

VESTIBULAR INFLUENCES DURING SLEEP

IV. FUNCTIONAL RELATIONS BETWEEN VESTIBULAR NUCLEI AND LATERAL GENICULATE NUCLEUS DURING DESYNCHRONIZED SLEEP¹

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INTRODUCTION

During desynchronized sleep a distinctive electrical pattern appears in different brain stem and cortical structures. This pattern consists of erratic monophasic potentials 100-300 μ V in amplitude, about 100 msec or less in duration, often grouped in bursts of 2 to 6 waves occurring at the frequency of about 7-8/sec. Described originally in the pontine reticular formation (62, 64, 63, 27, 55, 74, 78, 52, 58), these potentials have been found also at the level of the lateral geniculate nucleus (LGN) (76, 15, 25, 43, 24, 74, 78, 52, 58, 94, 104), of the superior colliculus (25, 74, 78), of the parietal (46) and visual cortices (79, 74, 75, 78, 52, 80, 104). As described first by Bizzi and Brooks (15), and later confirmed by Michel *et al.* (74) they occur synchronously in the pontine reticular formation and the LGN. The increase in the rate of discharge of single units recorded

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from the lateral geniculate nucleus (12; cf. 9) and the visual cortex (38, 39, 103, 102) during desynchronized sleep are likely to represent, in part at least, the microelectrode counterpart of the potential oscillations recorded with macroelectrodes.

Although the pontine and geniculate potentials mentioned above can precede electrocortical desynchronization and the disappearance of neck muscular activity by several tenths of seconds (25, 74), thus representing the first electrical sign of the appearance of desynchronized sleep, a striking time relation has been found between the bioelectric phenomena in the ponto-geniculo-visual system and the bursts of rapid eye movements (REM: 33) which characterize the desynchronized phase (15, 25, 74, 75, 103, 102). The erratic LGN waves, however, do not depend upon "on" and "off" discharges originating from the retina during the bursts of REM, nor are they due to proprioceptive reverberation originating from the extrinsic eye muscles, since they are present i) in complete darkness, ii) after total retinal inactivation (79, 11, 12, 52, 53), and iii) after eye enucleation followed by excision of the extrinsic ocular muscles (74, 78, 52, 53). These facts, together with the observation that geniculate responses having the same temporal behavior of the spontaneous potentials can be evoked by single shock stimulation of pontine structures during desynchronized sleep (15), indicate the existence of an extraretinal input upon the LGN during this phase of sleep.

An analysis of the localization of the brain stem region from which the monophasic potentials can be recorded and which upon stimulation evokes geniculate responses indicated that the pontine reticular formation is probably involved in the phenomenon (25, 47, 52, 61). These experiments were performed either in chronic (25, 47) or in acute animals (52, 61). In the latter case a phasic ponto-geniculo-visual activity similar to that occurring normally during desynchronized sleep was elicited by injection of reserpine (73, 32, 52, 61, 65, 104).

Recent experiments have shown that: i) neurons localized in the medial and descending vestibular nuclei discharge at high frequency during the REM (16, 17, 18) and that ii) bilateral destruction of these vestibular nuclei abolishes the large bursts of REM (86, 87, 88). The possibility therefore exists i) that the pontine potentials recorded in the intact preparation during desynchronized sleep may be regarded, in part at least, as the expression of bursts of high frequency discharge originating from second order vestibular neurons

and coursing along their ascending pathways, and ii) that vestibular volleys might contribute to the appearance of the lateral geniculate potentials at the time of the large bursts of REM.

In the present experiments the overall activity of the LGN during different backgrounds of sleep and wakefulness was recorded in unrestrained, unanesthetized cats, before and after vestibular lesions. It will be shown that the increase in discharge of the vestibular neurons that occurs during the REM periods of desynchronized sleep (16, 17, 18) is responsible for the phasic increases in the lateral geniculate activity which appear during the large bursts of REM. A rhythmic activity, however, which is apparently unrelated with the large bursts of REM, can still be recorded from the LGN following bilateral lesion of the vestibular nuclei.

METHODS

The experiments were performed on unrestrained, unanesthetized cats. EEG screw electrodes, EMG electrodes for the posterior cervical muscles, and in some experiments also for the tibialis anterior and the flexor digitorum brevis of both sides, as well as electrodes for recording ocular movements (electrooculogram: EOG) were implanted under Nembutal anesthesia, following a previously described technique (91). A bipolar electrode was inserted stereotaxically within the dorsal nucleus of the left LGN. This electrode consisted of two insulated stainless steel wires 125 μ in diameter (interelectrode distance less than 1 mm) introduced into a stainless steel tube support having an external diameter of 0.6 mm. The wires and the tube were insulated and bound together by applications of varnish. Since the tips of the wires extended about 10 mm beyond the end of the tube, the electrodes could reach LGN neurons without damaging the nucleus. During the introduction of the electrode, the spontaneous activity of LGN was continuously monitored at the C.R.O. The typical "on" and "off" discharges to flashes of light delivered at the repetition rate of one every five sec provided a physiological test for the proper localization of the electrode in the LGN. The electrode was then fixed on the skull with dental cement. All electrode leads were also soldered to tube sockets held tightly on the skull by dental cement.

The experiment started 48 hours after the end of the operation, when the effects of the anesthesia had worn off and the animal had adapted to its new condition. EEG and EMG potentials were amplified and recorded on a Grass electroencephalograph.

A method has been recently devised for the measurement of strictly all-or-nothing events occurring in a bundle of fibres such as the optic nerve (6). However in order to minimize the effects of gradual events, which are always present when recording from nuclear structures such as the LGN, the method introduced by Arduini and Pinneo (8) has been used. It is based on integration or rather averaging of the electric potentials at the output of the a. c. preamplifier after full-wave rectification. To eliminate the EEG frequency bands, the input to the integrator was filtered with a band-pass filter, whose cut-off frequencies were 500 cps and 10 Kcps, with a 12 db per octave attenuation. The d. c. output of the integrator was fed into a Hewlett Packard type 425A microvolt ammeter for dial reading of the d. c.

values. The output from the meter was also utilized for driving a Grass Polygraph with a 5 Pt d. c. preamplifier. The driver amplifier low-pass filter was set at 3 cps, 6 db per octave. The lateral geniculate activity after the first stage of amplification was also recorded through the EEG machine. Simultaneous recording was also made of the same activity through one channel of a 502 Tektronix C.R.O.; while the other channel was used for recording either the EEG during waking and synchronized sleep or the ocular movements during desynchronized sleep.

The recording sessions were made in complete darkness, following a one hour period of dark adaptation. The behavior of the animal was controlled with a sniperscope provided with an infrared source. At the end of each experiment the effects of diffuse illumination upon the level of activity of the LGN were recorded. For this purpose a 30 Watt tungsten filament lamp, heated at 6 volts, and placed 40 cm from the cornea was used.

Control records of lateral geniculate activity during different backgrounds of sleep and wakefulness were first taken for several days. The animals were then submitted, under Nembutal anesthesia, to chronic electrolytic destruction of the vestibular nuclei following a previously described technique (88). Experimental sessions started 24-48 hours postoperatively and were continued for as long as 9 days after the lesions.

The anatomical structures involved by the chronic vestibular lesions and placement of the recording geniculate electrode were controlled at the end of the experiment on serial histological sections, stained alternatively with Nissl's and Weil's techniques. A recent delimitation of the vestibular nuclei was adopted (23).

RESULTS

I. Lateral geniculate activity during quiet wakefulness and synchronized sleep. — It has been pointed out in the Methods that the activity of LGN was always recorded in darkness, while the behavior of the animal was controlled with a sniperscope. In this way changes of retinal stimulation due to ocular or pupillary movements were eliminated. The experiments we are going to report will show that LGN activity was nonetheless strongly affected by sleep.

During quiet wakefulness, characterized by a slightly synchronized EEG pattern and tonic contraction of the posterior cervical muscles (Fig. 1A), the integrated activity of the LGN reached a steady level, which appeared to be unmodified or only slightly depressed during synchronized sleep (Fig. 1B). Small irregular waves, occurring at the repetition rate of 1-2.5/sec, were observed in the geniculate records during both quiet wakefulness and synchronized sleep. The amplitude of these small potential oscillations increased when the spindle trains appeared on the EEG record (Fig. 2A), but no waxing and waning of the amplitude of the wavelets was found synchronously with the EEG spindle trains and the interspindle hulls. The amplitude of the LGN wavelets strongly decreased during steady illumination (Fig. 6A).

