XXII. COMMUNICATIONS BIOPHYSICS*

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RESEARCH OBJECTIVES

The past year has seen a diversification of the analytical studies of neuroelectric activity that characterize the efforts of our group. We continue to be interested in the response behavior and organization of sensory systems and in the development of tools that will enable us to give some kind of meaningful mathematical description of the electrical activity of the nervous system.

The role that computer techniques can play in research on brain function and behavior has been discussed by members of the group in two national conferences. Several papers (1-3) have been devoted to this topic, as well as to related problems of instrumentation (4, 5).

During the past year there have come from our group our first two papers on the analysis of firing patterns in single neurons (6, 7). On the other hand, averaging techniques have been applied to investigations of electrical events that occur later than the classical evoked primary responses (8-10). For problems that are related to these later events stimulus-locked averaging is not necessarily the only data-processing technique and one needs to consider other approaches, such as the detection of single or characteristic event patterns, or perhaps even processing techniques that depend in some sense upon the occurrence of a response. A critical examination of the assumptions that characterize the models implicit in these processing techniques is clearly indicated.

The past year has also seen the completion of our first major investigation in which averaging techniques have been used to study the behavior of cortical responses in man as a function of stimulus and state parameters (11).

Our studies of electrical phenomena and encoding mechanisms at the periphery of

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the auditory system have continued (12, 13) and a paper on responses to mechanical stimulation of the cat' s vibrissae has been published (14).

We have continued to examine man's sensory performance in relation to certain quantifiable aspects of the electrical activity of the nervous system (15, 16).

W. A. Rosenblith

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A. CORTICAL RESPONSES TO SHOCKS DELIVERED TO LATERAL AND MEDIAL GENICULATE BODIES UNDER DIFFERING RETINAL CONDITIONS

Unanesthetized cats with complete brain-stem transsections just in front of the trigeminal rootlets ("midpontine pretrigeminal" preparation) exhibit a predominance of the fast, low-voltage EEG patterns that are usually associated with an alert state in a behaving animal. This preparation has been the subject of considerable study in Professor Moruzzi's Institute at Pisa (1). Arduini and Hirao (2, 3) observed that although the "aroused" EEG pattern is typical of the midpontine pretrigeminal cat under conditions of retinal dark adaptation, a spread of EEG "sleep" pattern (spindling) followed indirect illumination (from above) by diffuse light or inactivation of the retina.

To probe the conditions of the nervous system during these different physiological states they delivered brief shocks to the lateral geniculate body, recording the evoked response from the corresponding visual cortex. They found that the retinal conditions that led to EEG spindling also led to an enlargement of the thalamocortical shock-evoked response (4). This finding for retinal illumination parallels that of Chang for cats under barbiturate anesthesia (5).

The present report relates to the following questions:

(a) To what extent does the enlargement of the thalamocortical shock-evoked responses appear in pathways other than those of the visual system?

Interest in this question follows in part a suggestion by Chang (5) that enlargement of the visual cortical response to lateral geniculate body stimulation is accompanied by enlargement of the auditory cortical response to medial geniculate body stimulation.

(b) Is the enlargement of the evoked response of the visual cortex strongly affected by the location of the stimulating electrode in the lateral geniculate body?

(c) What are the mechanisms that underlie the enlargement of evoked responses?

Most of the experiments were performed with cats in which a midpontine pretrigeminal section had been performed. In a few control experiments cats were anesthetized with nembutal. Acute and reversible deafferentation of the visual system was obtained by raising the intraocular pressure above that of the arterial blood; this produced an ischemic anoxia (a procedure that would normally be extremely painful but is allowable because of the pretrigeminal level of the section).

The potentials recorded from the surface of the cortex by monopolar electrodes were amplified and recorded on magnetic tape for processing at M. I. T. (6). The tape speed and preamplifier filters were set to give the system a passband of 1.5-1250 cps.

Electric pulses were delivered through isolating transformers to bipolar concentric electrodes in the lateral geniculate body or optic tract, and to bipolar electrodes (separation, less than 1 mm) in the medial geniculate body. The subcortical electrodes were placed by a stereotaxic instrument. Histological controls of electrode position were routinely performed with Nissl and Weil series stained preparations.

