PYRAMIDAL DISCHARGE FROM SOMATOSENSORY CORTEX AND CORTICAL CONTROL OF PRIMARY AFFERENTS DURING SLEEP [1]

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INTRODUCTION

During desynchronized sleep there is a *tonic* depression of the monosynaptic and polysynaptic reflexes (25, 26, 29, 19, 20). Phasic enhancements of such a depression occur during the desynchronized phase of sleep, particularly whenever the typical bursts of rapid eye movements (REM) appear (19, 20). Accumulated evidence has shown that the tonic reduction of the spinal reflexes is due to hyperpolarization of the α motoneurons, which is clearly related with processes of active inhibition arising from suprasegmental structures (27, 28, 30, 46, 21, 22, 38, 39). Thus tonic inhibition would be mainly postsynaptic in nature. The phasic depression of spinal reflexes during REM, however, has no counterpart in an increase of the postsynaptic inhibitory effects, as shown by the study of the response of motoneurons to antidromic volleys (21, 22) or direct electrical stimulation (38, 39). If phasic depression also results from active inhibitory processes, the mechanism of this inhibition must be entirely different.

Recent experiments have shown that during the bursts of REM the ventral horn terminals of group I*a* primary afferents become depolarized (40-42), an observation suggesting that presynaptic inhibition of these afferents might be responsible for the phasic depression of the monosynaptic reflexes (19, 20).

The problem that arises is whether a mechanism of presynaptic inhibition also affects the high threshold muscular and the cutaneous afferents (flexion reflex afferents, FRA: 16), thus accounting for the striking depression of the polysynaptic flexion reflexes at the time of the bursts of REM (19, 20).

A likely though not exclusive source of such inhibition would be the corticospinal fibers arising from the somatosensory cortex and travelling along the pyramidal tract. It has been shown recently that the increase in the pyramidal discharge which occurs during desynchronized sleep (4, 17) is related in time with the appearance of the bursts of REM (34-36). This effect is due in part to corticospinal volleys arising from the motor cortex because it can still be observed after bilateral ablation of the sensory cortical areas S_I and S_{II} (34-36). The corticospinal fibers, however, are not exclusively concerned with the transmission of volleys arising from the motor cortex to α motoneurons. Recent experiments have shown i) that electrical stimulation of the sensory-motor cortex of the cat is followed by depolarization of the primary afferent endings of both cutaneous and high threshold muscle afferents, never of group I*a* muscle afferents (2, 9, 10, 3) and ii) that the motor cortex depolarizes these primary afferents only indirectly through synaptic activation of neurons of the somatosensory cortex (3). As a result, the afferents involved in the polysynaptic reflex can be blocked presynaptically by corticofugal volleys arising from sensory cortex.

The present experiments were designed to determine i) whether the phasic enhancement of pyramidal activity occurring during the bursts of REM could still be observed after chronic unilateral ablation of the motor cortex, when only corticospinal influences arising from S_I and S_{II} were available, and ii) whether in acute experiments performed on the same animals before sacrifice primary afferent depolarization could still be produced by pyramidal stimulation following degeneration of the corticospinal motor fibers.

These experiments have provided indirect evidence in support of the hypothesis that during the REM periods of desynchronized sleep the endings of the FRA are depolarized, thus leading to a presynaptic inhibitory control of the polysynaptic reflexes.

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METHODS

Each experiment consisted of a chronic and an acute stage.

Chronic experiments were performed on unrestrained, unanesthetized cats. EEG screw electrodes, EMG electrodes for the posterior cervical muscles and the tibialis anterior muscle of both sides as well as electrodes for recording ocular movements (electro-oculogram: EOG) were implanted, prior to the recording sessions, under Nembutal anesthesia following a previously described technique (47). At the same time unilateral ablation of the motor cortex (precruciate gyrus, rostral postcruciate gyrus and the depths of the cruciate sulcus: cf. 1) was performed.

A bipolar electrode was inserted stereotaxically within the medullary pyramid, ipsilateral to the cortical lesion (cf. 35). This electrode consisted of two insulated stainless steel wires 125 μ in diameter (interelectrode distance less than 0.5 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. The tips of the wires extended about 10 mm beyond the end of the tube so that the electrodes could reach the pyramidal tract without producing great damage to the brain stem. The electrode was usually placed in the pyramid at the level of the inferior olive, just rostral to the *decussatio pyramidum*. During the introduction of the electrode, repetitive stimulation of the brain stem with 300/sec, 1.0 msec rectangular pulses, provided a physiological test for the proper localization of the electrode in the pyramidal tract. The electrode was fixed in that position which produced an active flexion of the contralateral hindlimb. The level of Nembutal anesthesia used (25 mg/kg) was light enough to permit the pyramidal motor response. All electrode leads were then soldered to tube sockets held tightly on the skull by dental cement.

The experiments started 48 hrs after the end of the operation when the effects of the anesthesia had worn off and the animal had adjusted to its new condition. EEG and EMG potentials were amplified and recorded on a Grass electroencephalograph. Simultaneous recording of the integrated pyramidal activity was made in the following way. The electrical activity, amplified by an A. C. preamplifier, was fed to a band-pass filter whose critical frequencies were 500 cps and 10 Kcps with a selectivity of 12 db per octave. The output of the filter was measured by a Ballantine-type 320 RMS voltmeter whose output (proportional to the root mean square of the input voltages) was finally recorded in a D. C. channel of the EEG. A Grass D. C. 5 P 1 preamplifier was used, and the driver amplifier low-pass filter was set at 3 cps, 6 db per octave. With this technique (4, 34-36) the pen deflections are proportional to the root mean square of the voltages between the recording electrodes. The area underneath the curve is therefore proportional to the energy of the recorded activity in the explored region. The pyramidal activity was also recorded, after the first stage of amplification, through one channel of a 502 Tecktronix C.R.O., while the other channel was used for recording either the EEG during waking and synchronized sleep or the ocular movements appearing in desynchronized sleep. In one experiment single unit recording from pyramidal tract axons was also made at the C.R.O., following a method described by other authors (5).

Acute experiments started when the corticospinal fibers arising in the motor cortex had degenerated, after an interval of 15 to 49 days. Under ether anesthesia the animals were submitted to anemic decortication. The lumbosacral region of the spinal cord was exposed from L 4 to S 2 and the ventral roots L 7 or S 1 were severed and prepared for recording under paraffin oil at 37° C. The obturator, quadriceps and hamstring nerves were sectioned on both sides. The tibial and/or the deep peroneal nerves were dissected and mounted for stimulation. For recording of dorsal root potentials the caudal filament of L 6 or the rostral filament of L 7 dorsal roots were sectioned, dissected free to the point of entry into the cord, and prepared for recording. Silver electrodes were used for recording from spinal roots: in particular one of the electrodes was placed close to the spinal cord, while the other was near the cut end. The interelectrodic distance was about 15 mm.

The same electrode which had been used for recording the pyramidal activity following ablation of the motor cortex in the unrestrained, unanesthetized cat was utilized for stimulation in the acute experiment. Minimal skull removal, however, was also made for placement of a stimulating electrode in the contralateral pyramid, or for stimulation of corticospinal fibers at the mesencephalic or medullary level on either side in some animals which had not been preparad for chronic recording of the pyramidal activity after unilateral ablation of the motor cortex.

The acute experiments began 1-2 hrs after ether anesthesia was terminated. The animals were then paralysed with Flaxedil and artificially respired. The dorsal root filaments and the recording electrodes were carefully isolated from the cord surface by paraffin oil at 37° C. The dorsal root potentials and the ventral root discharges elicited by repetitive stimulation of the contralateral pyramid at various frequencies, or by single shock stimulation of the central end of the ipsilateral tibial or deep peroneal nerve, were compared on both sides. Conventional amplifying and recording equipment was used. The time constant of the amplifier used for recording the dorsal root potentials was 1 sec. In all pictures upward deflection of the C.R.O. beam corresponds to negativity of the proximal recording electrode.

Electrolytic lesions were made at the end the pyramidal stimulations (Fig. 1). Histological controls of the motor cortex lesions and the sites of pyramidal stimulation were made by means of serial sections, stained alternately with Nissl and Weil methods.

RESULTS

1. *Extent of cortical lesions.* — Although the ablations involved most of the motor cortex, they were necessarily incomplete because the cruciate sulcus, which contains electrophysiologically (48, 14) and cytoarchitectonically (51, 31) defined motor cortex, undercuts to a large extent the limb areas of the primary somatic sensory cortex (SI). In making the lesions the depths of the cruciate sulcus were partially aspirated with fine-bore pipettes held next to the pia mater lining the sulcus, but the lesions within the depths of the sulcus were left purposely incomplete in order to insure that the somatic sensory cortex would be unharmed. The term "ablation of the motor cortex" is used throughout the paper with these qualifications.

