

# DISCHARGE PATTERNS OF SINGLE GENICULATE NEURONS DURING THE RAPID EYE MOVEMENTS OF SLEEP<sup>1</sup>

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SEVERAL RECENT STUDIES HAVE SHOWN that sleep with EEG slow waves is periodically interrupted by brief episodes of sleep with low-voltage fast EEG activity and rapid eye movements (REMs) (7, 8, 18, 19). During these episodes, single waves or groups of two to three waves appear in the lateral geniculate body in association with the REMs (6, 21). Each wave has an amplitude of 100–200  $\mu$ V., a duration of about 150 msec., and is predominantly monophasic (6). During sleep with REMs the monophasic waves appear synchronously in both geniculates (3, 23). It has recently been found that depolarization of optic tract terminals lasting about 150–200 msec. occurs during the monophasic geniculate waves (2, 17). Thus, the REMs of sleep are associated both with a change in polarization of optic tract terminals and with a monophasic wave in the lateral geniculate. The present experiment was performed in order to study the discharge of geniculate neurons while these two events are taking place. The findings indicate that the majority of geniculate neurons fire impulses in bursts during REM sleep and that the monophasic wave appearing in the lateral geniculate during the REM is correlated with this unitary discharge. These findings were obtained both in intact cats and in cats whose eyes had been enucleated.

## METHODS

Ten cats were used in this study. Under Nembutal anesthesia, electrodes for recording EEG were placed over the parietal cortex and EMG electrodes were implanted in the posterior cervical muscles. Screws for recording eye movements were fixed to the orbital surface of the frontal bone after opening the frontal sinus. A cylindrical base was cemented to the bone in the midline and during the recording session a hydraulic microdrive carrying a stainless steel microelectrode was mounted on this base (5, 11). The microelectrodes were made from 130- $\mu$ -diameter of stainless steel wire which was electrolytically sharpened to a tip size of 3–4  $\mu$ . and insulated with Insulex up to the tip. Unit recording was begun 3 days after the implantation of the electrodes. During the experimental sessions the cat was kept in a small box. Fifty-three units were recorded from the lateral geniculate of intact cats. All of these units were clearly affected by retinal illumination which induced "on," "off," or "on-off" discharges. After the effect of the light was determined, the cat was kept in complete darkness during the entire recording time to avoid retinal stimulation. Twelve units were recorded from two cats following bilateral enucleation of eyes and extraocular muscles. Several units considered in this paper were held for long periods of time in order to observe

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their pattern of discharge during at least two episodes of REM sleep. Units lost during this phase of sleep or without an adequate period of recording during synchronized sleep were not utilized. Records of EEG, EMG, and ocular activity were taken with a Grass polygraph. Unit activity and the slow geniculate waves which were recorded with the same electrode were displayed on an oscilloscope after appropriate filtering, and photographed on a Grass kymograph camera. Electrolytic lesions were made at the end of the experiment and serial sections were made in order to determine the location of the units. The cells considered in this paper were found in each of the three geniculate layers.

## RESULTS

*Activity of single geniculate units during rapid eye movement sleep in intact cats.* The temporal relationship between the wave pattern in the lateral geniculate and the other manifestations of REM sleep is shown in Fig. 1. The first sign, heralding the onset of an episode of REM sleep, was invariably the appearance of waves in lateral geniculate (Fig. 1A); after a variable delay of 20–90 sec. the cortical and EMG signs developed (Fig. 1B). Figure 2 gives a more detailed example of the monophasic geniculate waves and their relationship with the EMG of an extraocular muscle.

