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Neuronal Activity in the Chronic and Acute Epileptogenic Focus

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Activity of single neurons was recorded in the chronic (alumina) epileptogenic focus of unanesthetized monkeys with micropipettes. In some instances, intracellular recordings were obtained. Most of the bursting units had long interspike intervals between the first spikes in the burst. The following part of the burst consisted of a high-frequency train of spikes riding on a small membrane-depolarizing shift in many cases. Some units did not show the long initial intervals and differed in other respects as well. The activity in the chronic focus of the monkey was compared with that in the acute penicillin focus of the cat. A distinct difference between the two types of foci was found in the interspike interval patterns of bursting units. In some instances, movement-related trains of bursts separated by quiet periods, occurred in the the chronic focus. These cyclically occurring groups of bursts had a repetition rate of 25–35 per min. They were regarded as drug-induced (Sernylan). Within the trains, interburst intervals and the number of spikes in each burst were significantly reduced. In one cycling neuron, there was a negative correlation between trains of bursts and paroxysmal discharges in the EEG. The different types of activity in the chronic and acute focus are seen in parallel with some presumed structural differences.

INTRODUCTION

Microelectrode studies in monkeys with chronic epileptogenic foci produced by cortical injection of aluminum hydroxide gel show stereotyped high-frequency burst patterns in many neurons of the focus (6, 21, 24, 27, 30). Similar burst patterns have been found in foci of epileptic patients (5, 27). Some of these bursts in monkey and man have a long interval between the first and second action potential. Few attempts have been

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made to record intracellularly from the chronic alumina focus. Atkinson and Ward (1) reported that intracellular recording from units exhibiting typical burst firing was characterized exclusively by very short action potentials arising abruptly from a stable baseline suggestive of axon membrane. However, Prince and Futamachi (20) reported unit firing superimposed on agumented membrane depolarizing shifts which were of much smaller amplitude than usually encountered in the acute penicillin focus (2, 7, 13–15, 18). Neuronal bursts in the acute focus are closely time-locked to the interictal paroxysmal surface discharges (13, 19), whereas no consistent temporal relationship between these phenomena has been found in the chronic focus (27). An inherent tendency of penicillin surface spikes to occur in cycles of spike and no-spike periods has been reported (17, 19). No counterpart of this cycling phenomenon in the chronic focus has been reported so far. The present study was designed to further compare the burst patterns in the chronic and acute focus and provides some insight into the slower changes of membrane potential in epileptic neurons. A new technique (10) enabled us to record from cells in the alumina focus in unanesthetized monkeys with micropipettes by means of a chronically implanted recording chamber.

METHODS

Three adult rhesus monkeys (*Macaca mulatta*) were used to record from the chronic focus. The monkeys underwent sterile craniectomy and aluminum hydroxide gel was injected into the left precentral and postcentral cortex, approximately in the hand and arm area. Four months later two animals had developed epilepsy with partial seizures involving the right side of the body and generalized convulsions. Small twitch-like involuntary movements were observed interictally in the fingers contralateral to the focus. Interictal encephalographic recordings showed focal spike potentials. The remaining animal showed focal spiking and infrequent partial seizures. Six months after alumina injection, a stainless steel bone-fixed adaptor (25 mm diam) was aseptically implanted over the injection site (30). The exposed dura was sealed with a removable sheet of silastic rubber to retard infection. Three epidural EEG recording electrodes were implanted at the same time, approximately equally spaced around the circumference of the adaptor (Fig. 1). A concentric bipolar stimulating electrode was stereotactically implanted in the ipsilateral peduncle at the coordinates of the pyramidal tract (9). During recording sessions the silastic membrane was removed and a Trent–Wells hydraulic microdrive mounted to the adaptor. The dura was penetrated by a glass guide pipette, using a technique described by Glötzner and Calvin (10). The concentric recording micropipette was then advanced out of the guide into the cortex. To stabilize the head

