CHANGES IN THE ORTHODROMIC AND ANTIDROMIC RESPONSE OF OPTIC TRACT DURING THE EYE MOVEMENTS OF SLEEP[1]

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PREVIOUS STUDIES HAVE SHOWN that for each rapid eye movement of low-voltage fast sleep there is a corresponding monophasic wave of 100–140 msec. in the lateral geniculate body of the cat (8). These waves do not depend upon the presence of the retina or the eye muscle afferents (5, 22). In fact, following either retinal photocoagulation of the optic disc or enucleation of the eyes, these geniculate slow waves persist unmodified for 3 days, grow smaller in the next 3–5 days, and then disappear after the sixth day (5, 22). Since the time course of wave disappearance correlates precisely with the time course of optic nerve degeneration following enucleation (25), it was suggested that optic tract terminals are involved in the genesis of lateral geniculate waves (5).

The experiments to be reported here were designed to test whether impulses going through the optic tract terminals and the lateral geniculate were modified as a consequence of changes taking place in the presynaptic terminals of the optic tract during the slow geniculate waves and the related eye movements. The findings indicate that depolarization of optic tract terminals and depression of transmission through the lateral geniculate occur during the appearance of these waves.

METHODS

Ten adult cats were used. Electrodes were chronically implanted under pentobarbital anesthesia in the optic tract, in the lateral geniculate body, and over the parietal and visual cortex. The EMG activity of the ocular muscles was recorded from wires inserted in the medial rectus muscles. The subcortical electrodes consisted of either three or four stainless steel wires (250 μ. diameter) insulated to the tips and kept together by varnish. The separation between the tips was approximately 1 mm. The positioning of the recording electrodes in the visual pathways was based on observation of responses to light flashes as well as responses to electrical pulses. After positioning, the electrodes were secured to the skull with dental cement, and connected to a Sheatz pedestal (24). A period of 1 week was allowed for recovery following electrode implantation. All experiments were carried out in a shielded cage, where the cats slept in complete darkness. The EEG was constantly monitored on a Grass polygraph. The geniculate waves appearing during low-voltage fast sleep (or the EMG from the ocular muscle) were amplified and led to a Schmitt trigger. The out-

[1] A preliminary note describing the result of these experiments has appeared (4). A report by other investigators, who independently arrived at results similar to those reported here, has recently been published (16).

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put taken from the Schmitt trigger was then fed into a Grass stimulator which delivered short pulses (10 μsec.) either to the optic tract or to the lateral geniculate. The use of the Schmitt trigger, together with appropriate stimulus delays, allowed stimuli to be initiated at various phases of the geniculate wave. The voltage of the optic tract stimulus (orthodromic) was adjusted so as to evoke the presynaptic and postsynaptic responses in the lateral geniculate due to activation of optic tract fibers of larger diameter. Stimuli of higher strength were not delivered in order to avoid the contamination of the postsynaptic geniculate response with the presynaptic spike due to the activation of fibers of smaller diameter.

The light flashes were given by means of a small neon bulb mounted on a translucent contact lens. The flashes were triggered either by the geniculate wave or the EMG of an eye muscle. The cats' pupils were routinely dilated with atropine or neosynephrine.

The orthodromic lateral geniculate and the antidromic optic tract responses to electrical stimulation in the lateral geniculate, as well as the light-evoked potentials, were displayed on a Tektronix 502 oscilloscope and photographed with a Grass model II camera.

At the end of each experiment, iron was electrolytically deposited at the electrode tips. The brain was then fixed *in situ* and removed for histological verification of electrode placement.

Results

Amplitude changes of the pre- and postsynaptic spike in the lateral geniculate during eye movements. Figure 1 shows an example of slow geniculate waves and their relationship with the EMG activity of an ocular muscle. When stimuli were delivered to the optic tract during the interval between these geniculate waves, the response recorded in the lateral geniculate consisted of an early diaphasic positive-negative wave. This first wave represents the arrival at lateral geniculate of the impulses traveling along the optic fibers (presynaptic spike). A negative postsynaptic wave then follows the presynaptic spike (Fig. 2, left) (2, 3, 21).