An entirely different phenomenon, this time phasic in nature, appeared occasionally on the LGN records when the EEG was fully synchronized. It was generally associated with an instability of the eyes, different in kind from that observed during desynchronized

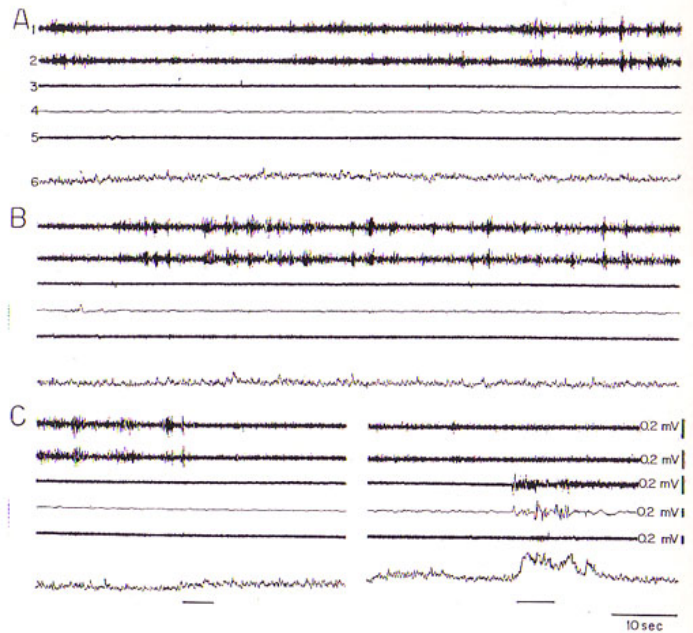


Fig. 1. — Activity of LGN during quiet wakefulness, synchronized sleep and induced arousal.

Unrestrained, unanesthetized cat. Experiment made 4 days after chronic implantation of the electrodes. Bipolar inkwriter records. 1: left parieto-occipital; 2: right parieto-occipital; 3: EMG of the posterior cervical muscles; 4: electrooculogram (EOG); 5: conventional recording from lateral geniculate nucleus (LGN) through a. c. preamplifier; 6: integrated activity of the LGN recorded through the same electrodes as in 5.

A, B: slight tonic increase in the level of LGN activity during quiet wakefulness (A) and its gradual reduction during transition from relaxed wakefulness to synchronized sleep (B). C: effects of weak (left side) and strong (right side) arousing stimuli (whistle) on the lateral geniculate activity. The horizontal bars indicate the duration of the stimuli.

sleep, but which could be clearly seen on the electrooculogram. Fig. 2 gives an example of this phenomenon.

Large, irregular potential oscillations appeared on the LGN record, superimposed on the steady level of activity which characterizes the synchronized phase of sleep (Fig. 2 *B*). These waves had a

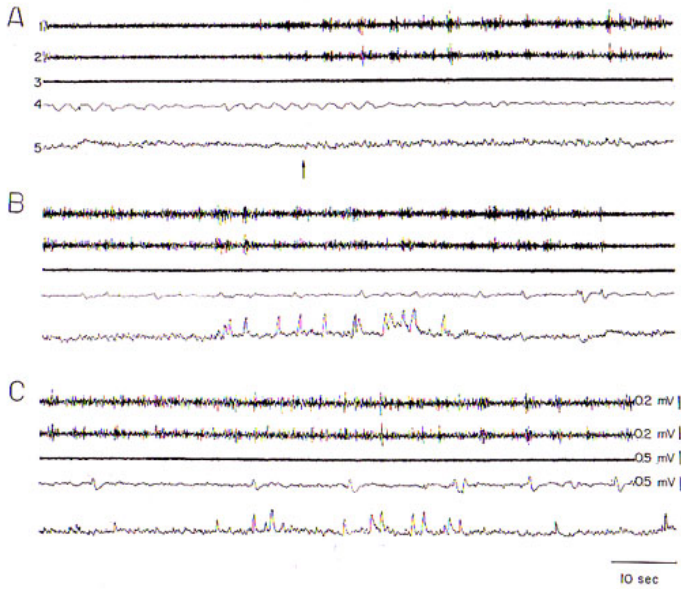


Fig. 2. — Activity of LGN during quiet wakefulness and synchronized sleep.

Unrestrained, unanesthetized cat. Experiment made 3 days after chronic implantation of the electrodes. 1-4: bipolar records as in Fig. 1; 5: integrated activity of the LGN.

A: transition from quiet wakefulness to synchronized sleep as indicated by the arrow. When the EEG spindles appear, small amplitude fluctuations can be seen in the lateral geniculate record, larger in amplitude than those occurring during quiet wakefulness. *B*, *C*: sharp peaks of lateral geniculate activity on a background of synchronized sleep. Note the absence of any time relationship between these transient enhancements of geniculate discharge and the cortical spindles.

repetition rate of 2 to 6 every 10 seconds and 5 to 15 of them were usually grouped in a train. No correlation could be found between these large peaks of geniculate activity and the typical spindles and interspindle lulls of the cerebral cortex. Most of the records taken during the synchronized EEG period did not present the high voltage, irregular LGN waves. Actually the trains of irregular waves were generally observed for about 20-25 seconds and then disappeared.

Because these bursts of geniculate waves are similar to those that occur during desynchronized sleep, the hypothesis was made that the onset of desynchronized sleep could be heralded during the synchronous phase by one or more of these trains. This hypothesis is supported by the observations i) that these bursts of LGN activity may be associated with a slight reduction of cervical EMG activity and ii) that these waves were followed after an interval of 10 to 90 seconds (average 20-30 sec) by the onset of a full episode of desynchronized sleep. This cannot be regarded as a proof, however, because the interval is too long and inconstant to provide convincing evidence of the existence of such a causal relation. Moreover, in other instances the EEG remained synchronized for a much longer period of time (see Fig. 2 *B*, *C*) after one of these episodes of geniculate activity and was eventually replaced by typical EEG activation, with behavioral arousal. On purely morphological grounds these potentials will be referred to as type I LGN waves, for reasons to be developed below.

2. *Lateral geniculate activity during transition from synchronized to desynchronized sleep.* — Three episodes of desynchronized sleep of progressively increasing durations are illustrated in Fig. 3. The large waves of the LGN records generally precede by a few seconds the onset of the EMG silence and the appearance of the desynchronized EEG pattern (see Fig. 3 *A*). An exception to this rule is seen in Fig. 3 *B*. It is of interest that the bursts of LGN waves are not to be found during the ocular movements occurring during wakefulness or synchronized sleep. There is, however, a good time correlation between these LGN waves and some ocular jerks which may precede the appearance of the desynchronized phase of sleep. These eye jerks are usually accompanied by twitch like contractions of the ear muscles, of the vibrissae and of the foot muscles (see 41 for references).

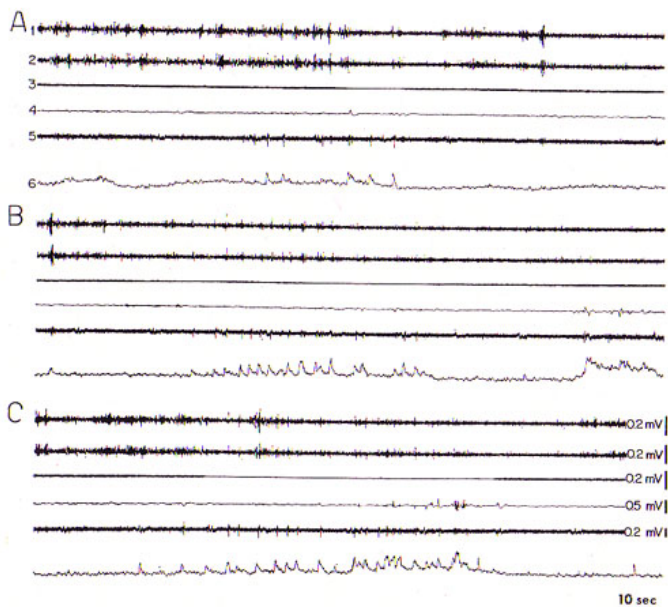


Fig. 3. — Activity of LGN during short-lasting episodes of desynchronized sleep.

Same animal as in Fig. 1, same bipolar records. Experiment made 2 days after chronic implantation of the electrodes.