The dark-adapted preparation was stimulated by a series of single shocks to the lateral geniculate body on one side interleaved with a series of single shocks to the

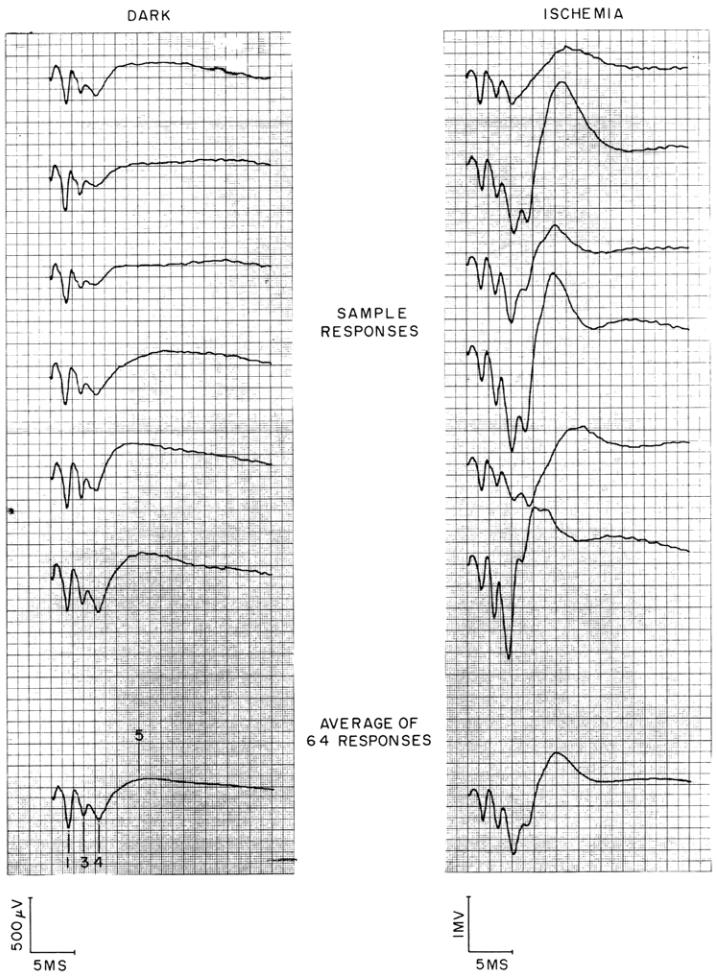

Fig. XXII-1. Stability of the average of responses. Potentials recorded by monopolar electrodes from striate cortex after delivery of shocks to the corresponding lateral geniculate body. Start of each trace is synchronous with delivery of a shock. In the experiments illustrated the rectangular pulses to the stimulating electrodes were 0.2 msec long. Shock amplitude was 5 volts, and rate of delivery was 1 pulse every 4 seconds. The waveforms at the left were recorded during retinal conditions of dark adaptation; those on the right were recorded after application of intraocular pressure. (Cat 79, midpontine pretrigeminal preparation.)

medial geniculate body on the other. Recording was from the corresponding cortical projection areas. The time between shocks in each series was usually 4 sec, and the interleaving such that a lateral geniculate body or medial geniculate body shock was delivered every 2 seconds. Activity was recorded for 5 minutes. After this, either a retinal ischemia was produced or the animal's eyes were illuminated and another five-minute series was recorded. At the end of this period the animal was returned to darkness and after 15 minutes a control record was run. Figure XXII-1 illustrates cortical responses to lateral geniculate body shocks for conditions of retinal dark adaptation and inactivation. Sample responses, as well as averages of responses, are shown for each condition. The usefulness of the average as a more stable measure of activity than the individual responses is illustrated in Fig. XXII-1, and is especially evident for the case of retinal inactivation.

These waveforms are typical of cortical responses to shocks delivered to the visual pathway. Other locations of stimulating electrodes for which cortical responses with similar waveforms are obtained include optic nerve, optic tract, and optic radiations. The waveform is not observed for physiological stimulation, even with very brief flashes. The various events in the waveform (numbered in Fig. XXII-1) have been the subject of extensive study (7-10), especially concerning their relationship to activity of cells in the cerebral cortex and the input connections to these cells.