When stimuli were delivered to the optic tract during the occurrence of the geniculate waves, amplitude changes of the presynaptic as well as of the postsynaptic response were observed. The presynaptic spike remained unmodified during the first 10 msec. after the beginning of a geniculate wave, but subsequently showed a gradual decrease in amplitude. Maximum reduction of presynaptic spike amplitude (about 10%) was reached 20–30 msec. after the start of the geniculate wave (Fig. 2, Table 1). Later, in the

FIG. 1. Lateral geniculate slow waves are recorded in the upper trace and the EMG of the medial rectus in the lower one. Voltage calibration 100 μV.

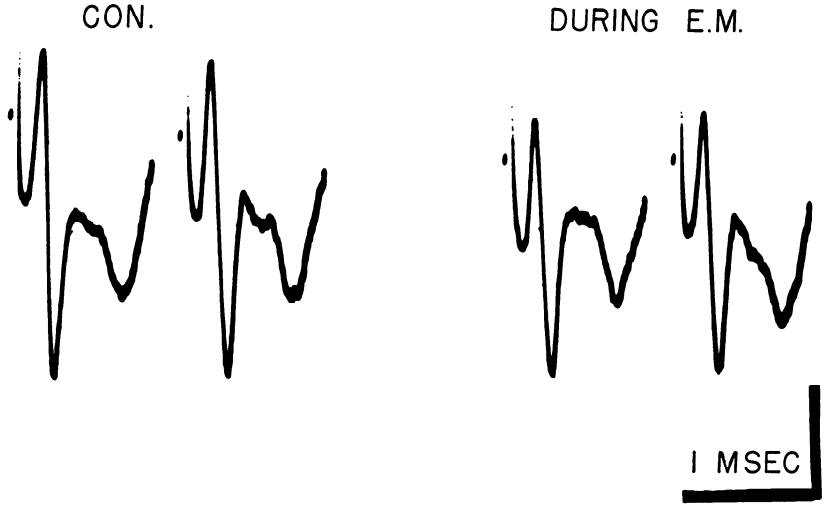

FIG. 2. Four geniculate responses following single shocks to the optic tract. The diphasic positive-negative wave represents the presynaptic spike; the wave following it represents the postsynaptic potential (negativity down). CON. = control; E.M. = eye movements. Voltage calibration 100 μV.

following 40 msec., a gradual recovery of the presynaptic spike occurred. Although the reduction of the presynaptic spike was observed throughout the entire lateral geniculate nucleus (dorsal part), the greatest effect was recorded from those electrodes which were in the region where the slow geniculate waves reached their maximal amplitude (7).

In order to study the changes of the postsynaptic response in the lateral geniculate, trains of three stimuli (0.1 msec. 300/sec.) were delivered to the optic tract during eye movements and for control purposes in the intervals between eye movements. The postsynaptic responses elicited by these trains in these two stages were then compared. It was found in general that the postsynaptic response to the first of the three pulses delivered during eye movements showed an increase or no change in spite of the clear decrease of the presynaptic spike (Fig. 2, right; and Fig. 3, left column, first and second train from the bottom). However, in those instances when the presynaptic spike was considerably reduced, the postsynaptic wave also showed a clear reduction (Fig. 3, left column).

Table 2 indicates the mean amplitude of the first postsynaptic wave. The second postsynaptic response showed a tendency to decrease and the third was found to be significantly reduced ($P = <.01$) when compared with the responses recorded in the intervals between the eye movements (Table 2).