A, B, C: three short-lasting episodes of desynchronized sleep showing the occurrence of sharp peaks of integrated activity in the LGN, which precede and accompany the cervical atonia. There is a good correlation between these peaks of integrated LGN activity and the spikes recorded from the same structure with the conventional technique. They can be related with the appearance of ocular movements during desynchronized sleep (C) but they occur even during those episodes (A, B) in which ocular movements are lacking. Simultaneously with these peaks in the lateral geniculate records, synchronous waves can be recorded from the parieto-occipital cortex in B. The increase in geniculate activity at the end of this record is related to the state of alertness of the animal.

3. Lateral geniculate activity during desynchronized sleep. —

Two kinds of geniculate activity can be found during a full episode of desynchronized sleep (Figs. 4, 5).

The *first type of activity* is represented by large LGN waves

similar in amplitude, duration and frequency to those which have been found, occasionally, during the synchronized phase of sleep, frequently 10 to 90 sec before the onset of the cervical muscular atonia and the flattening of the EEG (see paragraph 1). These waves, which will be referred to as type I LGN waves, are sometimes, but by no means always, associated with single ocular jerks or isolated twitches of the somatic musculature.

The *second type of geniculate activity* is characterized by waves 1.5 to 3.0 times larger in amplitude and 2 to 6 times longer in duration than those described above (Figs. 4 B-D, 5). Only this type of wave, which will be designated as type II LGN wave, appears to be strictly related in time with the large bursts of REM. The type II LGN waves usually precede slightly the onset of the train of REM; when present, myoclonic twitches generally occur synchronously with the peaks of these large geniculate waves.

When the EEG is recorded from the parieto-occipital cortex, it does not appear to be completely desynchronized during the two types of LGN waves. Synchronous waves, smaller in amplitude and shorter in duration than those recorded during the typical spindle trains of the synchronized phase of sleep can be seen on the record. They appear isolated or grouped in bursts and are clearly related in time with the LGN waves (Figs. 3 B, 4).

It should be noted that the LGN waves that occur during desynchronized sleep are generally superimposed on a stable level of geniculate activity comparable to that occurring during synchronized sleep. In some instances, however, the LGN waves are superimposed on a "tonic" enhancement of the integrated geniculate discharge (see Fig. 6 B). This "tonic" enhancement is observed when the frequency of LGN waves is high.

Fig. 6 is also of particular interest because a comparison can be made between the LGN waves occurring before and during the desynchronized phase of sleep and the "on" and "off" discharges induced by diffuse illumination. The amplitude and duration of type I LGN waves is of the same order as that of the "on" discharges, which under conditions of quiet wakefulness are evoked by flashes of light. They are, however, smaller in amplitude than the "off" discharges, which start from a level of tonic activity depressed by the steady illumination. Type II LGN waves, which occur synchronously with the bursts of REM, are longer in duration and quite different in shape from the "on" and "off" responses.

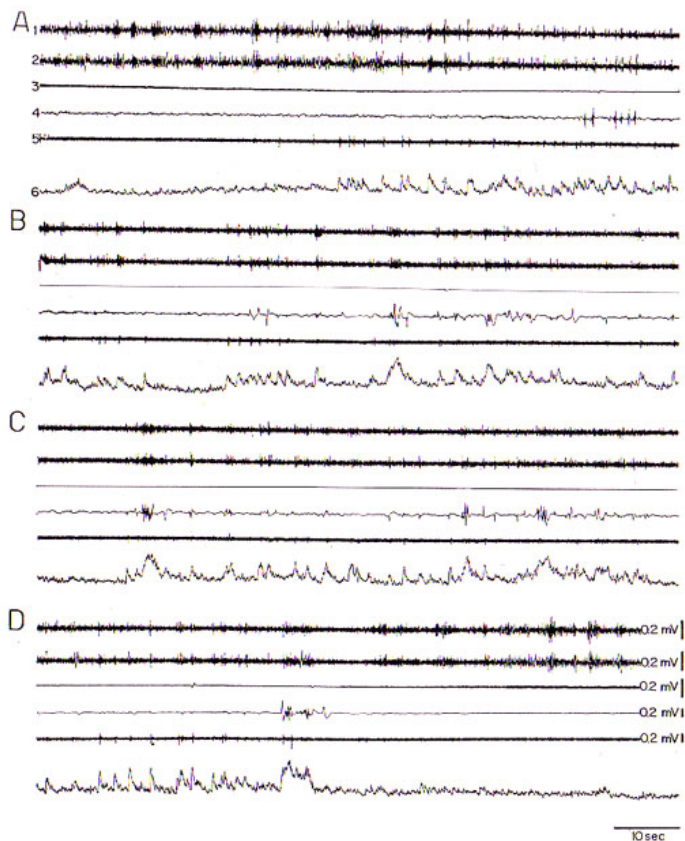


Fig. 4. - Activity of LGN during a long-lasting episode of desynchronized sleep.

Same animal as in Fig. 1, same bipolar records. Experiment made 4 days after chronic implantation of the electrodes.

A-D: continuous records showing a full developed episode of desynchronized sleep. Two kinds of activity can be recorded from LGN during desynchronized sleep. The first type is made by regular sharp peaks of integrated LGN activity which precede by several seconds the appearance of cervical atonia (A) and last throughout the episode; they are unrelated with the bursts of REM. The second type is represented by phasic increases of LGN activity which are larger in amplitude and longer in duration than those described above. They are related in time with the large bursts of

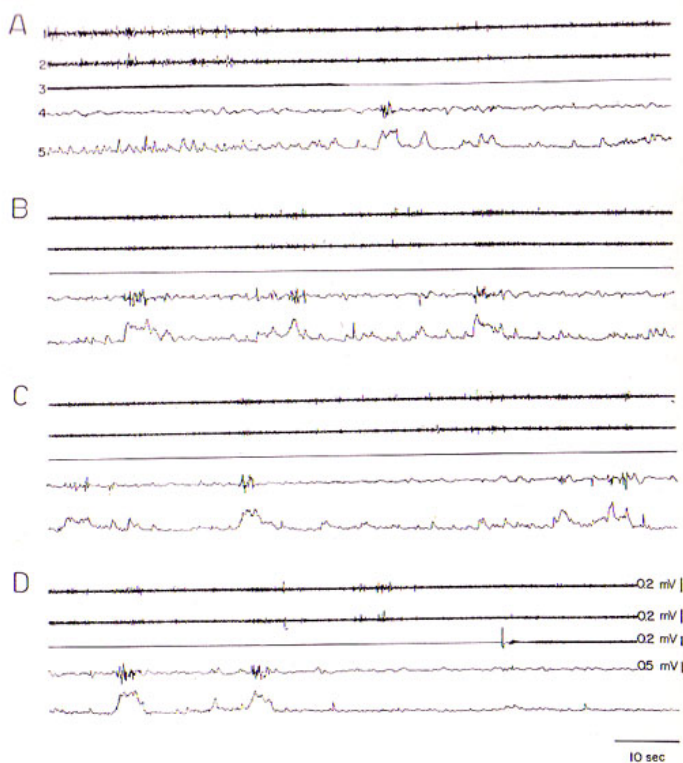


Fig. 5. - Correlation of large phasic increases in LGN activity with REM, during desynchronized sleep.

Unrestrained, unanesthetized cat. Experiment made 2 days after chronic implantation of the electrodes. Bipolar records as in Fig. 2.

Note the appearance in the lateral geniculate record of a regular rhythmic activity which precedes the cervical atonia and lasts throughout the desynchronized phase of sleep (type I LGN waves). The phasic increases in LGN activity which are larger in amplitude and longer in duration than those described above are clearly related in time with the large bursts of REM (type II LGN waves).

REM (B-D). Note that during the episode of desynchronized sleep the parieto-occipital records are not fully desynchronized as during wakefulness, because of the appearance of cortical waves synchronous with the phasic increases in the lateral geniculate activity.