Fig. 2 illustrates surface views of three representative lesions and Fig. 3 demonstrates with cross-sections the rostrocaudal extent of one of the largest lesions (Fig. 2 *C*). Note in Figs. 2 and 3 *D-F* that the hindlimb sensory cortex (1, 52, 11, 13) lying in the medial postcruciate gyrus is untouched by the lesion although some of the fibers arising from this region were probably interrupted by the lesion within the depths of the cruciate sulcus.

Most of the motor cortex was removed in the brain illustrated in Figs. 2 *C* and 3. Even the motor cortex within the cruciate sulcus was largely undercut by the lesion (Fig. 3 *B-E*). The cat bearing this lesion was used to illustrate the typical changes in integrated pyramidal activity during sleep and wakefulness following ablation of the motor cortex (Figs. 4-8).

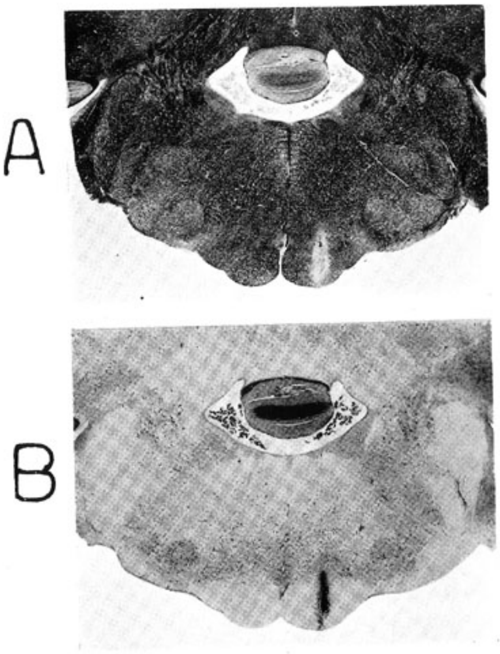

Fig. 1. – *Localization of the recording pyramidal electrode in one experiment with ipsilateral chronic ablation of the motor cortex.*

Same cat as in Figs. 2 *C* and 3. *A*: Weil method. *B*: Nissl method: 6 x.

2. *Integrated pyramidal activity during wakefulness and synchronized sleep in cats with chronic ablation of the motor cortex.* — The integrated activity recorded during quiet wakefulness from the pyramidal tract after ablation of the motor cortex appeared to be stabilized at a steady high level and showed only small and irregular oscillations (Fig. 4 *A*). During drowsiness the pyramidal activity decreased slightly, but appeared to be less regular because of the appearance of large amplitude deflections related in time with the sporadic trains of cortical synchronous waves (Fig. 4 *B*).

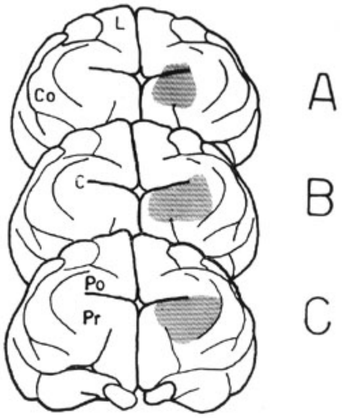

Fig. 2. – *Schematic representation of cortical ablations in three different cats from which the integrated pyramidal activity was recorded.*

Pr: precruciate gyrus; Po: postcruciate gyrus; Co: coronal gyrus; L: lateral gyrus; C: sulcus cruciatus.

During synchronized sleep the integrated pyramidal activity was characterized by the presence of large, irregular oscillations (Fig. 4 *C*) similar to those recorded from the pyramidal tract of animals with the motor cortex intact (34-36). The integrated activity decreased to a minimum during the interspindle lulls and reached a maximum during the spindle bursts. There was a clear-cut relationship between trains of synchronous waves and peaks in the integrated pyramidal activity, the large spindle trains corresponding to large peaks of pyramidal activity (Fig. 4 *C*).

Arousing sensory stimulations, which desynchronized the synchronous EEG rhythms, increased the background activity in the pyramidal tract so that it became stabilized at a level similar to that achieved during the spindle trains (Fig. 5 *A*). A steady increase in pyramidal activity was seen when the EEG arousal occurred in the absence of muscular movements and orienting reaction, detected by observation of the animal with a sniperscope in complete darkness and by electromyographic records (Fig. 5 *A*).

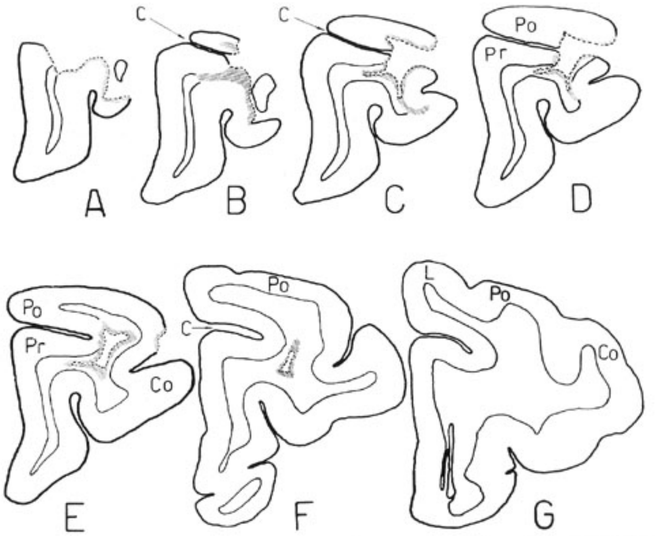

Fig. 3. – *Schematic representation of transverse sections of the brain showing the extent of the cortical ablation in the cat illustrated in Fig. 2* C.

The transverse sections are labelled in rostro-caudal direction from *A* to *G*. Much of the left motor cortex was removed. In particular the ablation involved the left precruciate gyrus and the rostral lip of the left postcruciate gyrus. Even the motor cortex within the cruciate sulcus was largely undercut by the lesion.

Stronger arousing stimulations produced not only EEG desynchronization but also a clear orienting response with widespread muscular activity. At these times a phasic enhancement of the pyramidal discharge was observed. It lasted throughout the sensory stimulation and gradually decreased later, to reach a steady level similar to that occurring during the stage of quiet wakefulness (Fig. 5 *C*). Similar phasic changes in pyramidal activity occurred when arousing stimuli eliciting an orienting reaction were applied on a background of quiet wakefulness (Fig. 5 *B*).

Oscillographic controls clearly confirmed the changes in the integrated records described above. They particularly showed fluctuations of the background activity of the pyramidal tract following ablation of the motor cortex during the EEG spindles (Figs. 9 *a*,

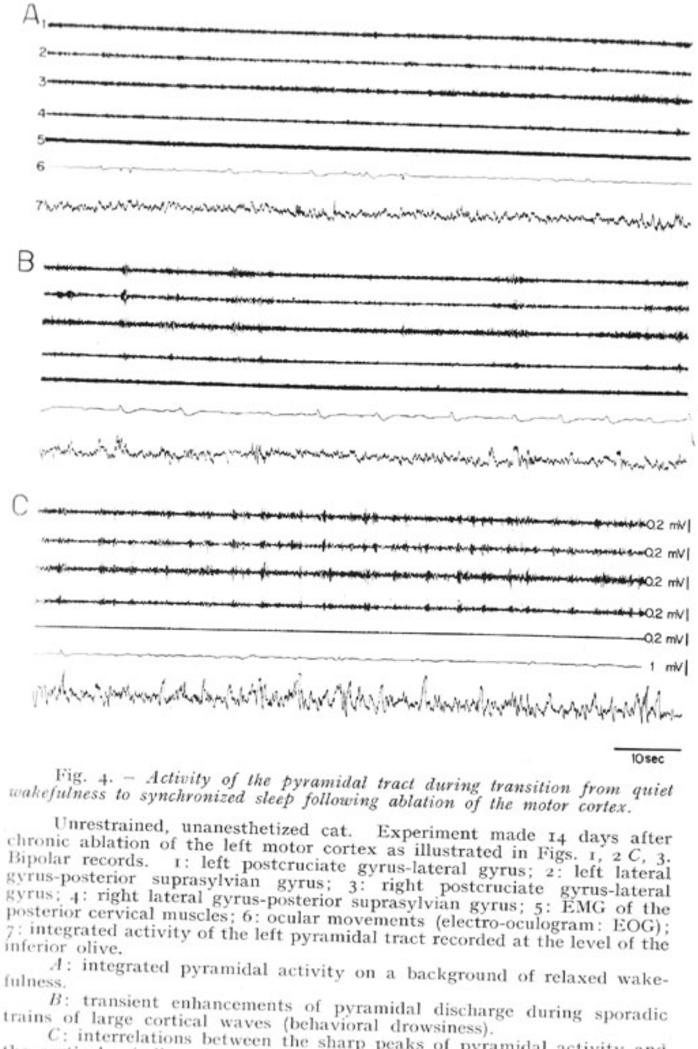

Fig. 4. – *Activity of the pyramidal tract during transition from quiet wakefulness to synchronized sleep following ablation of the motor cortex.*

Unrestrained, unanesthetized cat. Experiment made 14 days after chronic ablation of the left motor cortex as illustrated in Figs. 1, 2 *C*, 3. Bipolar records. 1: left postcruciate gyrus-lateral gyrus; 2: left lateral gyrus-posterior suprasylvian gyrus; 3: right postcruciate gyrus-lateral gyrus; 4: right lateral gyrus-posterior suprasylvian gyrus; 5: EMG of the posterior cervical muscles; 6: ocular movements (electro-oculogram: EOG); 7: integrated activity of the left pyramidal tract recorded at the level of the inferior olive.