When the intact cats passed from synchronized sleep into rapid eye movement sleep, the majority of geniculate cells (68%) fired impulses in bursts which were synchronous with the geniculate waves. Each burst began at the

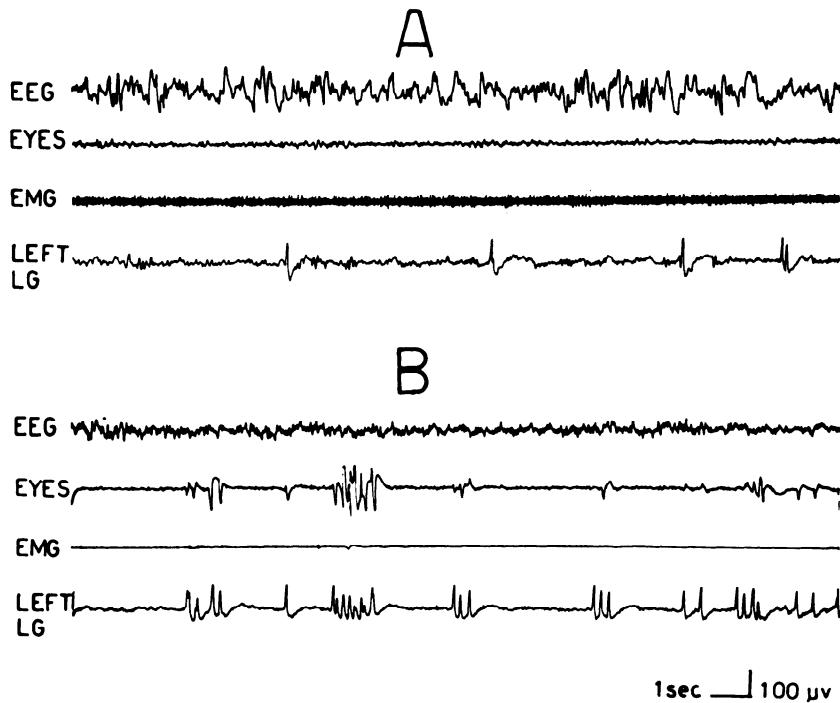


FIG. 1. Temporal relationship between the geniculate waves and the other manifestation of REM sleep. A: single geniculate waves appearing 40 sec. before EEG desynchronization; B: fully developed REM sleep. EMG = electrical activity of neck muscles.

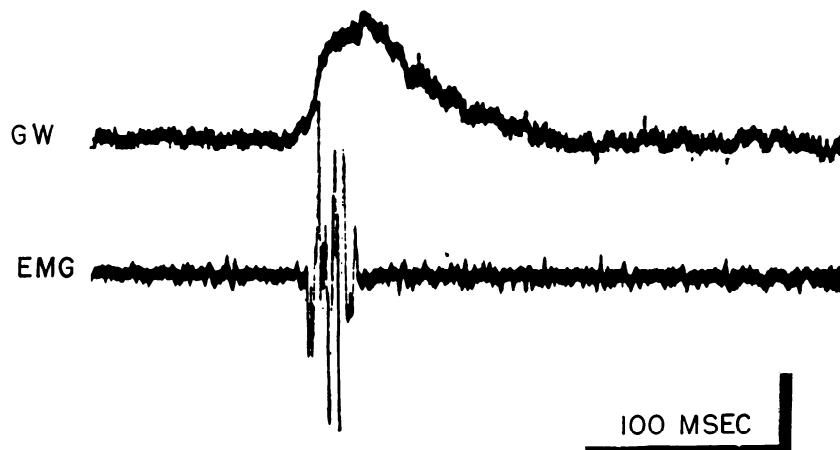


FIG. 2. Lateral geniculate slow wave in the upper trace and the EMG of the medial rectus in the lower one. Voltage calibration: 100  $\mu$ V.

peak of the wave or immediately after it and continued on the descending phase of the wave for about 100 msec. On the rising phase of the geniculate wave there was a silent period of about 15–20 msec. (Fig. 3C). This pattern of pause and burst replaced the firing in brief high-frequency clusters which occurred during synchronized sleep (Fig. 3A) (16). In general, the firing rate and the discharge patterns of geniculate units were constant for a given cell