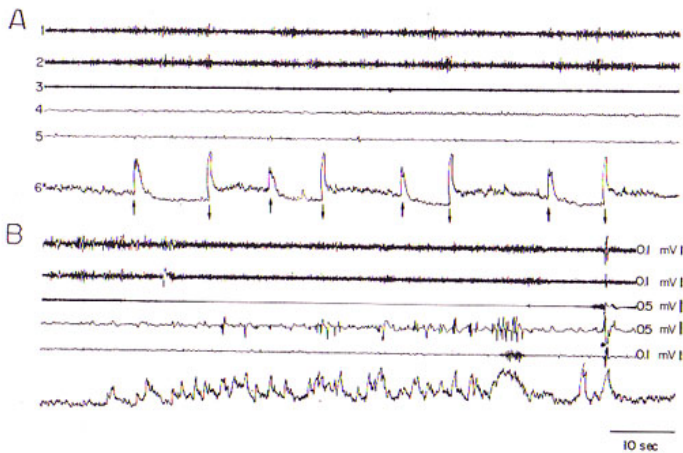


Fig. 6. — Comparison between the "on" and "off" discharges recorded from the LGN and the rhythmic phasic increases in LGN activity in darkness, during desynchronized sleep.

Unrestrained, unanesthetized cat. Experiment made 3 days after chronic implantation of the electrodes. 1-4: bipolar records as in Fig. 1; 5: EMG of the left flexor digitorum brevis; 6: integrated activity of the LGN.

A: relaxed wakefulness. Signals that diffuse light is turned on or off are given respectively by arrows \uparrow and \downarrow . Note large "on" and "off" discharges and striking reduction during steady illumination of background activity of LGN as compared to that recorded in darkness.

B: desynchronized sleep, in darkness. The amplitude of the sharp peaks of integrated LGN activity, typical of this phase of sleep, is lower than that of the "on" and "off" responses recorded in *A*. The LGN waves occurring during the large trains of REM are almost as large as the "on" and "off" responses and much longer in duration.

4. *Lateral geniculate activity during induced arousal.* — The effects of arousing stimuli on the LGN activity have been studied during different EEG backgrounds. When strong arousing stimuli are applied during quiet wakefulness or synchronized sleep, there is a great variability in the animal's behavior. When arousal is associated with a typical orienting reaction, there is a large, long lasting deflection of the integrated geniculate record which is similar in shape to type II LGN (Fig. 1 C, right). On the other hand, when EEG arousal has little behavioral counterpart, the integrated geniculate discharge simply increases smoothly to a steady level higher

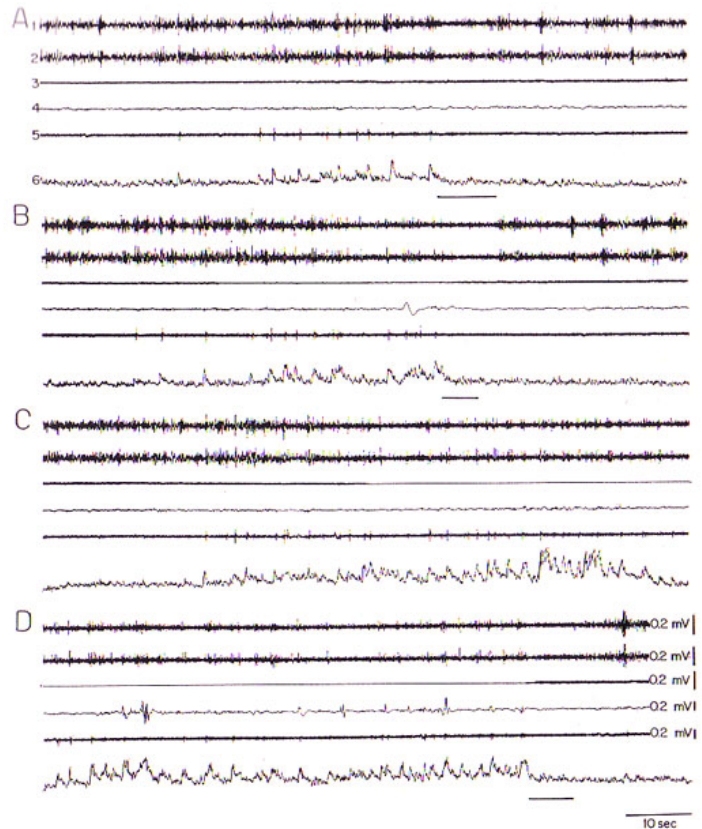


Fig. 7. — Abolition of LGN waves during arousal from synchronized or desynchronized sleep.

Same animal as in Fig. 1, same bipolar records. Experiment made 4 days after chronic implantation of the electrodes. The sharp peaks of integrated geniculate activity which occur on a background of EEG synchronization (*A*) or on a background of EEG desynchronization associated with reduction (*B*) or abolition (*C, D*: continuous records) of cervical EMG activity typical of desynchronized sleep are abolished during arousal induced by prolonged whistles. The horizontal bars indicate the duration of the auditory stimuli.

than that attained during quiet wakefulness or synchronized sleep (Fig. 1 C, left).

When arousing stimuli subthreshold for producing a clear behavioral response are applied on a background of type I LGN waves, either during synchronized sleep (Fig. 7 A), or at the transition from the synchronized to desynchronized phase (Fig. 7 B), the geniculate rhythms are suddenly disrupted. A similar effect is observed when the same type of arousing stimulation is applied on a typical background of desynchronized sleep (Fig. 7 D). In all these instances the geniculate activity returns to the steady level typical of the background of quiet wakefulness.

5. *Effects of vestibular lesions on the lateral geniculate activity during desynchronized sleep.* — It has been shown in a previous paper (88) that bilateral electrolytic lesion of the vestibular nuclei does not prevent the occurrence of the different episodes of sleep and wakefulness.

Fig. 8 shows the activity of LGN during quiet wakefulness (A) and synchronized sleep (B-D), after complete bilateral lesion of the vestibular nuclei. Note in D the occurrence of a prolonged period characterized by LGN waves similar to the type I waves which had been recorded from the same animal before the vestibular lesion (Fig. 7). As will be pointed out in the next section these episodes of synchronized sleep associated with type I LGN waves actually appeared to be more frequent and long lasting after the vestibular lesion (90 sec in Fig. 8 D). Fig. 9 shows continuous tracings of such an episode in which type I LGN waves were recorded almost constantly for about 180 sec, on a background of EEG synchronization.

As demonstrated in our previous paper (88) the most remarkable change produced by the complete bilateral lesion of the vestibular nuclei is the abolition of the large bursts of REM during desynchronized sleep. Only slow ocular movements or isolated ocular jerks can be detected after this lesion. The phase of desynchronized sleep in these preparations is still characterized by desynchronized electrocortical activity and by complete relaxation of the antigravity tonus of the posterior cervical muscles. The most prominent alterations in LGN activity produced by this vestibular lesion is the abolition during desynchronized sleep of type II waves, which before the lesion were definitely related in time with the bursts of REM. Type I LGN waves, on the other hand, persist throughout the epi-

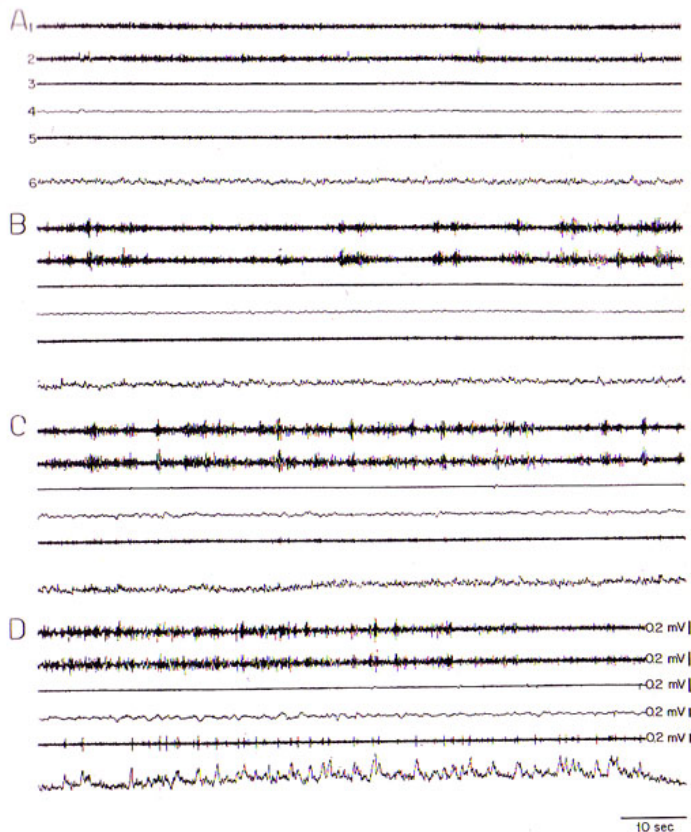


Fig. 8. — Activity of LGN during quiet wakefulness and synchronized sleep after vestibular lesion.