A: integrated pyramidal activity on a background of relaxed wakefulness.

B: transient enhancements of pyramidal discharge during sporadic trains of large cortical waves (behavioral drowsiness).

C: interrelations between the sharp peaks of pyramidal activity and the cortical spindles of the synchronized stage of sleep. The increase of pyramidal discharge is clearly related in time with the larger cortical waves, an effect particularly evident when spindling patterns prevail.

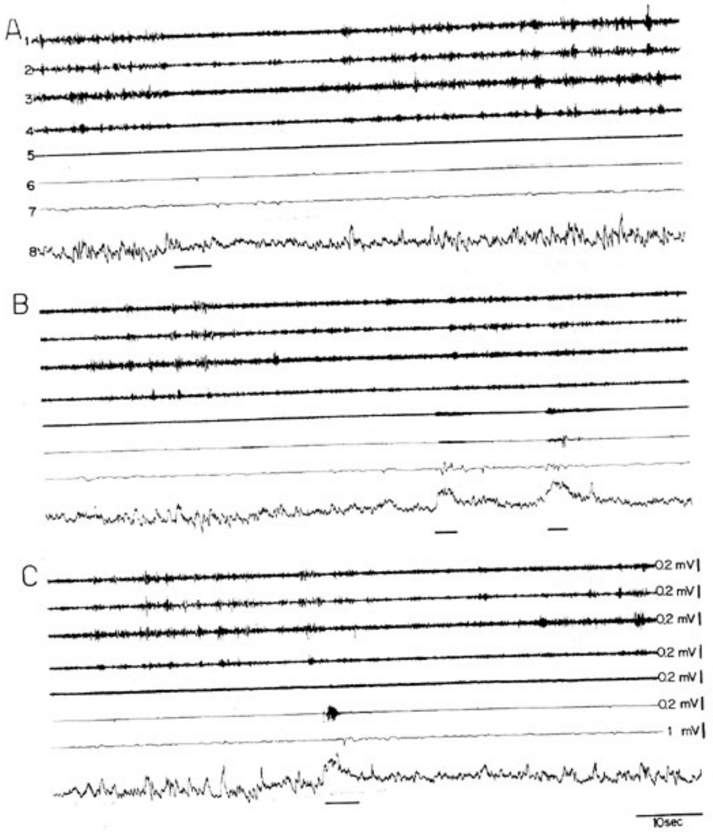

Fig. 5. – *Activity of the pyramidal tract during induced arousal following ablation of the motor cortex.*

Same animal as in Fig. 4, same experiment. 1-5: bipolar records as in Fig. 4; 6: EMG of the right tibialis anterior; 7: ocular movements (EOG); 8: integrated activity of the left pyramidal tract. The horizontal bars indicate acoustic stimulation of increasing intensity (whistles).

A: the arousal reaction induced by weak acoustic stimulation produced EEG desynchronization without muscular contractions. *B*, *C*: stronger arousing stimuli applied on a background of quiet wakefulness (*B*) or of synchronized sleep (*C*), besides desynchronizing the EEG, produced contraction of limb muscles, orienting reaction and eye movements.

The sharp peaks in the pyramidal record, occurring on a background of EEG synchronization, disappear during spontaneous (*B*) or induced wakefulness (*A*), as soon as the EEG becomes desynchronized. The pyramidal activity is then stabilized at a level comparable to that attained during the former peaks. A gradual decrease of this basic activity together with the appearance of periodic elevations of progressively increasing amplitude parallel the return of electrocortical synchronization (*A*). In *B* and *C* phasic increases in pyramidal activity appear during muscular contractions induced by stronger arousing stimuli. The peaks of these pyramidal deflections always reach a level higher than that achieved during the peaks that occur synchronously with the EEG spindles.

10 *a*) and a phasic enhancement during induced arousal (Figs. 9 *f*, 10 *f*). At this time the background activity could reach an amplitude 2.0 times that reached during the peaks synchronous with the EEG spindles (signal-to-noise ratio equal to 4).

3. *Integrated pyramidal activity during transition from synchronized to desynchronized sleep in cats with chronic ablation of the motor cortex.* — When synchronized sleep was replaced by a desynchronized episode, the peaks of integrated pyramidal activity that occurred synchronously with the EEG spindles disappeared, and only smaller, irregular deflections appeared. The average level was only slightly higher than that occurring during the interspindle lulls (Fig. 6 *A*). When isolated ocular movements or bursts of REM occurred at the beginning of the episode of desynchronized sleep, the baseline of the record rose irregularly, but always above the level reached during the peaks associated with the EEG spindles in the synchronized phase (Fig. 7 *A*).

4. *Integrated pyramidal activity during the REM periods of desynchronized sleep in cats with chronic ablation of the motor cortex.* — As soon as the outbursts of REM appeared, the pyramidal activity increased phasically to a level much higher than that occurring during the EEG spindles (Figs. 6, 7). There was always a clear-cut relationship between increase in pyramidal activity and the number, amplitude and frequency of the ocular movements (Fig. 8). The myoclonic twitches (18) also occurred during these periods of augmented pyramidal activity (Fig. 6 *B*). As previously reported (18), they involved mainly the flexor muscles. The occurrence and the amplitude of the twitches were not markedly different in the muscles of the hindlimb contralateral to the cortical ablation as compared

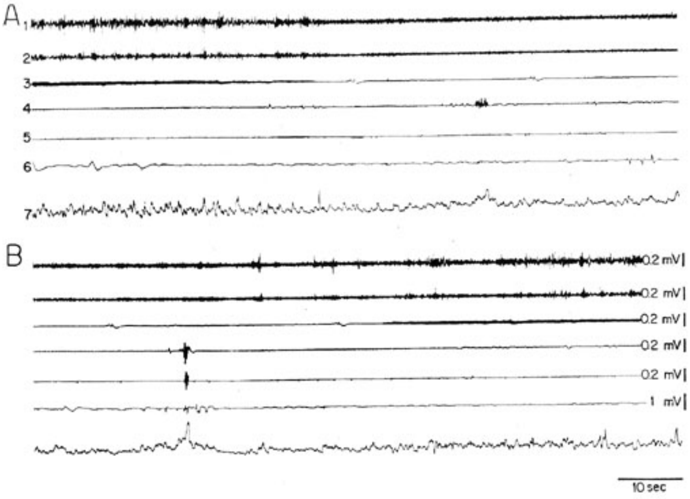

Fig. 6. – *Slight depression in the activity of the pyramidal tract, after chronic ablation of the motor cortex, during transition from synchronized to desynchronized sleep, in the absence of bursts of REM.*

Same animal as in Figs. 4, 5, same experiment. 1: left postcruciate gyrus-lateral gyrus; 2: right postcruciate gyrus-lateral gyrus; 3: EMG of the posterior cervical muscles; 4: EMG of the left tibialis anterior; 5: EMG of the right tibialis anterior; 6: ocular movements (EOG); 7: integrated activity of the left pyramidal tract.