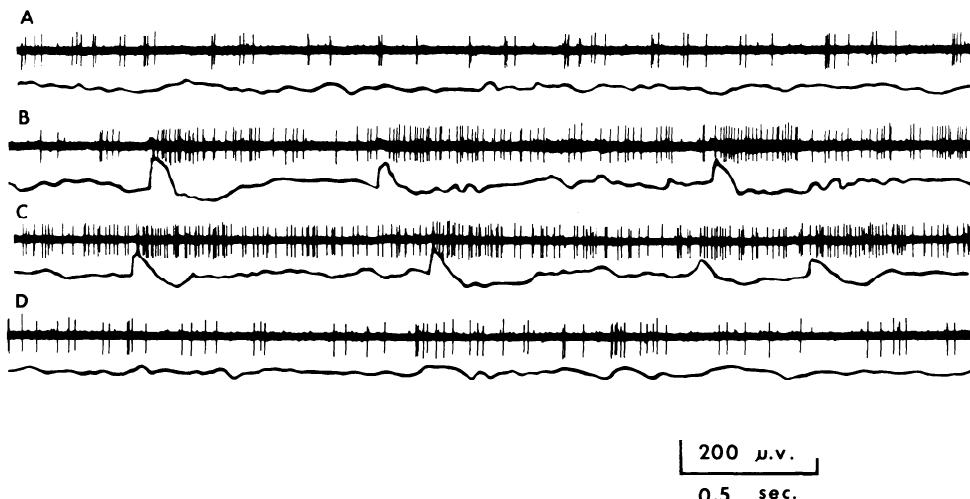


FIG. 3. Single unit activity recorded from the lateral geniculate during natural sleep. In all the records, the upper trace corresponds to unit activity, the lower one to the slow geniculate activity recorded with the same electrode after appropriate filtering. Record A obtained during synchronized sleep; B, just before the beginning of the cortical manifestation of REM sleep; C, during REM sleep; D, quiet waking. Voltage calibration: left vertical bar refers to slow activity; right vertical bar to units.

from one episode of rapid eye movement sleep to the next. Furthermore, regardless of whether on-, off-, or on-off-units were observed, the same change in discharge pattern and in the rate of firing occurred during rapid eye movement sleep. The frequency within each burst varied between 80–140 spikes/sec., and for a given cell it approached the firing rate seen after presentation of a light stimulus. It was also observed that a burst of unitary discharge was clearly correlated with the monophasic waves which, as shown in Fig. 1A, appeared 20–90 sec. before the electroencephalographic and electromyographic signs of REM sleep (Fig. 3B).

In 12% of geniculate neurons in this sample a phasic decrease in the

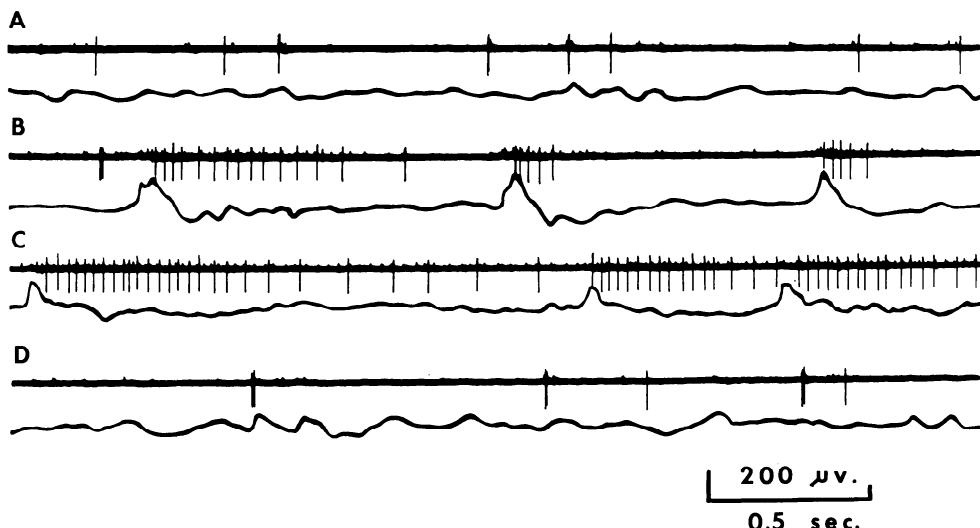


FIG. 4. Activity of single geniculate neuron during REM sleep in a bilaterally enucleated cat. Upper trace corresponds to unit activity; the lower one to the slow geniculate activity. A, synchronized sleep; B and C, REM sleep; D, quiet waking. Voltage calibration: left vertical bar refers to slow activity; right vertical bar to units.