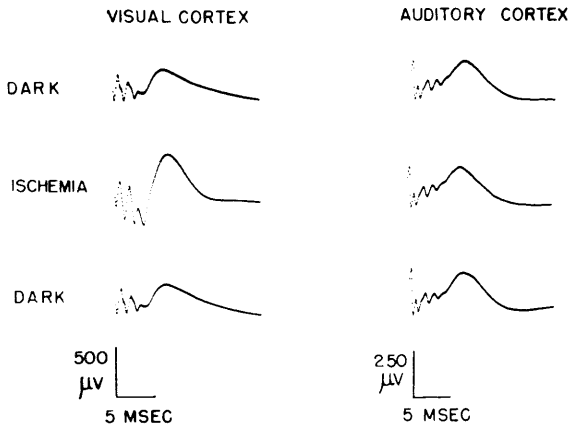

Fig. XXII-2. Averages of cortical responses from shocks delivered to the lateral geniculate body and the medial geniculate body for different retinal conditions. Shock amplitudes were 5 volts and 3 volts, respectively. In the experiments illustrated the rectangular pulses to the stimulating electrodes were 0.2 msec long. Averages of 64 responses for retinal conditions of dark adaptation, and of 32 responses for ischemia are shown. The set of responses averaged during ischemia was recorded approximately 30 sec after application of intraocular pressure. (Cat 82, midpontine pretrigeminal preparation.)

Figure XXII-2 illustrates the constancy of the average of shock-evoked responses from the auditory cortex while the responses from the visual cortex are enlarged during retinal ischemia. The same constancy of the averaged responses from auditory cortex is observed when the visual cortical responses are enlarged by diffuse illumination. Similar results were obtained from cats under nembutal anesthesia.

The relative enlargement of the responses in the visual cortex depends on the voltage of the shocks near threshold levels giving greatest increase in size. We did not seem to find a "maximal" response, in the sense that even for quite high levels of shock there was some enlargement, as illustrated in Fig. XXII-3.

The enlargement of responses was not equally great for shocks delivered to all regions of the lateral geniculate body. We consistently found enlargement when stimulating the posterior three-quarters of the lateral geniculate body, but it was entirely absent or hardly evident when we stimulated the anterior quarter. Figure XXII-4 illustrates this result. In this experiment electrodes were placed simultaneously in the anterior and posterior sections of the lateral geniculate body. Interleaved stimuli were presented and responses averaged separately for the two locations. The enlargement effects were also strong if the shock stimulus was delivered to the optic tract rather than to the lateral geniculate body. Presumably these shocks excite all of the lateral geniculate body including the posterior part.

A series of experiments was performed with flickering rather than steady illumination used. The beam of the illuminating lamp was mechanically chopped at a rate that was under the control of the experimenters, and with an approximate on-off ratio equal to 1. Since the light intensity and on-off ratio were held constant, the average intensity of illumination was constant for different flickering rates. Figure XXII-5 illustrates averages of the cortical responses to shocks to the lateral geniculate body for different rates of flicker. For flicker at a rate of 12/sec, the responses are smaller than the control responses obtained in the dark. As the flicker rate is increased the averaged responses gain in amplitude and finally reach maximum. Under conditions for which there is a large increase of the responses for illumination with steady light, there is an equally large increase for illumination with a high rate of flicker.

Our results lead us to make some suggestions about the mechanism of the enlargement of the early evoked response recorded from visual cortex. A first hypothesis might postulate that the activation of retinal units brought about by steady illumination would lower the threshold of the postsynaptic neurons of the lateral geniculate body. One would expect the greatest enlargement with light flickering at a low rate, for which the retina responds to each "on" and "off" of the flickering light (5). The experimental findings with flicker are in opposition to this interpretation.