A, *B*: short-lasting episode of desynchronized sleep. As soon as the synchronous rhythms are disrupted (*A*) there is a simultaneous disappearance of the peaks of pyramidal activity. The background activity is rather steady, with only minor oscillations, at a level lower than that reached by the former peaks accompanying the spindles. The reverse occurs at the end of the episode of desynchronized sleep (*B*). Note absence of REM during transition from synchronized to desynchronized sleep and enhancement of pyramidal activity during myoclonic twitches, with (*B*) or without (*A*) REM. The twitches occur synchronously with the peaks of the pyramidal record.

with those of the intact side. The jerks appeared only when the peaks in the pyramidal record had reached their maximum amplitude. A phasic enhancement of the integrated pyramidal discharge was observed, during desynchronized sleep, even when the myoclonic twitches were not associated with bursts of REM (Fig. 6 *A*).

The phasic enhancements of the integrated pyramidal activity during the bursts of REM recorded on the ink-writer were also

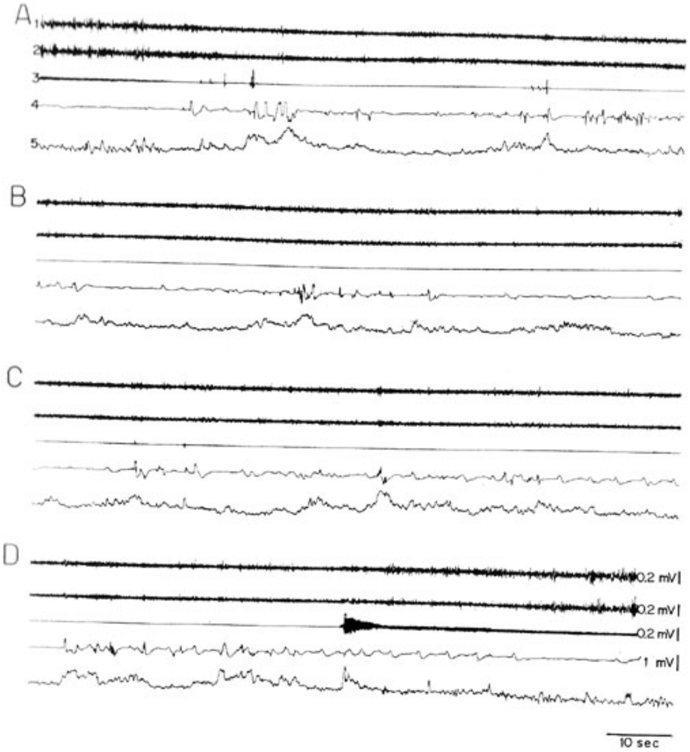

Fig. 7. – *Increase in the activity of the pyramidal tract, after chronic ablation of the motor cortex, during transition from synchronized to desynchronized sleep, associated with bursts of REM.*

Same animal as in Figs. 4-6. Experiment made 18 days following chronic ablation of the left motor cortex. Bipolar records. 1: left lateral gyrus-posterior suprasylvian gyrus; 2: right lateral gyrus-posterior suprasylvian gyrus; 3: EMG of the posterior cervical muscles; 4: ocular movements; 5: integrated activity of the left pyramidal tract.

A-D: an episode of desynchronized sleep. Soon after transition from synchronized to desynchronized sleep (*A*), synchronous with a burst of REM, a strong, long lasting enhancement of the pyramidal activity occurs. The integrated activity reaches a level much higher than that observed during the former peaks accompanying the spindles. Several prolonged pyramidal discharges appear later, synchronous again with the outbursts of REM (*B-D*).

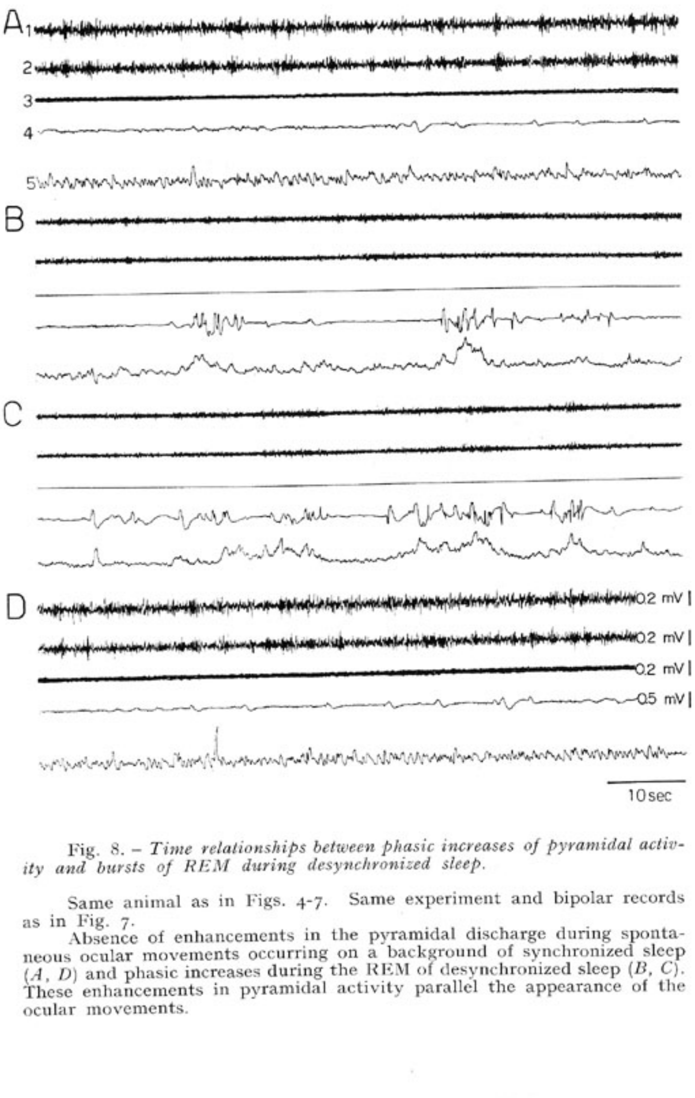

Fig. 8. – *Time relationships between phasic increases of pyramidal activity and bursts of REM during desynchronized sleep.*

Same animal as in Figs. 4-7. Same experiment and bipolar records as in Fig. 7.

Absence of enhancements in the pyramidal discharge during spontaneous ocular movements occurring on a background of synchronized sleep (*A*, *D*) and phasic increases during the REM of desynchronized sleep (*B*, *C*). These enhancements in pyramidal activity parallel the appearance of the ocular movements.

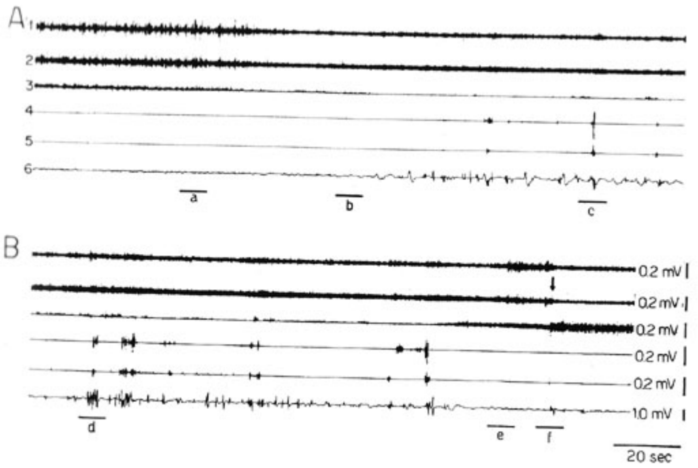

Fig. 9. – *Relationship between increase in background activity of the pyramidal tract and bursts of REM during desynchronized sleep after chronic ablation of the motor cortex.*

Unrestrained, unanesthetized cat. Experiment made 9 days after the implantation of the electrodes and ablation of the left motor cortex as illustrated in Fig. 2 *B*.

Ink-writer records. 1: left lateral gyrus-suprasylvian gyrus (EEG); 2: right lateral gyrus-suprasylvian gyrus (EEG); 3: EMG of the posterior cervical muscles; 4: EMG of the left tibialis anterior; 5: EMG of the right tibialis anterior; 6: ocular movements (EOG). The horizontal lines indicate the periods during which the integrated activity of the left medullary pyramid was recorded with the C.R.O. as shown in Fig. 10.

A: transition from synchronized to desynchronized sleep as monitored by disappearance of EMG cervical activity, followed by outbursts of REM and clonic twitches. *B*: continuation of the episode of desynchronized sleep. Note clear time correlation between myoclonic twitches and large bursts of REM. The reappearance of the tonic EMG activity of the neck musculature (*B*, right) indicates the end of the episode of desynchronized sleep. The arrow indicates the arousal reaction produced by an auditory stimulus (whistle).

accompanied by similar changes in the multiple spike discharge recorded on the C.R.O. with conventional techniques (Figs. 9 *c*, *d*; 10 *c*, *d*). Fig. 10 shows that the signal-to-noise ratio increased transiently up to 4 during the bursts of REM. At this time the background activity reached values as high as 2.0-2.5 times that occurring during the spindle trains of synchronized sleep.