Same animal as in Fig. 1, same bipolar records. Experiment made 10 days after chronic implantation of the electrodes and 3 days after complete bilateral destruction of the vestibular nuclei.

A-D: continuous recording showing transition from wakefulness (A) to synchronized sleep (B-D). The small amplitude fluctuations which are seen in the geniculate record in A-C, are replaced in D by sharp peaks of geniculate activity which last for about 90 sec. The appearance of a background of relaxed wakefulness at the end of record D is followed by abolition of the LGN waves.

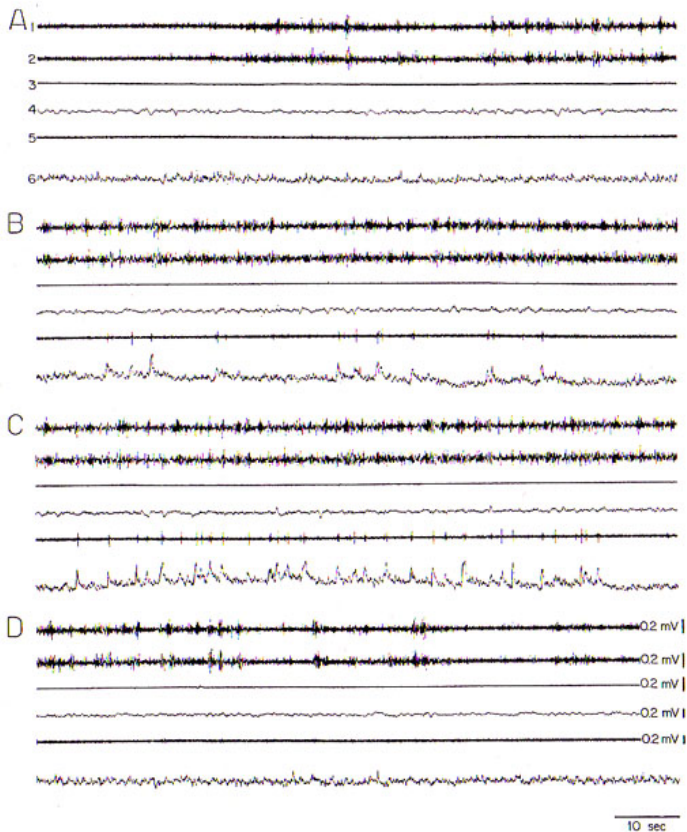


Fig. 9. — Prolonged episode with type I LGN waves recorded on a background of synchronized sleep, after vestibular lesion.

Same animal as in Fig. 1, same bipolar records. Experiment made 10 days after chronic implantation of the electrodes and 3 days after complete bilateral lesion of the vestibular nuclei.

A-D: continuous recording showing the prolonged appearance for about 180 sec of sharp peaks of geniculate activity on a background of synchronized sleep.

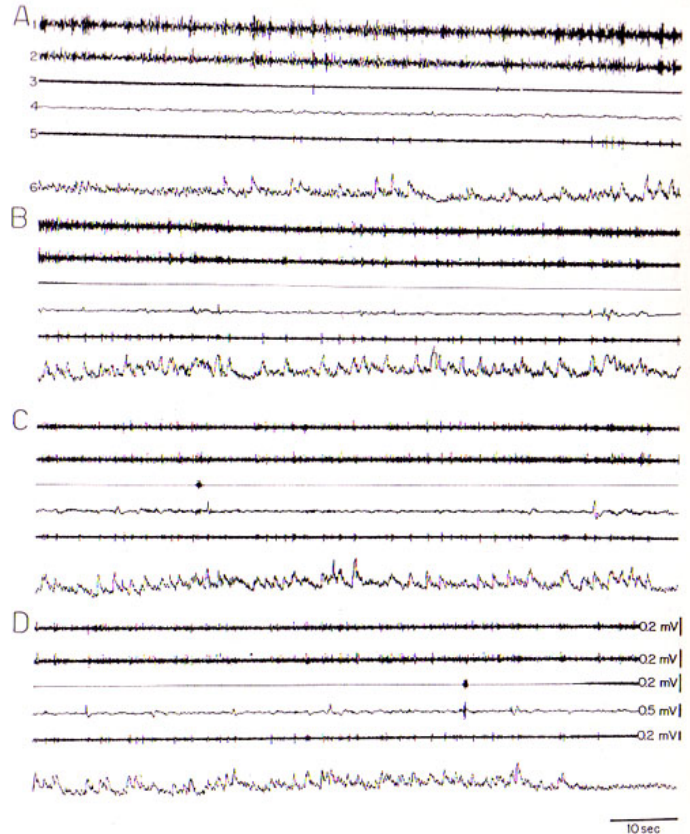


Fig. 10. — Absence of type II LGN waves and related REM, with presence of type I waves, during desynchronized sleep, after vestibular lesion.

Same animal as in Fig. 1, same bipolar electrodes. Experiment made 6 days after chronic implantation of the electrodes and 2 days after bilateral partial lesion of the vestibular nuclei.

A: sharp peaks of geniculate activity (type I LGN waves) on a background of EEG synchronization, preceding desynchronized sleep.

B-D: episode of desynchronized sleep, shown by flattening of the EEG and appearance of cervical atonia. Type I LGN waves are still present and remain throughout the episode of deep sleep. Note, however, the absence of the large bursts of REM and of related type II LGN waves activity. The incompleteness of the vestibular lesion accounts for the persistence of small groups of ocular jerks.

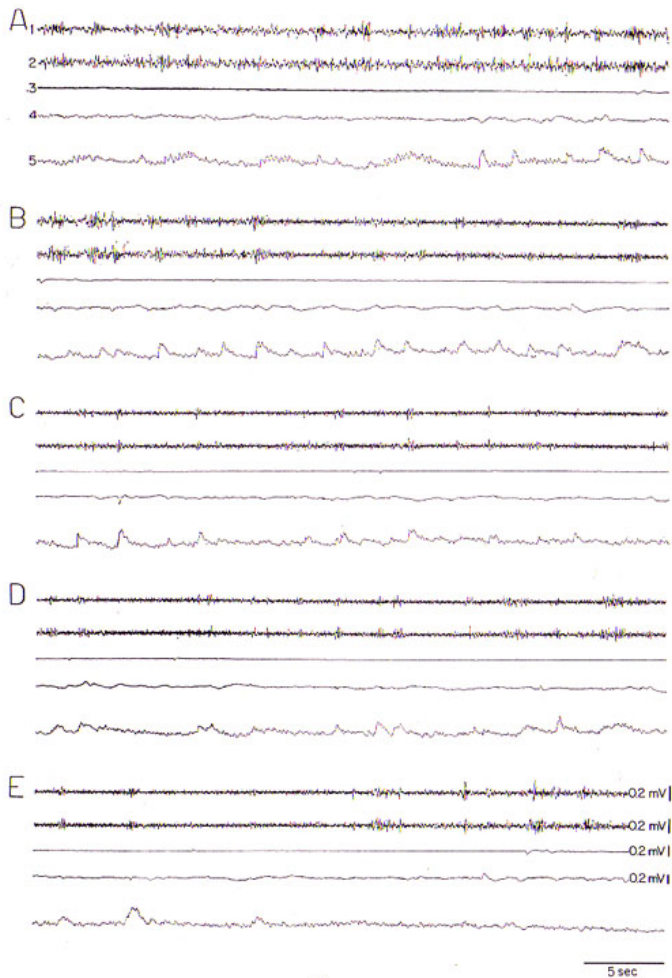


Fig. 11.

sodes of desynchronized sleep. Figs. 10 and 11 show these effects resulting respectively from partial and complete bilateral destruction of the vestibular nuclei. It will be shown in the next section that both the occurrence and the duration of the typical episodes of desynchronized sleep are apparently reduced following the vestibular lesion.

6. *Effects of vestibular lesions on the relative occurrence of the different EEG backgrounds of sleep associated or not with the lateral geniculate waves.* — Table I shows the typical effects of partial and complete bilateral lesions of the vestibular nuclei on LGN activity recorded from the same animal during different EEG backgrounds. The total recording time was divided in five parts according to the following EEG backgrounds. *A*: wakefulness, including both active and relaxed wakefulness, characterized by absence of LGN waves of any type. *B*: typical episodes of synchronized sleep, characterized by absence of LGN waves. *C*: episodes of synchronized sleep associated with trains of type I LGN waves. *D*: episodes of synchronized sleep associated with trains of type I LGN waves immediately preceding the appearance of desynchronized sleep. *E*: typical episodes of desynchronized sleep (with type II LGN waves in the normal animal).