Augmentation of antidromic optic tract response following lateral geniculate stimulation during eye movements. The excitability of optic tract terminals in the lateral geniculate body was tested by recording the antidromic response in the chiasma to lateral geniculate stimulation during the rapid eye move-

ments; stimulus again being triggered either by lateral geniculate waves or by the EMG of the eye muscle via the Schmitt trigger. Figure 4 (left) shows an example of an antidromic response recorded in the optic tract during the intervals between eye movements. The shape and the size of this antidromic response did not change when a brief 300/sec. train of stimuli was delivered to the lateral geniculate. The response was composed of two deflections, which suggests that the lateral geniculate stimulation activated two groups of fibers with different conduction velocities. When the same stimulus was delivered during eye movements, the antidromic response revealed an augmentation lasting 60 msec. This augmentation started 10

Table 1. Amplitude of presynaptic spike

	I. Presyn. Spike		II. Presyn. Spike		III. Presyn. Spike	
	Mean	SD	Mean	SD	Mean	SD
Cat 1						
During E.M.	245	15	246	7	241	6
Control, between E.M.	278	11	261	5	260	11
Cat 2						
During E.M.	271	16	214	15	263	12
Control, between E.M.	303	11	241	12	295	14
Cat 3						
During E.M.	236	6	185	10	236	11
Control, between E.M.	274	9	210	9	265	8

Train of three stimuli delivered to the optic tract during eye movements and in the intervals between eye movements. Mean amplitude of the first, second, and third presynaptic spikes and their standard deviations. Each value represents the mean of 30 presynaptic spikes. The differences are statistically significant ($P = <.01$). SD = standard deviation. E.M. = eye movement.

msec. after the beginning of an eye movement and reached a peak 25–35 msec. later, and involved the first as well as the second deflection (Fig. 5).

Change of photically evoked responses in the visual pathways during eye movements. The evoked response to light was recorded in the optic tract, in the lateral geniculate, and in the visual cortex. Whenever the EMG of an eye muscle or the slow geniculate wave was used to trigger a flash of light the evoked response was found to be reduced in the lateral geniculate and in the visual cortex, but unchanged in the optic tract (Fig. 6). The time course of the reduction was about 40 msec. and the decrease in amplitude during eye movements varied between 20–40%. These results confirm previous observations by Mouret *et al.* (23). No variation of light intensity was attempted in the course of these experiments.

Discussion

The form of the potentials recorded in the lateral geniculate following optic tract stimulation appears to be comparable to those reported by other

authors (2, 3, 21). There is general agreement in the interpretation of the waves of Fig. 2, namely, the first positive-to-negative potential indicates the arrival of impulses in the optic tract terminals (presynaptic spike), while the second negative wave corresponds to the postsynaptic response (2, 3, 21).

In the first part of the DISCUSSION the significance of the decrease of the presynaptic spike and the increase of the antidromic response during rapid eye movements will be examined. Later, the depression of transmission through the lateral geniculate will be considered.

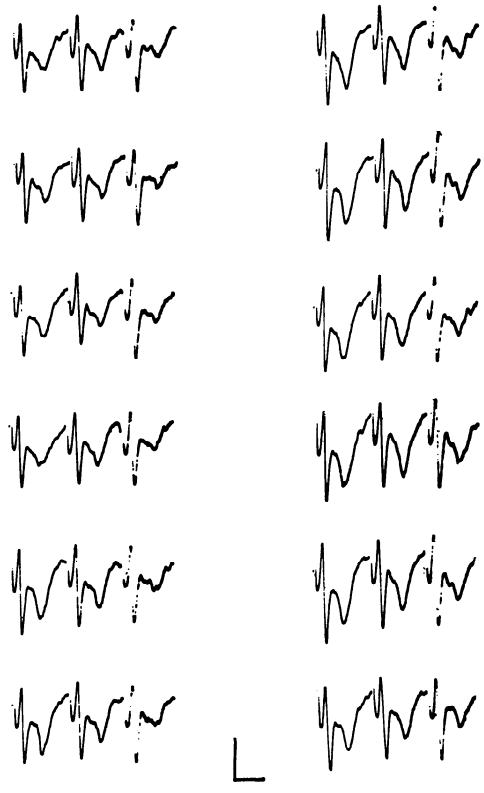

FIG. 3. Groups of three geniculate responses following a brief high-frequency train (0.1 msec., 300/sec.) to the optic tract during eye movements (left column) and control (right column). The train was delivered 15 msec. after the beginning of an eye movement. Voltage calibration 100 μV. Time calibration 1.6 msec.