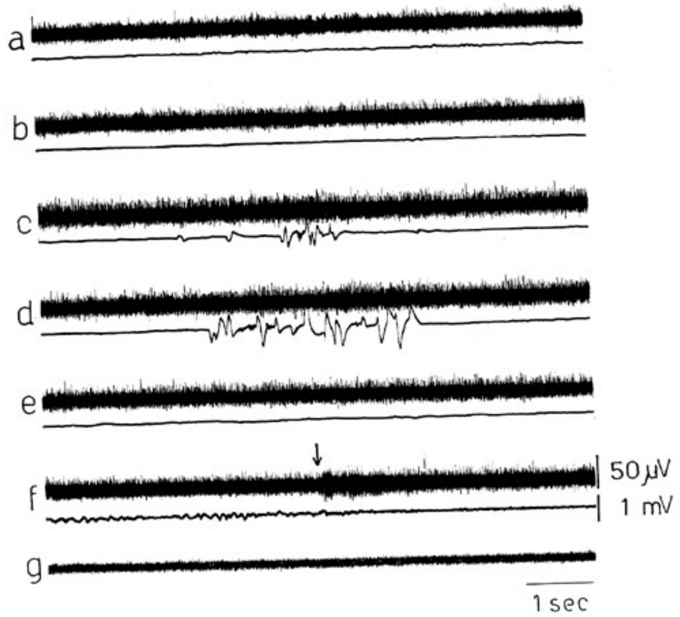

Fig. 10. – *Oscillographic records of the overall pyramidal activity taken during different EEG backgrounds, as illustrated in Fig. 9.*

Upper beam: integrated pyramidal activity recorded with a bipolar electrode from the left pyramidal tract, through an A. C. preamplifier (low-pass filter at 10 Kcps and high-pass filter at 500 cps, 12 db per octave). Lower beam: eye movements (EOG). *a*: synchronized sleep; *b*: beginning of the episode of desynchronized sleep; *c*, *d*: increase in the background activity of the pyramidal tract during bursts of REM; *e*: spontaneous wakefulness; *f*: increase of the pyramidal activity during arousal induced by acoustic stimulation (whistle) as indicated by the arrow; *g*: noise of the recording system.

5. *Single unit activity of pyramidal tract fibers during sleep and wakefulness in cats with chronic ablation of the motor cortex.* — The firing patterns of single units recorded from the pyramidal tract of unrestrained, unanesthetized cats after ablation of the motor cortex was affected by sleep and wakefulness in a manner very

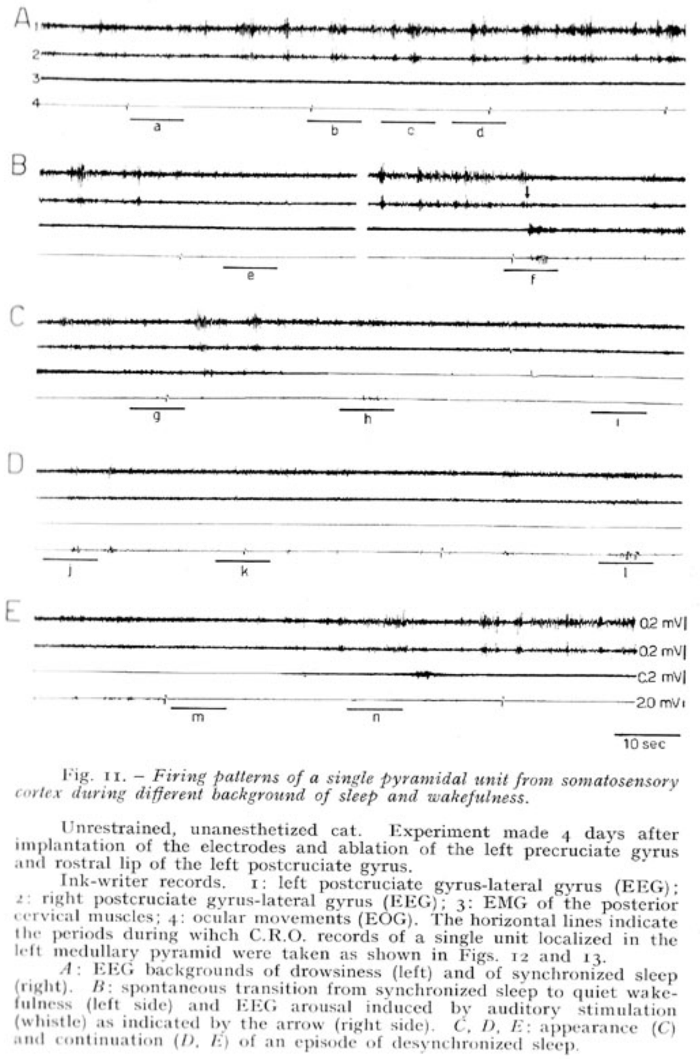

Fig. 11. – *Firing patterns of a single pyramidal unit from somatosensory cortex during different background of sleep and wakefulness.*

Unrestrained, unanesthetized cat. Experiment made 4 days after implantation of the electrodes and ablation of the left precruciate gyrus and rostral lip of the left postcruciate gyrus.

Ink-writer records. 1: left postcruciate gyrus-lateral gyrus (EEG); 2: right postcruciate gyrus-lateral gyrus (EEG); 3: EMG of the posterior cervical muscles; 4: ocular movements (EOG). The horizontal lines indicate the periods during wihch C.R.O. records of a single unit localized in the left medullary pyramid were taken as shown in Figs. 12 and 13.

A: EEG backgrounds of drowsiness (left) and of synchronized sleep (right). *B*: spontaneous transition from synchronized sleep to quiet wakefulness (left side) and EEG arousal induced by auditory stimulation (whistle) as indicated by the arrow (right side). *C*, *D*, *E*: appearance (*C*) and continuation (*D*, *E*) of an episode of desynchronized sleep.

similar to that of the pyramidal tract neurons recorded by Evarts (17) from the precentral gyrus (motor cortex) of the monkey.

The discharge patterns of a pyramidal tract fiber, originating from the somatosensory cortex, are illustrated by the records of Figs. 12 and 13; while the corresponding EEG, EMG and EOG records (ink-writer) are given in Fig. 11. Unit firing is correlated with the EEG in Fig. 12 and with the EOG in Fig. 13.

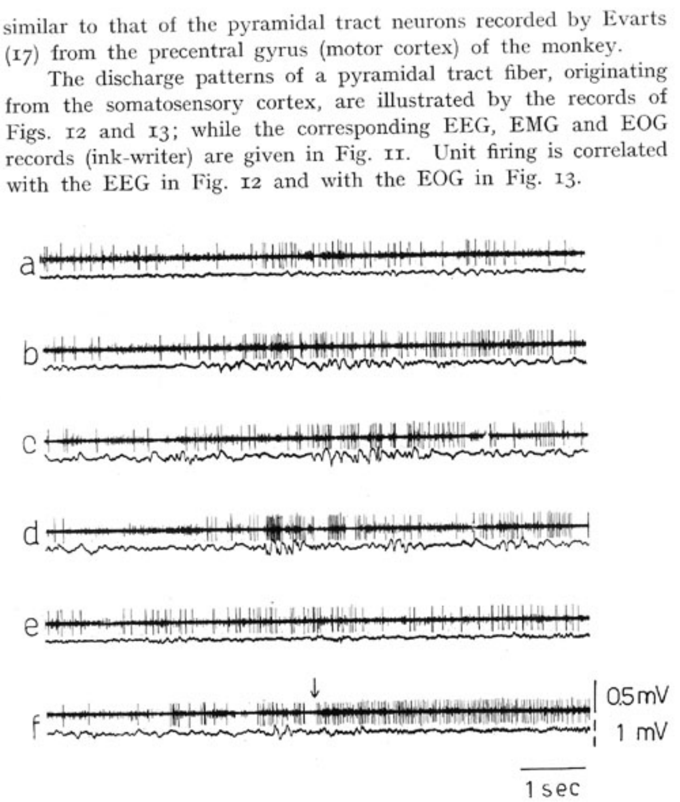

Fig. 12. – *Firing patterns of a single pyramidal unit from somatosensory cortex during wakefulness and synchronized sleep.*

Same animal as in Fig. 11. C.R.O. recording of firing of pyramidal unit (above) and of electrocortical activity from posterior sigmoid gyrus of the left side (below).

a: pattern of pyramidal discharge on a background of drowsiness (see Fig. 11 *A*); *b, c, d*: bursts of discharge during spindles of synchronized sleep (see Fig. 11 *A*); *e*: pattern of pyramidal discharge during quiet wakefulness (see Fig. 11 *B*). Note absence of high-frequency bursts and the rate of background activity higher than in *a*; *f*: the electrocortical desynchronization induced by a whistle (arrow; see Fig. 11 *B*) is accompanied by an increase in rate of firing of the pyramidal unit, which discharges quite regularly.