firing rate took place during REM sleep. The appearance of each monophasic wave was accompanied by a transitory arrest in the spontaneous activity of the geniculate units. On-, off-, and on-off-cells were all represented in this group. Ten per cent of cells did not show any kind of correlation with geniculate waves, but there was a slight increase in their firing rate during REM sleep. The remaining 10% of cells exhibited neither a change in their discharge pattern during geniculate waves nor in their spontaneous firing rate during the transition from synchronized to desynchronized sleep.

*Activity of single geniculate neurons during rapid eye movement sleep in bilaterally enucleated cats.* Since the EEG and the EMG of neck muscles were constantly monitored during each experimental session, it was possible to identify the episodes of REM sleep in cats without eyes or extraocular muscles. In addition, the geniculate waves, which represent an electrical event

highly correlated with the REM (Figs. 1 and 2), could also be recorded for a few days following bilateral enucleation because they are not dependent upon the presence of the retina or the eye muscles (3, 23). Therefore, the activity of geniculate units in the blind cats was recorded, as before enucleation, in relation with the monophasic waves. During REM sleep 11 of these cells showed the same characteristic changes as described for the units of intact cats, i.e., a burst of impulses correlated with geniculate waves (Fig. 4, B and C). In one cell an arrest of this spontaneous activity took place during the monophasic waves.

#### DISCUSSION

*Significance of phasic increase of unitary activity occurring in the lateral geniculate during rapid eye movement of sleep.* The results of the present investigation show that when recordings are made in complete darkness the majority of geniculate neurons fire impulses in bursts which begin 15–20 msec. after the initiation of an eye movement and its related monophasic geniculate wave. Since the phasic increase in the discharge of geniculate neurons was present not only in the intact but also in the blind cats, this activation cannot be the result of a modulation of tonic, retinofugal discharges and must therefore be a consequence of an extraretinal input which is timed to occur during a rapid eye movement. Furthermore, these bursts of unitary discharge cannot be the result of afferent discharges from eye muscle proprioceptors because the extrinsic ocular muscles were carefully dissected and removed from the blinded cats.

It is well known that during REM sleep there are phasic changes in the muscular activity (8, 13). It might therefore be assumed that the geniculate bursts are a consequence of exteroceptive or proprioceptive stimulation produced by the myoclonic twitches impinging first on the reticular formation and from there upon the lateral geniculate. It does not appear probable, however, that this assumption is correct. In fact, if exteroceptive and proprioceptive impulses could activate the neurons in the lateral geniculate then these ascending impulses would not reach the lateral geniculate in perfect synchrony with the REMs—a synchrony shown by the close correlation between an eye movement, the related slow geniculate wave, and the unit discharge. Furthermore, since there are myoclonic twitches which occur without relationship to the REM (and vice versa) (13), the assumption that myoclonic twitches led to geniculate unit discharge would imply that we should have recorded bursts of unitary activity independent of the geniculate wave and the associated REM. Since this was not observed, it follows that it is highly unlikely that the phasic activation of geniculate neurons is the consequence of exteroceptive or proprioceptive impulses.

Alternatively, the hypothesis can be put forward that the phasic discharges of lateral geniculate neurons are the result of the activity of oculomotor centers located either in the cortex or in the brain stem, or in both. Indeed, there is some evidence that the oculomotor centers of the pons and the

mesencephalon might be functionally connected with the lateral geniculate during REM sleep (4). A possible anatomical basis for this connection is seen in those Golgi studies which have indicated that reticular axons give off collaterals which terminate in the lateral geniculate (25). Furthermore, it has been shown that a change of the animal's state of arousal (1, 16) as well as electrical stimulation of the reticular formation can modify the discharge of geniculate neurons (24, 27, 32). It has also been found that the monophasic geniculate waves which are associated with bursts of unitary discharge in the majority of geniculate units 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 the firing rate of geniculate neurons (31).