Recording sessions 1 and 2 were taken 2 and 4 days respectively after chronic implantation of the electrodes. Recording sessions 3 and 4 were taken 2 and 3 days respectively after bilateral *partial* lesion of the vestibular nuclei. Finally recording sessions 5, 6 and 7 were taken 2, 3 and 6 days respectively after *complete* bilateral lesion of the vestibular nuclei. The completeness of the vestibular lesion was documented by the abolition of the residual bursts of REM (compare Figs. 10 and 11) and by the histological control taken at the end of the experiment (see Fig. 13).

Fig. 11. — Abolition of type II LGN waves related with the REM after complete vestibular lesion.

Same animal as in Fig. 1; bipolar electrodes as in Fig. 2. Experiment made 10 days after chronic implantation of the electrodes and 3 days after complete bilateral lesion of the medial and descending vestibular nuclei.

A-E: episode of desynchronized sleep showing the complete abolition of the REM and of related large amplitude phasic increases in lateral geniculate activity. The background rhythmic activity, however, persists throughout the episode of desynchronized sleep. Note that the EEG spindles outlast the abolition of the cervical muscular activity (*A, B*) and reappear before the end of cervical atonia (*E*).

TABLE I *

RECORDING SESSIONS	1	2	3	4	5	6	7
DATE	3-XII-64	5-XII-64	7-XII-64	8-XII-64	10-XII-64	11-XII-64	14-XII-64
TOTAL RECORDING TIME (sec)	21240	29160	11102	13380	15210	13355	13450
Wakefulness	6483 (30.52%)	6780 (23.25%)	3715 (33.46%)	4365 (32.62%)	6790 (44.64%)	3805 (28.49%)	3250 (24.16%)
Synchronized sleep without LGN waves	9468 (44.30%)	14115 (48.41%)	4391 (38.65%)	6229 (46.56%)	6306 (41.46%)	6825 (51.10%)	8235 (61.23%)
Synchronized sleep with type I LGN waves	90 (0.42%)	100 (0.34%)	413 (3.72%)	220 (1.64%)	618 (4.06%)	1125 (8.42%)	600 (4.46%)
Synchronized sleep with type II LGN waves leading to desynchronized sleep	491 (2.31%)	431 (1.48%)	256 (2.31%)	328 (2.45%)	223 (1.47%)	360 (2.70%)	590 (4.39%)
Desynchronized sleep	4768 (22.45%)	7734 (26.32%)	2427 (21.86%)	2238 (16.73%)	1273 (8.37%)	1240 (9.29%)	775 (5.76%)
NUMBER OF EPISODES OF DESYNCHRONIZED SLEEP (E)	15	20	4	8	5	5	5
frequency of these episodes calculated on the basis of the recorded time B+C+D+E	1/684 sec	1/1119 sec	1/1847 sec	1/1127 sec	1/1684 sec	1/1010 sec	1/2040 sec
mean duration of the episodes (E) calculated on the basis of the duration of the cervical atonia (sec)	318	388	398	396	255	248	155
mean duration of the periods (D) of synchronized sleep with type I LGN waves leading to desynchronized sleep (sec)	32.7	21.5	64.0	41.0	44.6	72.0	118.0
NUMBER OF EPISODES OF SYNCHRONIZED SLEEP WITH TYPE I LGN WAVES (C)	4	5	12	4	8	9	8
frequency of these episodes calculated on the basis of the recorded time B+C+D+E	1/3689 sec	1/4476 sec	1/615 sec	1/2254 sec	1/1052 sec	1/1061 sec	1/1275 sec
frequency of these episodes calculated on the basis of the recorded time B+C	1/2374 sec	1/2843 sec	1/392 sec	1/1612 sec	1/865 sec	1/883 sec	1/1104 sec
mean duration of the episodes (sec)	23	20	34	55	77	125	75

* Results taken from experiment No. 19. The cat had been submitted to chronic implantation of the electrodes the first of December 1964, to bilateral partial lesion of the vestibular nuclei the fifth of December 1964 after recording session 2, to complete bilateral lesion of the vestibular nuclei the eighth of December 1964 after recording session 4. Absolute time values and percentages of recording time (in parenthesis) are given.

The recording sessions were made continuously in a quiet, dark room, at constant temperature (22° C) and after the animal had been regularly fed. The exact duration of each of them is given in Table I. They lasted from a minimum of 3 to a maximum of about 8 hours. On the average the animal was spontaneously awake during 31.2% of the recorded time, while it spent the remaining periods under different backgrounds of sleep.

It is of interest that after partial, and particularly after complete, bilateral lesion of the vestibular nuclei the percentage of time spent in desynchronized sleep (E) clearly decreased; while the percentage of time spent in synchronized sleep with type I LGN waves (C, D) increased after the same operations. Table I also shows that the number of episodes of desynchronized sleep (E) decreased after the first (incomplete) lesion. A clear-cut reduction of their mean duration occurred, however, only when the lesion had been completed. On the contrary, the mean duration of the episodes (D) which immediately precede the appearance of the desynchronized phase of sleep, was increased after the lesion. Table I, finally, shows that even the occurrence of those episodes of synchronized sleep associated with type I LGN waves but not leading to the desynchronized phases (type C background) is particularly enhanced after the vestibular lesion. This effect is paralleled by an increase in the mean duration of the same episodes.

The most significant among these results are presented diagrammatically in Fig. 12, A and B. Fig. 12 A shows in particular that a progressive relative increase in duration of the typical pattern of synchronized sleep occurs following partial and complete lesion of the vestibular nuclei, while the sum of the periods of desynchronized and synchronized sleep associated with type I LGN waves is reduced. Mere inspection of Fig. 12 B shows also that the desynchronized phase of sleep is greatly reduced following the vestibular lesion while the synchronized phase with type I LGN waves is greatly enhanced. It should be pointed out, however, that the decrease in number and duration of the desynchronized phases of sleep is only partially compensated by the increase in number and duration of those episodes of synchronized sleep associated with type I LGN waves.

7. Vestibular structures responsible for the phasic enhancements in the geniculate discharge during the bursts of REM. — The abolition

TABLE 1*

RECORDING SESSIONS	1	2	3	4	5	6	7
DATE	3-XII-64	5-XII-64	7-XII-64	8-XII-64	10-XII-64	11-XII-64	14-XII-64
TOTAL RECORDING TIME (sec)	21240	29160	11102	13380	15210	13355	13450
A: Wakefulness	6483 (30.52%)	6780 (23.25%)	3715 (33.46%)	4365 (32.62%)	6790 (44.64%)	3805 (28.49%)	3250 (24.16%)
B: Synchronized sleep without LGN waves	9408 (44.30%)	14115 (48.41%)	4291 (38.65%)	6229 (46.56%)	6306 (41.46%)	6825 (51.10%)	8235 (61.23%)
C: Synchronized sleep with type I LGN waves	90 (0.42%)	100 (0.34%)	413 (3.72%)	220 (1.64%)	618 (4.06%)	1125 (8.42%)	600 (4.46%)
D: Synchronized sleep with type I LGN waves leading to desynchronized sleep	491 (2.31%)	431 (1.48%)	256 (2.31%)	328 (2.45%)	223 (1.47%)	360 (2.70%)	590 (4.39%)
E: Desynchronized sleep	4768 (22.45%)	7734 (26.52%)	2427 (21.86%)	2238 (16.73%)	1273 (8.37%)	1240 (9.29%)	775 (5.76%)
NUMBER OF EPISODES OF DESYNCHRONIZED SLEEP (E)	15	20	4	8	5	5	5
Frequency of these episodes calculated on the basis of the recorded time B+C+D+E	1/984 sec	1/1119 sec	1/1847 sec	1/1127 sec	1/1684 sec	1/1910 sec	1/2040 sec
Mean duration of the episodes (E) calculated on the basis of the duration of the cervical atonia (sec)	318	388	398	396	255	248	155
Mean duration of the periods (D) of synchronized sleep with type I LGN waves leading to desynchronized sleep (sec)	32.7	21.5	64.0	41.0	44.6	72.0	118.0
NUMBER OF EPISODES OF SYNCHRONIZED SLEEP WITH TYPE I LGN WAVES (C)	4	5	12	4	8	9	8
Frequency of these episodes calculated on the basis of the recorded time B+C+D+E	1/3689 sec	1/4476 sec	1/615 sec	1/2254 sec	1/1052 sec	1/1061 sec	1/1275 sec
Frequency of these episodes calculated on the basis of the recorded time B+C	1/2374 sec	1/2843 sec	1/392 sec	1/1612 sec	1/865 sec	1/883 sec	1/1104 sec
Mean duration of the episodes (sec)	23	20	34	55	77	125	75

* Results taken from experiment No. 19. The cat had been submitted to chronic implantation of the electrodes the first of december 1964, to bilateral partial lesion of the vestibular nuclei the fifth of december 1964 after recording session 2, to complete bilateral lesion of the vestibular nuclei the eighth of december 1964 after recording session 4. Absolute time values and percentages of total recording time (in parenthesis) are given.

