frequently result in a marked decrease in the fluorescence efficiency of the solution with a concomitant reduction in the absolute counting efficiency.

It is patently advantageous to assay the activity of the sample with a

minimum amount of purification or special preparation. In varying degrees, suspension of the active material in gels (4), or thickened systems (5), or the use of plastic capillary detectors (6) to count aqueous solutions of beta emitters, achieves this desired result.

An alternative technique (1) is to wet a filter paper containing an active deposit with a liquid scintillator solution. The organic solvent renders the paper relatively transparent, and surprisingly good light collection is possible. The method suffers from the evaporation of the solvent on a warm phototube surface and this results in a change in solute concentration with an accompanying change in detection sensitivity.

In order to overcome this weakness in the method, monoisopropylbiphenyl, which was recently reported as a scintillation solvent by Swank (7), was tested for its suitability for filter paper counting. This solvent possesses a vapor pressure about 1/1000 that of toluene at room temperature, and has a correspondingly lower rate of solvent loss by evaporation.

To test the counting method, samples of beta emitters of differing energy were chosen. A series of aliquots of aqueous solutions of calcium-14, sodium-22, iodine-131, and phosphorus-32 were pipetted onto No. 1 Whatman filter paper 1 3/8 inches in diameter. The

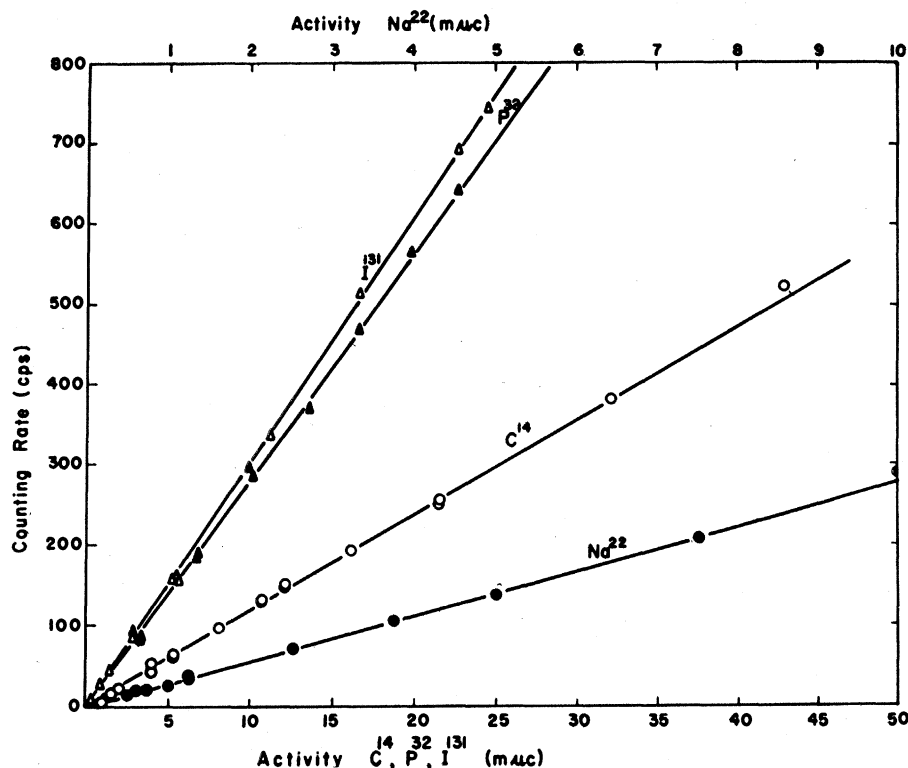


Fig. 1. Linear dependence of counting rate on activity of four beta emitters on filter paper.

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