The reduction of the presynaptic spike in the lateral geniculate following orthodromic stimulation during geniculate waves can be interpreted as a sign of optic tract terminal depolarization. There is direct evidence, obtained by recording from inside the presynaptic component of the giant synapse of the squid, that spike amplitude is reduced by the application of currents which depolarize the axon (14). Furthermore, it has been found that electric depolarization of the spinal cord decreases the spike potential recorded from the primary afferent fibers (11). Alternatively, it is conceivable that the decrease of the presynaptic spike observed in our experiments during rapid eye movements might be due to a reduction in the number of fibers activated by

Table 2. Amplitude of postsynaptic spike

	I. Postsyn. Spike		II. Postsyn. Spike		III. Postsyn. Spike	
	Mean	SD	Mean	SD	Mean	SD
Cat 1						
During E.M.	71	17	44	9	22	8
Control, between E.M.	78	15	51	6	32	9
Cat 2						
During E.M.	59	15	42	10	20	7
Control, between E.M.	67	12	58	9	36	8
Cat 3						
During E.M.	65	12	30	7	15	5
Control, between E.M.	60	12	41	8	26	4

Train of three stimuli delivered to the optic tract during eye movements and in the intervals between eye movements. Mean amplitude of the first, second, and third postsynaptic waves. Each value represents the mean of 30 postsynaptic waves. The differences for the third postsynaptic wave are significant ($P = <.01$). SD = standard deviation. E.M. = eye movement.

the optic tract shock. In order to decide between these two alternatives, the excitability of optic tract terminals was tested with the method of antidromic stimulation (29). Since the antidromic response from the optic tract to stimulation of the lateral geniculate during rapid eye movements gave rise to a larger response, a larger number of fibers must have been activated. It is known, in fact, that when an electric pulse is delivered to nerve terminals during axonal depolarization, more fibers will respond (29). This finding rests on the notion that whenever a depolarization of nerve membrane occurs,

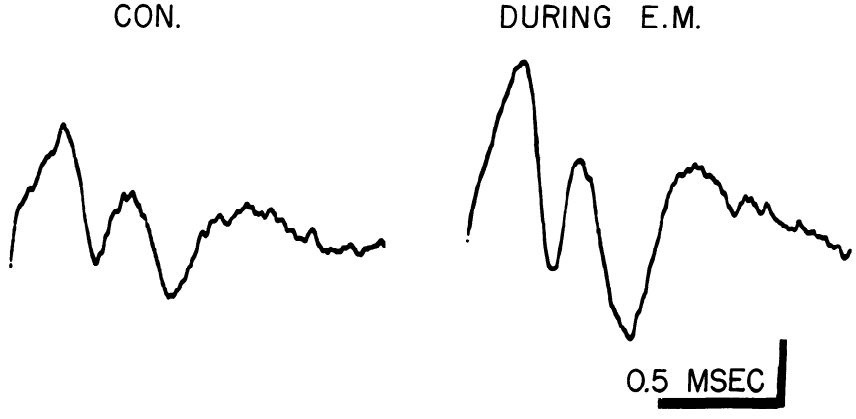

FIG. 4. On the left, the antidromic response of the optic tract following a shock to the lateral geniculate delivered in the intervals between eye movements. On the right is shown the antidromic response following an identical shock to the geniculate during eye movements (positivity up, negativity down). CON. = control; E.M. = eye movement. Voltage calibration 50 μV.