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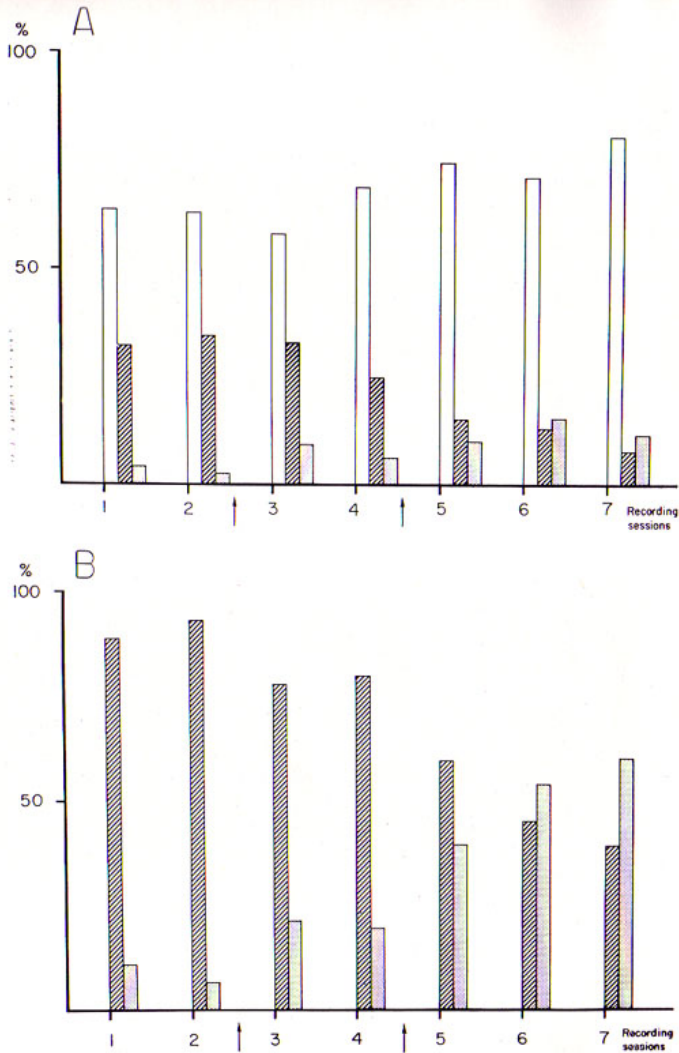


Fig. 12.

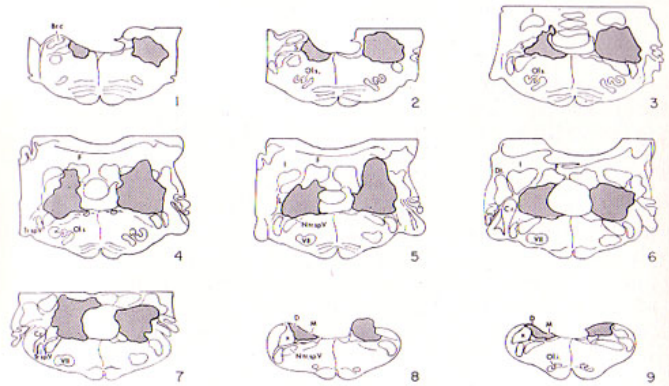


Fig. 13. - Bilateral destruction of the vestibular nuclei responsible for the REM and the related phasic enhancements in the lateral geniculate activity during desynchronized sleep.

Same animal as in Figs. 1, 3, 4, 7-11. Schematic representation of brain stem sections, taken at regular intervals and reproduced in a rostral-caudal direction. Shaded area represent the extent of the electrolytic lesion. C. r.: restiform body; D: descending vestibular nucleus; D_l: dentate nucleus; F: fastigial nucleus; I: interpositus nucleus; L: lateral vestibular nucleus (of Deiters); M: medial vestibular nucleus; N. tr. sp. V.: nucleus of spinal tract of trigeminal nerve; Ol. i.: inferior olive; Ol. s.: superior olive; p. h.: nucleus praepositus hypoglossi; S: superior vestibular nucleus; VII: motor nucleus of the facial nerve.

Fig. 12. - Relative occurrence of the different EEG backgrounds of sleep after vestibular lesions.

A: the relative durations of the different EEG backgrounds of sleep occurring during the recording sessions (see Table I), are plotted diagrammatically. For each recording session, numbered progressively, the white columns indicate the typical episodes of synchronized sleep without LGN waves, the hatched columns the typical episodes of desynchronized sleep, while the dotted columns give the episodes of synchronized sleep with type I LGN waves, either unrelated with or followed by a phase of desynchronized sleep. The first and the second arrows indicate the time at which the partial and the complete lesion of the vestibular nuclei were made.

B: the results illustrated above (A) are plotted here to show the relative changes in duration of the typical episodes of desynchronized sleep (hatched columns) and of synchronized sleep with type I LGN waves (dotted columns) following the vestibular lesions. The results are expressed in per cent of the total time in which LGN waves were recorded during both synchronized and desynchronized sleep.

of both Type II LGN waves and REM bursts during the desynchronized phase of sleep can be observed whenever the lesion is bilateral and affects the classical vestibular complex in its entire rostro-caudal extent (Fig. 13). This effect has been followed for as long as 9 days after the operation. Bilateral electrolytic lesion limited to the medial and descending vestibular nuclei may also be effective. As pointed out in a previous study (88) the medial and descending vestibular nuclei are responsible for the bursts of REM during desynchronized sleep. The electrolytic lesion of these vestibular nuclei must be complete in order to abolish completely the bursts of REM and the related type II LGN waves. No attempt has been made to limit the lesion to the superior or to the lateral vestibular nuclei of both sides, or to the whole vestibular complex of one side, since it has been shown previously that these destructions do not abolish the REM (88).

DISCUSSION

The limitations of the method utilized in these experiments to record the overall activity of the LGN have been pointed out by previous authors (8), and they will not be discussed here. Suffice it to say that although the contribution of graded electrical events to our integrated records cannot be completely ruled out simply on the basis of the filters used, most of the electrical activity recorded is due to all-or-none potentials. These are likely to originate from the LGN neurons, but some unknown percentage of activity due to action potentials in axon terminals is likely to contribute to our recordings.

The present experiments were carried out in complete darkness, under conditions of dark adaptation. Thus the changes in LGN activity cannot be attributed to peripheral effects of photic retinal stimulation. The effects related with sleep and wakefulness must be central in origin.

That the activity in the LGN is influenced by fluctuations of the level of wakefulness has been repeatedly demonstrated (22, 3, 4, 36, 44, 9, 106), although in several instances the authors did not state that the experiment had been carried out in complete darkness. The results of microelectrode recording are of particular significance. While the lateral geniculate units discharge at random during wakefulness, when the EEG is synchronized their sponta-

neous firing appears to be grouped in clusters (49, 50, 19, 70, 96). Bursts of high frequency discharge can also be recorded during desynchronized sleep particularly at the time of the REM (12).

When the overall activity of LGN is recorded with our technique, no major changes are observed on transition from quiet wakefulness to synchronized sleep. The wavelets which can be recorded during the synchronized phase are only slightly larger than those recorded during relaxed wakefulness. Because the wavelets are wiped out by steady illumination, which reduces the retinal dark discharge (cf. 5, 7), they are likely to be due to an extraretinal modulation of LGN units driven by the dark discharge.