During quiet wakefulness (Fig. 12 *e*) the discharge tended to be rather regular with absence both of short and of long interspike intervals. The mean discharge frequencies ranged from 4 to 8/sec. When an orienting reaction was produced by auditory stimulation (active wakefulness; Fig. 12 *f*), the regularity of the discharge became greater. Also the rate of firing increased, reaching mean values of 22-26/sec. Higher rates could be observed only at the very beginning of an arousal reaction. In all instances, however, there were neither bursts of high-frequency discharge nor long periods of inactivity.

During drowsiness the discharge became slightly irregular, but only during synchronized sleep was the discharge characterized by the appearance of short-lasting bursts of spikes alternating with short periods of complete inactivity (Fig. 12 *b-d*). The result was that the long and short interspike intervals increased. The bursts of pyramidal discharge were clearly related with the EEG spindles in confirmation of previous findings (cf. 17). However there was not always a strict relation between individual high voltage waves of the cortical spindles and single bursts of unit discharge. The mean discharge frequency during the whole episode of synchronized sleep ranged from 5 to 10/sec, but during the EEG spindles rates as high as 20-100/sec were attained.

During desynchronized sleep the bursts of discharge alternating with periods of silence were still present; however, the duration both of the bursts and of the intervals of silence was definitely greater. There was, therefore, as compared to synchronized sleep, a further increase in the proportion of very short and of very long interspike intervals, since the frequency of discharge increased during the bursts and these were interspersed with longer periods of inactivity. The bursts of high-frequency discharge were related in time with the bursts of REM. Fig. 13 (*h, j, l*) shows this relationship very clearly. There was, moreover, some relation between frequencies and overall duration of the pyramidal outbursts and amplitude and frequency of the groups of REM. This was not a constant finding, however. Occasionally isolated movements of the eyes were associated, during desynchronized sleep, with long lasting bursts of high-frequency discharge (Fig. 13 *k*). However, when isolated ocular movements occurred spontaneously on a background of light sleep, the pyramidal discharge was entirely unaffected (Fig. 13 *g*). The mean discharge frequency throughout the episodes of desynchronized sleep ranged

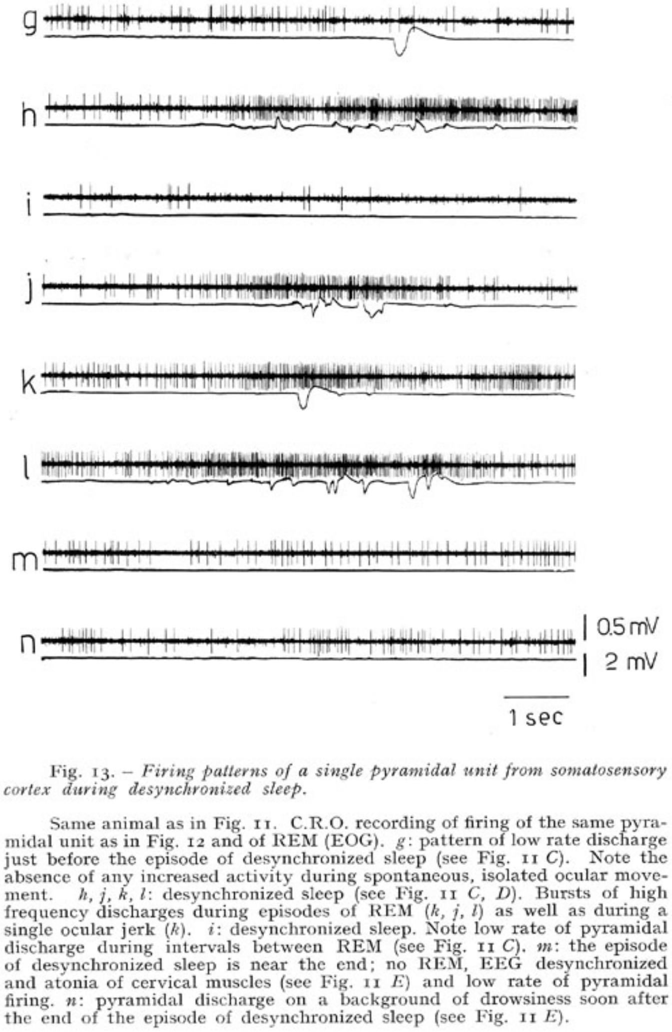

Fig. 13. – *Firing patterns of a single pyramidal unit from somatosensory cortex during desynchronized sleep.*

Same animal as in Fig. 11. C.R.O. recording of firing of the same pyramidal unit as in Fig. 12 and of REM (EOG). *g*: pattern of low rate discharge just before the episode of desynchronized sleep (see Fig. 11 *C*). Note the absence of any increased activity during spontaneous, isolated ocular movement. *h, j, k, l*: desynchronized sleep (see Fig. 11 *C, D*). Bursts of high frequency discharges during episodes of REM (*k, j, l*) as well as during a single ocular jerk (*k*). *i*: desynchronized sleep. Note low rate of pyramidal discharge during intervals between REM (see Fig. 11 *C*). *m*: the episode of desynchronized sleep is near the end; no REM, EEG desynchronized and atonia of cervical muscles (see Fig. 11 *E*) and low rate of pyramidal firing. *n*: pyramidal discharge on a background of drowsiness soon after the end of the episode of desynchronized sleep (see Fig. 11 *E*).

from 12 to 14/sec, but at the time of REM the rate reached values as high as 35-150/sec.

Summing up, the phasic increases of the integrated pyramidal discharge that occur synchronously i) with the spindles during synchronized sleep and ii) with the outbursts of REM during the desynchronized phases were related, at the unit level, with outbursts of high frequency impulses. During desynchronized sleep these outbursts were much longer in duration and higher in rate than during the EEG spindles.

6. *Dorsal root potentials evoked by pyramidal stimulation following chronic ablation of the motor cortex.* — The cats, which after ablation of the motor cortex had presented a modulation of the pyramidal discharge during sleep, similar in character to that occurring in intact preparations, were later decorticated with anemic procedure, paralyzed with Flaxedil, and artificially respired. The acute experiment was performed 15 to 49 days following removal of the motor cortex, after complete degeneration of the corticospinal motor fibers. Physiological evidence of the degeneration was provided by the fact that repetitive stimulation of the pyramidal tract, performed in the unrestrained, unanesthetized cat just before the anemic decortication, did not produce any detectable motor effect on the contralateral hindlimb, when the stimulation was performed with the same parameters which produced the typical flexor response soon after recovery from the cortical ablation. With higher stimulus intensities movements of the ear, of the vibrissae, as well as orbicular contractions were observed; but these effects were obviously due to spread of current to surrounding brain stem structures. Even with such strong stimuli, the typical pyramidal motor response of the contralateral hindlimb was always absent.

Repetitive stimulation of the pyramidal tract performed in the acute experiment with stimulus intensities similar to those which produced hindlimb flexion before degeneration of the corticospinal motor fibers evoked a dorsal root potential (DPR). Its amplitude approximated that of the DRP elicited by stimulating the pyramidal tract in the intact animal with the same parameters of stimulation. The latency from the onset of pyramidal stimulation was about 25 msec, and the total duration was the same as that of the DRP produced by afferent volleys in the limb nerves. The same parameters of pyramidal stimulation, however, either did not produce any ventral root discharge, or such an effect when present was much smaller in amplitude than that elicited in the control experiments. That this negative result was not due to damage of the spinal cord was shown by the normal amplitude of the monosynaptic and the polysynaptic reflexes recorded from a ventral root following stimulation of the central ends of the ipsilateral tibial and deep peroneal nerves.