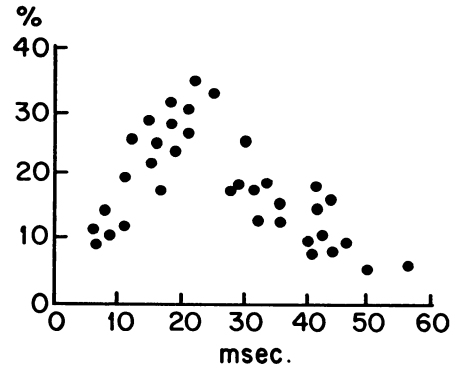

FIG. 5. Time course of the per cent change in amplitude of the first component of the antidromic optic tract responses. Each dot is an average of five responses at various times after the start of an eye movement. These data represent findings from three animals.

there is a corresponding decrease in the threshold for electrical excitation (12, 20).

Summing up, it can be concluded that both the reduction of the presynaptic spike in the lateral geniculate following orthodromic stimulation as well as the increase of optic tract antidromic response during rapid eye movement indicate a depolarization of optic nerve terminals.

Depression of transmission through the lateral geniculate during eye movements. In previous studies it has been shown that the EPSP of nerve cells set up by an afferent volley is diminished when the presynaptic membrane potential is displaced in the depolarizing direction (11, 14, 27). In our experiment we did not investigate the EPSP of geniculate neurons; we have only the postsynaptic gross response as an indication of the activity of geniculate neurons. The results show that during depolarization of the optic tract terminals some postsynaptic responses are depressed, namely, the second

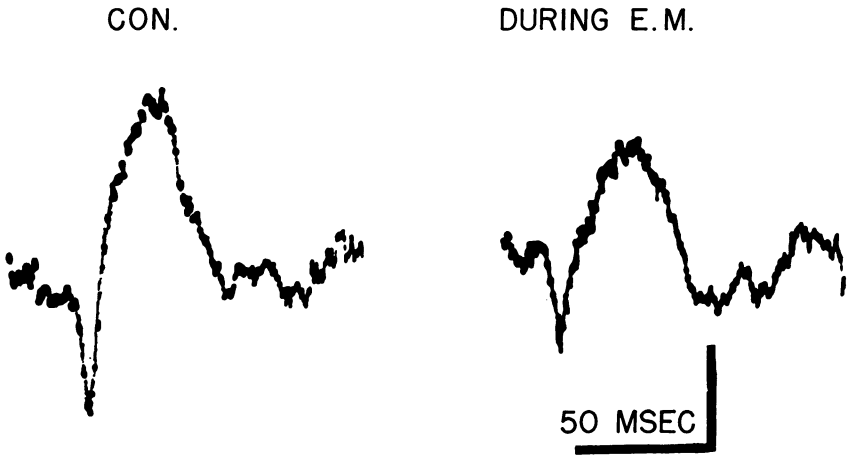

FIG. 6. On the left, the response to a flash of light recorded from the lateral geniculate in the intervals between eye movements. On the right, a similar flash of light was delivered during eye movements. CON. = control; E.M. = eye movement. Voltage calibration 100 μV.

and the third, while the postsynaptic response to the first stimulus of a train showed no change or an actual increase. It is difficult, at the present time, to interpret this differential behavior of the postsynaptic responses.

A less equivocal sign of depressed geniculate transmission is provided by the reduction in amplitude of the light-evoked response in the geniculate, but not in the optic tract, during eye movements. In spite of this association between depolarization of the presynaptic terminals and depressed transmission, it is impossible to say that the depolarization of the optic tract terminals is entirely responsible for the depressed transmission through the lateral geniculate. Indeed, since we did not record the membrane potential of the geniculate neurons we cannot rule out the hypothesis that a reduction of postsynaptic excitability might occur in geniculate neurons and be responsible, at least in part, for the depressed transmission.