The large potential changes which appear phasically on the LGN record in our experiments have been classified in two groups. Type I LGN waves are represented by short-lasting deflections, large in amplitude, which appear occasionally during the synchronized phase. They often precede by 10-90 sec the onset of a desynchronized episode and are constantly observed throughout the desynchronized period itself. They are sometimes related with single ocular jerks or with isolated, short-lasting twitches of the limb musculature.

Type II LGN waves are from 1.5 to 3.0 times larger in amplitude and from 2 to 6 times longer in duration than the type I deflections. They appear only at the time of the large bursts of REM and are sometimes associated with myoclonic twitches of the limb musculature. The differentiation of two types of LGN waves during desynchronized sleep was not made by the previous authors who recorded the erratic geniculate waves during desynchronized sleep (76, 15, 25, 43, 24, 74, 78, 52, 58, 94, 104) probably because of the limitation of the technique used.

Both kinds of LGN waves were not due to proprioceptive reverberations from the periphery, because they frequently appeared before the ocular movements. Nor were they due to retinal "on" and "off" discharges, for the reason stated above (cf. p. 448).

It has been previously shown that the REM are the consequence of inherent rhythms in the vestibulo-oculomotor system (16, 17, 18), and that a complete bilateral lesion of the medial and descending vestibular nuclei abolishes selectively the large bursts of REM that occur during the desynchronized phase of sleep (86, 87, 88). The most remarkable changes of geniculate activity produced by this vestibular lesion was the abolition of type II LGN

waves. Type I waves, which start occasionally several seconds before the occurrence of the other signs of desynchronized sleep and are clearly unrelated with the large bursts of REM, remain unmodified following the vestibular lesion. They persist throughout the episodes of desynchronized sleep. A vestibular influence on the LGN activity during sleep is therefore indicated.

Extraretinal inputs to the LGN have already been described by previous authors and they have been anatomically identified with reticulogeniculate and corticogeniculate paths (81, 72, 95, 107, 10, 37, 100). Moreover, physiological experiments have clearly shown that stimulations of the reticular formation (45, 2, 21, 35, 67, 22, 26, 68, 36, 97, 20, 98, 40, 83, 101, 82, 34, 48, 108), and of the visual cortex (107, 1, 66) have striking influences on the spontaneous and induced activity recorded from the LGN. Since the REM, as well as the geniculate activity typical of desynchronized sleep, persist after neocortical ablation, it has been assumed that this geniculate activity is due to ascending volleys originating from the reticular formation (cf. 55). This assumption is proved by the fact that the LGN waves can be triggered during the desynchronized phase of sleep by brain stem structures, mainly localized in the pontine reticular formation (25).

Thus at least two extraretinal inputs impinge upon the LGN during desynchronized sleep: 1) an extravestibular input, probably reticular in origin, which is responsible for the sleep modulation of geniculate activity after complete bilateral lesion of the vestibular nuclei, and 2) a vestibular input originating in the medial and descending vestibular nuclei, which influences the lateral geniculate neurons at the time of the large bursts of REM.

Recent experiments have shown that while the LGN waves still occur during desynchronized sleep after retrograde degeneration of geniculate neurons secondary to ablation of the visual cortex, they disappear after Wallerian degeneration of the optic nerve (14, 78, 52, 53). These findings suggest that the electrogenesis of the geniculate waves which are abolished by Wallerian degeneration of the optic nerve is related with the presynaptic side of the synapses. Although it cannot be excluded that postsynaptic structures are also inactivated by a process of transneuronal degeneration (cf. 42), this is not the critical factor since (as stated above) the LGN waves survive the severe retrograde atrophy of LGN cells following decortication. The presynaptic hypothesis is supported

by the observation (13, 94, 51) that the excitability of the intrageniculate endings of optic fibers is enhanced during the LGN waves, which are related in time with the REM. A positive Wall's test (105) is generally regarded as major evidence in favor of presynaptic inhibition. The other evidences are unfortunately more controversial since only LGN postsynaptic responses to a flash of light are reduced during REM (13), while the response to single shock stimulation of the optic nerve appears to be facilitated (94, 51; cf. 13). This last finding would actually indicate that presynaptic depolarization of the primary optic tract endings is accompanied by some process of postsynaptic facilitation in the LGN. That this might be the case is supported by the fact that some lateral geniculate neurons show bursts of high frequency discharge during the bursts of REM (12).

Since the method used in the present experiments integrates mainly all-or-none potentials, it can be concluded that the LGN waves elicited by the ascending vestibular volleys at the time of the REM may be related not only with the presynaptic impulses which are at least in part responsible for the depolarization of the primary optic tract endings, but also with the postsynaptic impulses which may originate from the lateral geniculate neurons. This problem will be discussed more fully in another paper (71).

The observation that sleep induced manifestations of geniculate activity, namely type I LGN waves, persist throughout the desynchronized phase of sleep in spite of the bilateral destruction of the vestibular nuclei, which abolish REM and type II LGN waves, should now be discussed. This finding, together with the evidence that destruction of the pontine reticular formation abolishes all phenomena associated with the desynchronized phase of sleep (29, 54, 55, 77, 84, 28, 92, 93, 78, 30, 31, 47, 56, 57, 59), suggests that the same brain stem center, which is possibly located in the pontine reticular formation and which triggers the geniculate activity (15), is also responsible for the phasic rhythmic activity in the vestibular nuclei. Anatomical interconnections between vestibular nuclei and brain stem reticular formation (69, 99, 23) makes this possibility a likely one. The mechanism of this interaction, however, is still unknown. One could postulate that the vestibular nuclei might be inserted "in parallel" in the ponto-geniculate circuit, thus contributing to the phasic enhancement of the lateral geniculate activity which occurs during REM.

The question might now be asked as to whether the vestibular nuclei, driven by the pontine reticular center, are capable of influencing in some way the occurrence of the desynchronized phases of sleep.

We have suggestive evidence from our experiments that a complete, bilateral destruction of the vestibular nuclei, in addition to abolishing REM and related type II LGN waves, also reduces the occurrence and the duration of the episodes of desynchronized sleep. On the contrary, type I LGN waves which are recorded during synchronized sleep or immediately precede the desynchronized phases are facilitated by the lesion. The hypothesis might be advanced, therefore, that the driven activity of the vestibular nuclei is responsible i) for the precipitation of the desynchronized phase of sleep, once the ponto-geniculate activity has appeared and ii) for its prolonged duration, once this episode is fully developed.

In this context, the outbursts of ponto-geniculate activity are likely to represent the initial event in the causal chain of phenomena leading to a full episode of desynchronized sleep. These phenomena still appear after complete destruction of the vestibular nuclei. Activity of these nuclei, however, would facilitate the appearance of the tonic manifestations of deep sleep, such as electrocortical desynchronization and posterior cervical muscle atonia. The vestibular nuclei would be responsible, alone, for REM and type II LGN waves.

It might be asked now whether the rhythmic ponto-geniculate activity is critically responsible for the tonic manifestations of desynchronized sleep. The results of some recent experiments provide only indirect evidence against this hypothesis (78, 47, 52, 57, 60, 61).

Future experiments should be devoted to the analysis of the central mechanisms responsible for the tonic manifestations of desynchronized sleep on the one hand, and for the phasic rhythmic activity in the ponto-geniculate system on the other hand. The linkage between the two mechanisms probably represents one of the crucial problems awaiting clarification.

SUMMARY

1. The overall activity of the lateral geniculate nucleus (LGN) has been recorded during different backgrounds of sleep and wakefulness, before and after bilateral destruction of the vestibular nuclei.

2. Two kinds of geniculate activity have been recorded: i) type I LGN waves represented by short-lasting potentials, which may occur sporadically during the synchronized phase, frequently preceding the onset of desynchronized sleep by 10-90 seconds, and which are constantly found throughout the desynchronized phase; ii) type II LGN waves characterized by phasic increases in the geniculate activity larger in amplitude and longer in duration than type I waves.

3. While the type I LGN waves could be related only with isolated ocular movements, type II waves appeared synchronously with the large bursts of REM.

4. Bilateral lesion of the medial and descending vestibular nuclei abolishes not only the REM but also type II LGN waves; while type I waves still remain, suggesting the presence of vestibular and extravestibular inputs to LGN. The functional significance of these inputs during desynchronized sleep is discussed.

5. The number and the duration of the episodes of desynchronized sleep are also reduced by the vestibular lesion. On the contrary type I LGN waves are observed more frequently and for longer periods of time during synchronized sleep. Thus the vestibular nuclei may be necessary for the normal manifestation of the tonic aspects of desynchronized sleep.

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