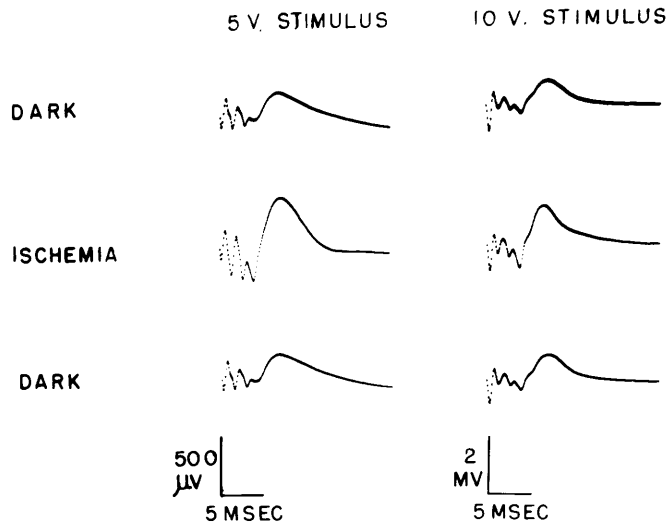

Fig. XXII-3. Enlargement of cortical responses to lateral geniculate body shocks for two shock amplitudes. Average of 64 responses for all records except for the middle left-hand column in which the average of 32 responses is shown. Note difference in amplitude calibration for the two columns. (Cat 82, midpontine pretrigeminal preparation.)

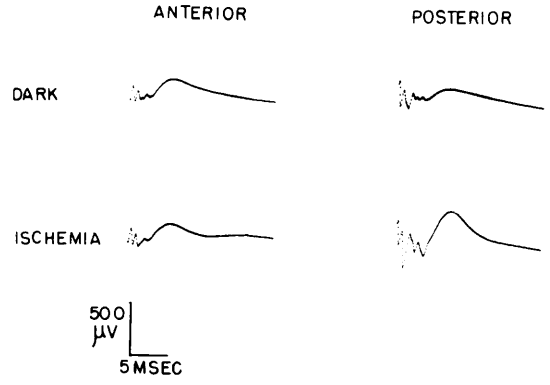

Fig. XXII-4. Illustration of lack of enlargement of responses from shocks to the anterior lateral geniculate body while there is a sizable enlargement for shocks to the posterior lateral geniculate body. Each waveform is the average of 64 responses. Shock amplitudes were 3 volts, anterior; 4 volts, posterior. (Cat 102, midpontine pretrigeminal preparation.)

According to an alternative hypothesis the enlargement of the evoked responses would be due to reduction or suppression of the afferent tonic activity originating in the retina. It would be assumed that this activity, the "dark discharge," exerts a depressant influence on the postsynaptic neurons (4).

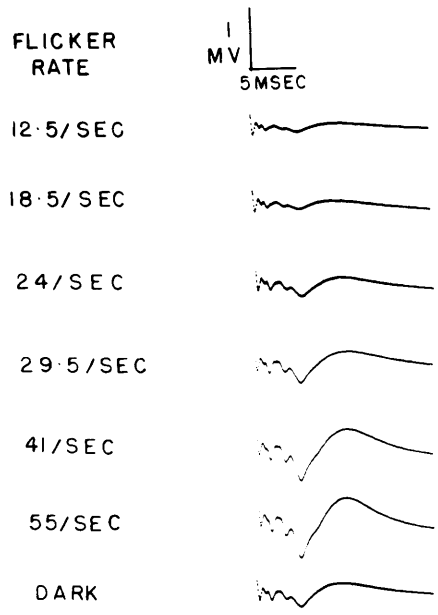

Fig. XXII-5. Evoked responses to lateral geniculate body shocks during retinal illumination by a diffuse flickering light. Illumination by a 30-watt tungsten filament lamp placed 50 cm from the cat's eyes at an angle of 60° to the line of sight. Each record is an average of 64 responses. Shock amplitude was 3 volts. (Cat 108, midpontine pretrigeminal preparation.)

Assuming an "inhibition" of the lateral geniculate body shock-evoked responses in the visual cortex by the dark discharge, we are led to ask whether this is inhibition in the Sherrington sense, or a reduction in the available responsive population as a result of refractoriness of neurons of the lateral geniculate body. The second explanation, which would imply the existence of phenomena of occlusion, would account for the striking reduction of the cortical responses to shocks delivered to the lateral geniculate body which is observed during low-rate flicker.

In the midpontine pretrigeminal preparation the pattern of spindling which follows retinal ischemia or illumination is a widespread phenomenon, while the enlargement of cortical responses to shocks delivered to thalamic nuclei seems directly related to events in the visual pathways. The evoked responses described

here occur within 50 msec of the shocks. There are later events in the evoked responses that seem more directly related to the general pattern of cortical activity. Study of these later events is in progress.

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(Prof. Arduini is a member of the Istituto di Fisiologia, Università di Pisa (Prof. Moruzzi, Director). Dr. Goldstein was Science Faculty Fellow of the National Science Foundation on leave from Massachusetts Institute of Technology while this research was carried out.)

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