Although these experiments do not provide any indication of the origin of the impulses inducing depolarization of the optic tract terminals, it is of interest to point out that during rapid eye movements of sleep there are functional connections between the oculomotor regions of the pons and mesencephalon and the lateral geniculate (6). It has also been reported recently that the slow geniculate waves depend critically on brain-stem pathways (15). The brain stem, however, might not be the only source for these impulses since electrical stimulation of the visual cortex has been shown to induce an increase in excitability of optic nerve terminals in the pretrigeminal cat (1), as well as paralyzed animals (17). Regardless of the region from which the impulses which depolarize optic tract terminals might originate, it should be pointed out that there is anatomical evidence indicating the presence of axoaxonic synapses in the lateral geniculate (26). This finding, together with our results on optic tract terminal depolarization during eye movements, raises the question of whether our data indicate the occurrence of presynaptic inhibition. The occurrence of this type of inhibition is inferred from a decreased EPSP in association with presynaptic depolarization (10, 13). From the considerations above it is clear that further investigations are needed in order to clarify the events occurring at the postsynaptic membrane of a geniculate neuron during optic tract depolarization. At the present time, therefore, the hypothesis of presynaptic inhibition can only be suggested.

In conclusion, it might be of interest to mention that psychophysiological investigations have indicated that, in man, visual thresholds are substantially elevated during rapid eye movements (9, 18, 19, 28). Since the impairment of vision occurs also when the effect of retinal blur is minimized, the existence of a central inhibitory mechanism has been postulated (28). Therefore, although our results have been found in the cat during the rapid eye movements of sleep, the hypothesis can be put forward that the same mechanism might account for the decreased visual perception during voluntary eye movements.

SUMMARY

1. Electrical stimuli delivered to the optic tract during rapid eye movement sleep gave rise to presynaptic and postsynaptic responses in the lateral geniculate. When these stimuli were given during the eye movements, the amplitude of the presynaptic spike was found to be decreased.

2. The antidromic response recorded in the optic tract to lateral geniculate stimulation showed an augmentation during eye movements.

3. The flash-evoked responses were found to be reduced in the lateral geniculate and in the visual cortex, but unchanged in the optic tract during the eye movements.

4. The reduction of the optic tract orthodromic response and the increase of the optic tract antidromic response, together with the changes in the flash-evoked responses, may indicate the occurrence of presynaptic inhibition during the rapid eye movements of sleep.

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REFERENCES

1. ANGEL, A., MAGNI, F., AND STRATA, P. Excitability of intrageniculate optic tract fibers after reticular stimulation in the mid-pontine pretrigeminal cat. *Arch. ital. Biol.*, 1965, *103:* 668–693.
2. BISHOP, G. H. AND O'LEARY, J. L. Factors determining the form of the potential record in the vicinity of the synapses of the dorsal nucleus of lateral geniculate body. *J. cell. comp. Physiol.*, 1942, *19:* 315–331.
3. BISHOP, P. O. Synaptic transmission—an analysis of the electrical activity of the lateral geniculate nucleus in the cat after optic nerve stimulation. *Proc. roy. Soc., Ser. B*, 1953, *141:* 362–392.
4. BIZZI, E. Changes in the orthodromic and antidromic response of optic tract during the eye movements of sleep. *Physiologist*, 1965, *8:* 113.
5. BIZZI, E. AND BOLLER, F. The effect of retinal photocoagulation on lateral geniculate deep sleep waves. *Arch. ital. Biol.* In press.
6. BIZZI, E. AND BROOKS, D. Functional connections between pontine reticular formation and lateral geniculate nucleus during deep sleep. *Arch. ital. Biol.*, 1963, *101:* 666–680.
7. BROOKS, D. C. Localization of lateral geniculate nucleus potentials during the "deep" phase of sleep. *Anat. Rec.*, 1964, *148:* 264.
8. BROOKS, D. C. AND BIZZI, E. Brain stem electrical activity during deep sleep. *Arch. ital. Biol.*, 1963, *101:* 648–665.
9. DITCHBURN, R. W. Eye movement in relation to retinal action. *Opt. Acta*, 1955, *1:* 171–176.
10. ECCLES, J. C., ECCLES, R. M., AND MAGNI, F. Central inhibitory action attributable to presynaptic depolarization produced by muscle afferent volleys. *J. Physiol.*, 1961, *159:* 147–166.
11. ECCLES, J. C., KOSTYUK, P. G., AND SCHMIDT, R. F. The effect of electric polarization of the spinal cord on primary afferent fibres and their monosynaptic excitatory action. *J Physiol.*, 1962, *162:* 138–150.
12. EISENMAN, G. AND RUDIN, D. O. The compound origin of potential in a stimulated dorsal root. *J. gen. Physiol.*, 1954, *37:* 781–793.
13. FRANK, K. AND FUORTES, M. G. F. Presynaptic and postsynaptic inhibition of monosynaptic reflexes. *Fed. Proc.*, 1957, *16:* 39.