Regardless of the region from which the extraretinal input to lateral geniculate might originate, it can be proposed that the lateral geniculate represents a region of visual-motor integration. It might be argued, of course, that the proposed integration represents a peculiarity of the eye movements of sleep—in some relation with the image-forming mechanism of dreams (22). On the other hand, the type of visual-motor integration under discussion might occur, perhaps in a more subtle and selective form, during the eye movements of the waking animal. If this were the case, the extraretinal input reaching the geniculate neurons would represent a case of a central discharge impinging on the visual system simultaneously with the efferent discharge which gives rise to an eye movement. The existence of such "corollary" central discharges has been postulated in order to account for the perceptual constancy of the environment during eye movements (26, 28).

*Relationship between activity of geniculate neurons and the occurrence of depolarization of optic tract terminals.* It has recently been shown that within 10–15 msec. following the beginning of the REM there is a decrease in the amplitude of the presynaptic component of the lateral geniculate response to electrical stimulation of the optic tract (2, 17). Associated with this reduction of presynaptic spike amplitude there is a facilitation of the antidromic optic tract response to lateral geniculate stimulation (2, 17). Both of these findings are consistent with the occurrence of a depolarization of optic tract terminals (2, 17). The depolarization of presynaptic terminals is generally regarded as a consequence of the repetitive firing of interneurons (9, 30). Since in our experiment the majority of geniculate neurons were found to increase their firing rate after the beginning of an eye movement, and since the average time course of a burst of unitary activity correlates rather well with the time course of optic tract terminal depolarization associated with the REMs, the hypothesis might be put forward that some of the units showing bursts of discharge with REMs were interneurons responsible for presynaptic depolarization. In the present study it is impossible to state what fraction (if any) of the 53 units were interneurons. However, several indirect lines of evidence suggest that a considerable proportion of these 58 units were the principal cells of the lateral geniculate. The points which favor this assumption are:

tion are: 1) the principal cells are larger and should be picked up more easily by the microelectrode; 2) the units recorded had responses to retinal illumination which are generally thought to arise in the principal cells; and 3) during REM sleep, single units in the visual cortex show discharges which are related to the activity of extraocular muscles in a manner very similar to that found in this experiment (10, 29). While it is possible that the visual cortex neurons might be activated by extrageniculate inputs (20), it seems more plausible to consider the discharge of neurons in the visual cortex as a consequence of the geniculate bursts.

In order to interpret the simultaneous occurrence of phasic discharges of what will be assumed to be the principal cells of the lateral geniculate and the depolarization of optic tract terminals, it may be useful to consider an analogous situation in the spinal cord. It was recently shown that during the myoclonic twitches of extremities which are present during REM sleep, there is presynaptic depolarization of primary afferent fibers simultaneously with an increased discharge of spinal motoneurons induced by descending reticular spinal volleys (14). Evarts (12), commenting on these findings, has proposed that presynaptic inhibition in this situation might represent a mechanism allowing for a partial uncoupling of the spinal motoneuron from segmental reflex control without depressing its postsynaptic excitability. If this line of thinking is extended to our findings in the lateral geniculate, it might be suggested that depolarization of optic tract terminals during the eye movements of sleep might decrease the amount of retinal activity impinging on geniculate neurons without depressing their excitability, because an extraretinal input, possibly from oculomotor centers (inducing the cell discharge shown in Fig. 3, *B* and *C*), must be relayed by the geniculate units.

Future investigations will reveal whether the simultaneous appearance of optic tract depolarization and the phasic increase in activity of geniculate neurons found during REM sleep occurs during the voluntary eye movements of waking as well.

#### SUMMARY

1. Using a microelectrode technique, records were obtained from 53 units in the lateral geniculates of 10 unrestrained cats. Sixty-eight per cent of the units fired impulses in bursts during REM sleep. Twelve per cent of geniculate cells decreased their firing rate.

2. Monophasic waves appearing in the lateral geniculate body during the REM phase of sleep have been correlated with the unitary discharge. Similar results were obtained in blind cats.

3. The phasic increase in the discharge of geniculate neurons is considered to be the consequence of an extraretinal input timed to occur during a rapid eye movement of sleep.

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