Fig. 14 demonstrates the results obtained with the cat, whose chronic lesion is illustrated in Figs. 2 *C* and 3 (position of the stimulating pyramidal electrode in Fig. 1). The experiment was performed 49 days after removal of the motor cortex of the left side. The dorsal root potentials elicited on the right side by stimulation of the left medullary pyramid with the chronically implanted electrode (Fig. 14 *a'*, *b'*, *c'*: upper traces) were similar in amplitude to DRP produced in a normal cat by stimuli of comparable intensities (Fig. 14 *a*, *b*, *c*: upper traces). The ventral root discharges, however, (see Fig. 14 *a'*, *b'*, *c'*: lower traces) were markedly reduced with respect to the ventral root discharges recorded in the intact cat (Fig. 14 *a*, *b*, *c*: lower traces). The last group of records in Fig. 14 (*d* and *d'*) shows that the DRP (upper traces) and the mono- and polysynaptic reflexes (lower traces) elicited by stimulating the right deep peroneal nerve reached the same amplitude, with the same intensities of stimulation, in the cat with the sensory-motor cortex intact (*d*) and in the animal with left motor cortex removed (*d'*).

Similar results were obtained when the acute experiment was performed on the same animal, which had previously been submitted to unilateral chronic ablation of the motor cortex. In the experiment of Fig. 15 the stimulating electrode was introduced into the midbrain stereotaxically, and the effects of stimulating the tegmentum and the basis pedunculi of both sides were studied 44 days after removal of the left motor cortex. The extent of the cortical lesion was comparable to that of Fig. 2 *C*. Traces *a*, *b* and *d*, *e* of Fig. 15 give the responses to repetitive stimulation, with the same electrical parameters, of points localized at different depths of the contralateral brain stem, as indicated in the diagram. As the electrode passed through the tegmentum, DRP and ventral root discharges could be recorded both on the right (Fig. 15 *a*, *b*) and on the left side (Fig. 15 *d*, *e*) by stimulating respectively the left and the right side of the mesencephalic reticular formation (depths from -1 to -4). The responses were of comparable amplitude on

both sides. On passing into the *substantia nigra* (depth -5) the responses vanished. When the electrode reached the corticospinal fibers in the basis pedunculi, DRP of comparable amplitude appeared (depths -6, -7). However the ventral root discharges elicited by

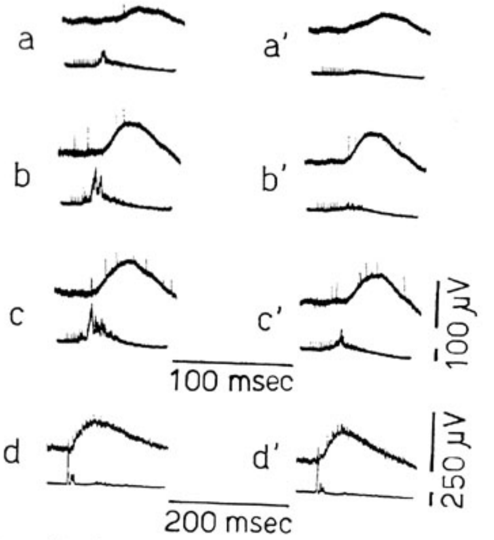

Fig. 14. – *Dorsal root potentials and ventral root discharges evoked by pyramidal stimulation.*

The upper traces were recorded from a dorsal root filament (upper L 7), on the right side. The filament was cut 15 mm from the dorsal root entry zone and placed on two electrodes, one close to the entry zone and the other on the cut end. In this and the following figure upwards deflection denotes negativity of the central electrode. The lower traces were recorded from ventral roots L 7-S 1, on the right side.

a-d: control records taken from a cat with sensory-motor cortex intact.

a'-d': records taken from the same cat as in Figs. 4-8 after ablation of the left motor cortex (see Figs. 2 *C*, 3). Experiment made before sacrifice, 49 days after cortical topectomy.

a-c and *a'-c'*: effects of repetitive stimulation of the left pyramid at the medullary level above the *decussatio* with a train of 10 shocks at 500/sec, 1.0 msec in duration, and at intensities 1.5 (*a*, *a'*), 2.5 (*b*, *b'*) and 3 (*c*, *c'*) times the threshold for dorsal root potentials. *d* and *d'*: effects of single shock stimulation of central end of the right common peroneal nerve, with single shock of 0.5 msec, 4 times the threshold for the monosynaptic reflex, to prove that segmental stimulation was equally effective in both animals. The cats were anesthetized with Nembutal, paralyzed with Flaxedil, and artificially respired.

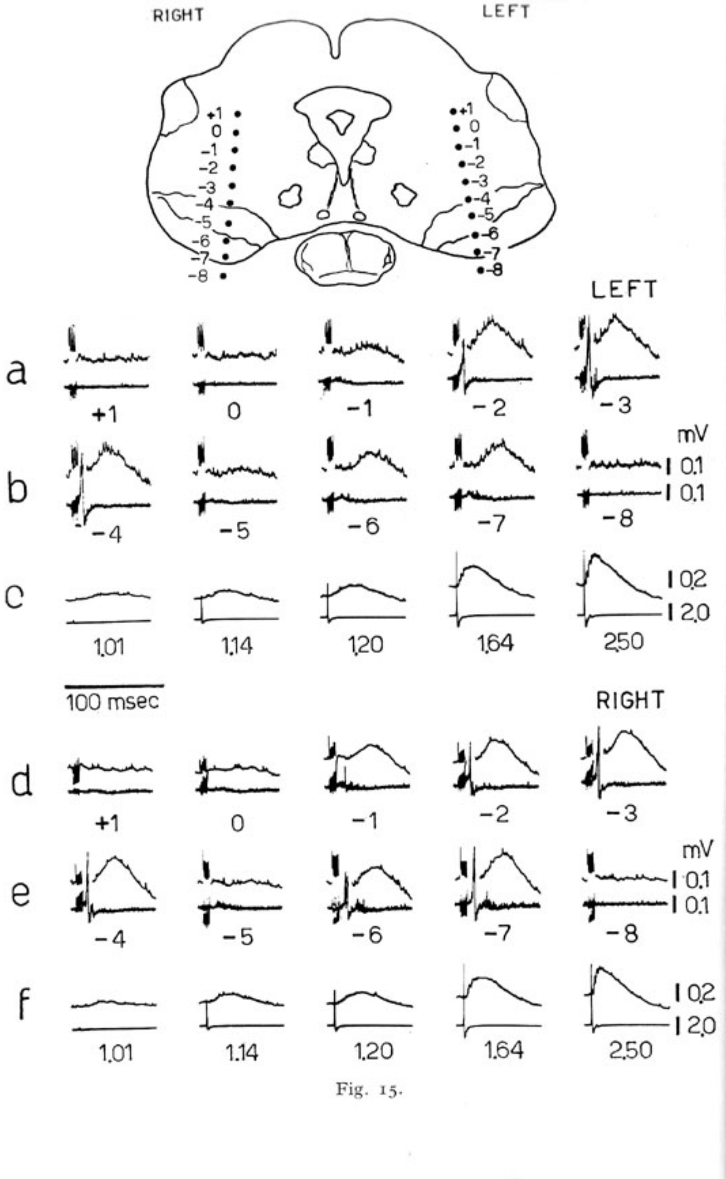

Fig. 15.

stimulation of the mesencephalic corticospinal tract were not bilaterally equivalent. On the side contralateral to the cortical ablation (Fig. 15 *b*: -6, -7) the ventral root discharge was almost nonexistent, but stimulation of the intact pyramid produced on the contralateral side a well-developed motor discharge (Fig. 15 *e*: -6, -7). Fig. 15 *c* and *f* show the similarity in the development of the monosynaptic and polysynaptic reflexes, as well as of the DRP, after stimulation of both tibial nerves.

Summing up, the experiment illustrated in Fig. 15 indicates that sufficient motor cortex was removed to abolish almost entirely the motor component of the corticospinal response, but that the depolarizing effect on the primary afferents was nevertheless almost unmodified. Incidentally the similarity in the amplitude of the

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Fig. 15. – *Absence of ventral root discharge with persistence of dorsal root potentials following stimulation of the basis pedunculi in cat with chronic ablation of corresponding motor cortex.*

Cat submitted to chronic ablation of the left precruciate gyrus and the rostral lip of the left postcruciate gyrus. The ablation extended deep into the ventral bank of the cruciate sulcus. The experiment was performed 43 days after cortical ablation, *i. e.* when degeneration of the pyramidal fibers arising from the motor cortex had occurred. The animal was submitted to anemic decortication, paralyzed with Faxedil and artificially respired.

Upper traces are dorsal root potentials (DRP) recorded from the most caudal dorsal rootlet at L 6. Lower traces are potentials recorded from the whole ventral root at S 1.