14. HAGIWARA, S. AND TASAKI, I. A study of the mechanism of impulse transmission across the giant synapse of the squid. *J. Physiol.*, 1958, *143:* 114–132.
15. HOBSON, J. A. The effect of chronic brain stem lesions on cortical and muscular activity during sleep and waking in the cat. *Electroenceph. clin. Neurophysiol.*, 1965, *19:* 41–62.
16. IWAMA, I. AND SAKAKURA, H. Impulse transmission in cat lateral geniculate and so-called deep sleep wave. *Proc Japan Acad.*, 1965, *41:* 499–502.
17. IWAMA, K., SAKAKURA, H., AND KASAMATSU, T. Presynaptic inhibition in the lateral geniculate body induced by stimulation of the cerebral cortex. *Jap. J. Physiol.*, 1965, *15:* 310–322.
18. LATOUR, P. L. Visual threshold during eye movements. *Vision Res.*, 1962, *2:* 261–262.
19. LETTVIN, J. Y. Research Laboratories of Electronics, M. I. T. Quarterly Progress Report, July, 1960.
20. LORENTE DE NÓ, R. A study of nerve physiology. *Stud. Rockefeller Inst. med. Res.*, 1947, pp. 131–132.
21. MARSHALL, W. H. Excitability cycle and interaction in geniculate-striate system of cat. *J. Neurophysiol.*, 1949, *12:* 277–288.
22. MOURET, J. *Les mouvements oculaires au cours du sommeil paradoxal* (Thesis). University of Lyon, 1964.
23. MOURET, J., JEANNEROD, M., AND JOUVET, M. L'activite electronique du systeme visuel au cours de le phase paradoxale du sommeil chez le chat. *J. Physiol., Paris,* 1963, *55:* 305–306.
24. SHEATZ, G. C. Multilead techniques for large and small animals. In: *Electrical Stimulation of the Brain,* edited by D. E. Sheer. Austin, Univ. of Texas Press, 1961, pp. 45–50.
25. SMITH, J. M., O'LEARY, J. L., HARRIS, A. B., AND GAY, A. J. Ultrastructural features of the lateral geniculate nucleus of the cat. *J. comp. Neurol.*, 1964, *123:* 357–378.
26. SZENTÁGOTHAI, J. The structure of the synapse in the lateral geniculate body. *Acta anat.*, 1963, *55:* 166–185.
27. TAKEUCHI, A. AND TAKEUCHI, N. Electrical changes in pre- and postsynaptic axons of the giant synapse of *Loligo. J. gen. Physiol.*, 1962, *45:* 1181–1193.
28. VOLKMANN, F. Vision during voluntary saccadic eye movements. *J. opt. Soc. Amer.*, 1962, *52:* 571–578.
29. WALL, P. D. Excitability changes in afferent fibre terminations and their relation to slow potentials. *J. Physiol.*, 1958, *142:* 1–21.