The records in *a, b, c* were taken from the roots of the *right* side, while those in *d, e, f* came from the roots of the *left* (control) side.

a, b: show the effects of repetitive stimulation (6 rectangular pulses at 650/sec, 1 msec, 2 V) of the *left* side of the brain stem at the coordinates indicated in the diagram. DRP associated with ventral root discharge occur on the right side by stimulation of the left mesencephalic reticular formation (-1, -2, -3, -4). No effect on stimulation of the *substantia nigra* (-5), and selective appearance of DRP, not associated with a ventral root discharge, by stimulating the left basis pedunculi (-6, -7). *c*: DRP and ventral root discharges elicited by stimulation of the central end of right tibial nerve with rectangular pulses, 0.05 msec in duration. The stimulus intensities are expressed in terms of time threshold (T) for the monosynaptic reflex. The growth of the monosynaptic reflex is paralleled by the development of the DRP. Note further increase in amplitude of the DRP at 2.50 T, together with the appearance of the polysynaptic reflex.

d, e: show the effects of repetitive stimulation (same parameters as in *a, b*) of the right side of the brain stem at the coordinates indicated in the diagram. Note appearance of DRP and ventral root discharge on stimulating the right mesencephalic reticular formation (-1, -2, -3, -4) as well as the right pyramid (-6, -7). *f*: DRP and ventral root discharges elicited by stimulation of the central end of left tibial nerve with the same parameters of stimulation as in *c*.

DRP elicited contralaterally by stimulating the corticospinal tract of the intact side and of the decorticated side strongly indicate that the precruciate (motor) cortex does not contribute significantly to the dorsal root response.

DISCUSSION

The present study was undertaken in order to ascertain i) whether there is a modulation during sleep of the corticofugal fibers arising in the somatosensory cortex and coursing along the pyramidal tract, and ii) whether this modulation, if present, might contribute to the depression during sleep of the polysynaptic spinal reflexes through presynaptic depolarization of the central endings of the flexion reflex afferents (FRA). The first question has been definitely and positively answered by our experiments, while an affirmative reply to the second question rests upon the acceptance of a working hypothesis which will be discussed below.

The data of the literature and the original observations which have prompted these investigations have been reviewed in the introduction. Let us simply mention here the main results of our investigations. The *chronic* experiments have shown that the pyramidal tract neurons of the somatosensory cortex are affected, as are the corresponding units of the motor cortex (17), by wakefulness and by the synchronized and desynchronized phases of sleep. These conclusions have been drawn by recording both the integrated activity and the discharge of single units of the pyramidal tract in the unanesthetized, free-moving cat after chronic destruction of the motor cortex.

The *acute* experiments have shown, on the other hand, that stimulation of the fibers arising from the somatosensory cortex yields clear-cut dorsal root potentials (DRP), which are generally attributed to depolarization of the intraspinal endings of the afferent fibers (see 15). As mentioned in the introduction this effect, which would be responsible for presynaptic inhibition (see 15), is limited to group I *b*, group II and III proprioceptive fibers and to cutaneous fibers, *i. e.* to the flexion reflex afferents (FRA).

Depolarization of the primary afferent endings has been found by stimulating not only the postcruciate cortex (2), but also the precruciate motor cortex (9, 10, 3). The DRPs evoked by precruciate stimulation were abolished, however, by removal of the postcruciate cortex, thus suggesting that the effect of stimulation of the motor cortex was mediated indirectly through synaptic activation of neurons in the postcruciate cortex (3). This conclusion is supported by the present experiments, which showed that the DRPs elicited by pyramidal stimulation following degeneration of the corticospinal fibers originating from the motor cortex do not differ in amplitude from the DRPs elicited by stimulating in the same animal the intact corticospinal tract with the same parameters of stimulation. The intraspinal pathways of the presynaptic inhibition of the FRA arising in the somatosensory cortex have recently been thoroughly investigated in an anatomical study (44: see also 33).

Although the entire cerebral cortex may send fibers to pyramidal tract (49; see however 12), it is known that the sensory-motor area is the most important source of pyramidal fibers (cf. 37, 49, 6, 7, 44). Therefore only pyramidal fibers arising in the somatosensory cortex would remain after complete ablation of the motor cortex. It is of interest that the modulation of the integrated pyramidal discharge during sleep is practically abolished after complete destruction of both the motor and the somatosensory cortices (34-36).

The results of the chronic and acute experiments complement each other, though, only if one assumes that the volleys of electrical pulses applied to the pyramidal tract in the acutely decorticated, unanesthetized cats exerted an effect on the spinal endings of the FRA which was similar in kind, though possibly different in extent, to that of the outbursts of high frequency impulses which occurred in the chronic experiments during the REM periods of desynchronized sleep. If this assumption is accepted one may conclude that the phasic depression of the polysynaptic reflexes usually associated with the bursts of REM (19, 20) is due, in part at least, to corticofugal volleys arising in the somatosensory cortex synchronously with the phasic ocular phenomena, coursing along the pyramidal tract, and inhibiting presynaptically the spinal endings of the FRA.

The much shorter bursts of high frequency pyramidal discharge occurring during the spindles of synchronized sleep, do not seem to produce an effect on the FRA comparable to that seen during REM. This conclusion is also supported by the observation that the polysynaptic reflexes are of the same amplitude during the spindles and the interspindle lulls (19, 20). This statement is not necessarily true for the cortical regulation during sleep of other systems, such as the γ motoneurons (cf. 23, 24).

Thus our working hypothesis on the presynaptic inhibition of FRA elicited by pyramidal volleys, arising in the somatosensory cortex, might explain the phasic depression of the flexion reflexes occurring during desynchronized sleep. Furthermore it has the advantage of leading to three predictions which might be verified experimentally:

i) dorsal root potentials will be present in the unrestrained, unanesthetized cat during the bursts of REM of the desynchronized sleep;

ii) the antidromic response of the flexion reflex afferents to intraspinal stimulation will be enhanced during these bursts, as it has been shown to occur for group I *a* muscle afferents (40-42);

iii) the enhancement of the antidromic responses of the FRA in this experimental condition should be reduced by removal of the contralateral somatosensory cortex, if the presynaptic inhibition of the FRA is mainly related with corticofugal volleys arising from that area of the neocortex.

Concerning point iii) we want to emphasize that the phasic depression of the polysynaptic reflexes during the bursts of REM is not exclusively due to presynaptic inhibition arising in the somatosensory cortex. This conclusion is supported by the observation that a phasic depression can still be observed after bilateral ablation of the sensorymotor cortex (45).

The same structures localized in the lower brain stem which depolarize the central endings of the group I *a* primary afferents might also depolarize the flexion reflex afferents (40-42; cf. 8). The cutaneous and high threshold muscular afferents are likely to be affected also by structures of the rostral brain stem, for the present experiments show that depolarization of the primary afferents is also elicited by stimulation of the mesencephalic reticular formation. Excitability measurements of primary afferents utilizing Wall's technique (50) or intrafibre recordings at varying depths within the spinal cord have not been made during these brain stem stimulations. It is of interest, however, that neurons in the mesencephalic reticular formation show outbursts of discharges synchronous with the REM during desynchronized sleep (32) and there may be a causal or cognate relationship between increase in this neuronal activity and the depolarizing effect on the flexion reflex afferents.

SUMMARY

1) Pyramidal activity has been recorded at the medullary level in unrestrained, unanesthetized cats following unilateral chronic ablation of the motor cortex, with the aim of determining whether the modulation during sleep and wakefulness of the pyramidal discharge originating from the somatosensory cortex could be referred to volleys exerting presynaptic depolarization of the flexion reflex afferents.

2) The integrated activity of the pyramidal tract fibers coming from the somatosensory areas of the cortex reaches a steady level during quiet wakefulness, and increases transiently during induced arousal.

3) During synchronized sleep there is a gradual decrease in the pyramidal activity when peaks of discharge synchronous with the EEG spindles occur.

4) During desynchronized sleep there is phasic enhancement of the pyramidal discharge, occurring at the time of the bursts of REM.

5) The changes in the background activity of the pyramidal tract following ablation of the motor cortex are paralleled by changes in rate and pattern of discharge recorded from single units during the different phases of sleep in the same kind of preparation.

6) Stimulation of the pyramidal tract following chronic degeneration of the corticospinal motor fibers elicits contralateral dorsal root potentials of the same amplitude as those induced by stimulation of the intact pyramid. This effect has been recently referred to presynaptic depolarization of the flexion afferents. The ventral root discharge, on the other hand, is greatly reduced or completely abolished on the side opposite to the cortical ablation.

7) The modulation during sleep and wakefulness of pyramidal activity following ablation of the motor cortex is thus likely to reflect changes in the level of depolarization of the flexion reflex afferents. In particular the increase in the pyramidal discharge originating from the somatosensory cortex during the bursts of REM may contribute, through a mechanism of presynaptic inhibition, to the phasic depression of the polysynaptic reflex that occurs at the time of the bursts of REM.

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