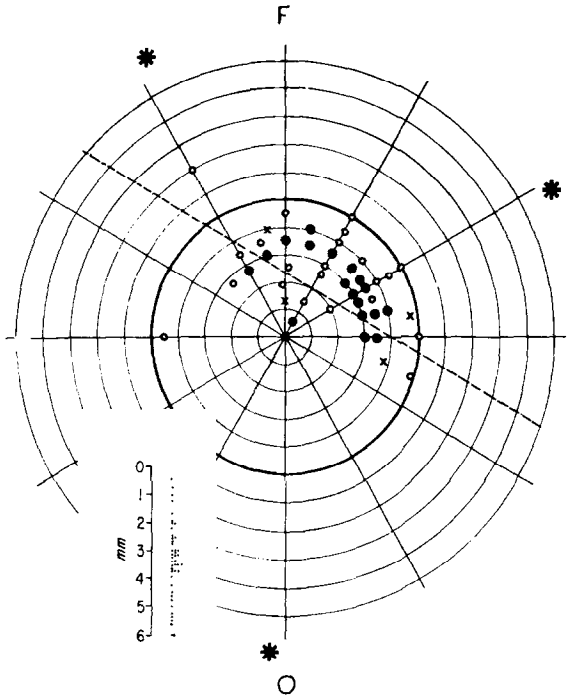

FIG. 1. Topography of the presumed recording sites in the left central cortex of the monkey. Mapping of the central fissure (interrupted line), of the alumina injection sites (x) and of the three implanted EEG electrodes (asterisks) are approximations relative to the chamber. Sites of microelectrode recording are indicated by circles. Open circles—normal neuronal activity but no bursting units encountered, filled circles—bursting and normal units; F—frontal, O—occipital. *Inset:* Distribution of about 40 bursting units in cortical depth relative to first activity in the track. Diameter of outer circle is 20 mm.

during recording sessions, four Allen-head screws were placed in the skull—two in a frontotemporal position and two occipital. The cavities of these screws received four adjustable pins of a metal frame affixed to a primate chair. This device effectively abolished all head movements. Stable recordings did not exceed 15 min. During recording sessions, one monkey had to be tranquilized with 1 mg/kg, im, Sernylan (Phencyclidine hydrochloride), a primate tranquilizing agent. This drug produced a nystagmus and transient rhythmic involuntary movements in the right arm and hand and, to a lesser extent, on the left side. In electromyographic recordings from both hands, periods of activity about 1 sec in duration occurred synchronously on both sides at a rate of 25–40 per min. In normal monkeys, the drug did not induce rhythmic movements.

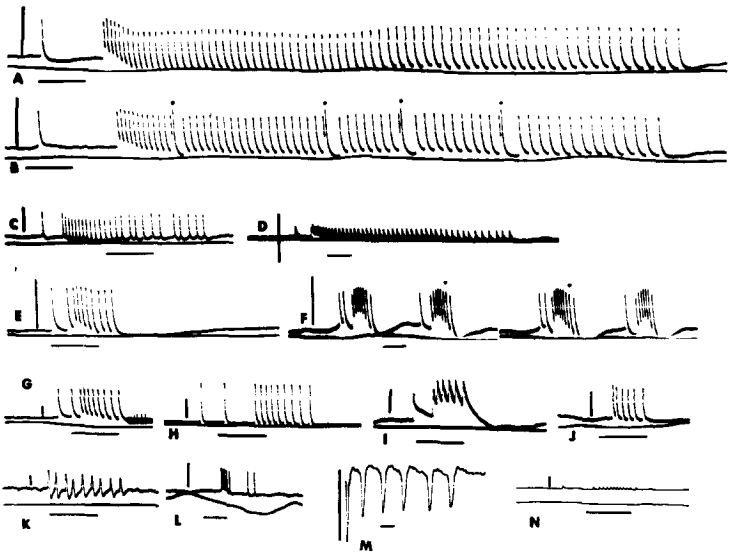

FIG. 2. Types of bursts encountered in different neurons of chronic foci in three monkeys, including bursts with long initial intervals (A–I, N), and bursts, without long initial intervals (J–L). D.C. recordings except for C which is RC coupled. Each capital represents a different unit with the exception of A and B. A: long burst with very long first interval. B: same unit as A showing "fixed coupling" with complete compensatory pause. C and D: two medium length bursts. F: two consecutive double bursts. Each double burst consists of two segments which are separated by a pronounced hyperpolarization. G and H: intracellular recordings from two cells, bursts with long first and second intervals. Membrane potential 40 mv. I: Long first interval burst. J: burst. without long first interval. K: burst with biphasic action potentials and unusual pattern of interspike intervals. L: burst with unusually long terminal intervals. M: exceptional burst because of negative spikes of extremely short duration. Note progressive increase of spike duration. In K and L there also is a progressive decrease in spike amplitude. Calibration in A–H: 10 mv, in I–L: 2 mv. Membrane potentials in A–C, 20 mv and in E, F, 25 mv. D, I–N are extracellular recordings. Time scale: 20 msec in all recordings, except burst M (1 msec). Vertical bar in G represents 200 mv for the EEG in all recordings.

The penicillin experiments were performed acutely in adult cats under light barbiturate anesthesia (Surital, iv). The animals were intubated, immobilized with gallamine triethiodide, and artificially respirated. A burr hole exposed the dura over the anterior sigmoid gyrus. The penicillin focus was produced by penetrating the dura with a micropipette of about 400 μm tip diam, containing less than 0.05 ml of an aqueous penicillin solution (250,000 units/ml). The EEG was recorded from the center of the focus by means of a silver wire placed into the penicillin solution in the pipette. In cat and monkey, the EEG signals were fed into a Grass a-c preamplifier at a low frequency cutoff of 0.3 Hz and recorded on tape or a Brush ink-

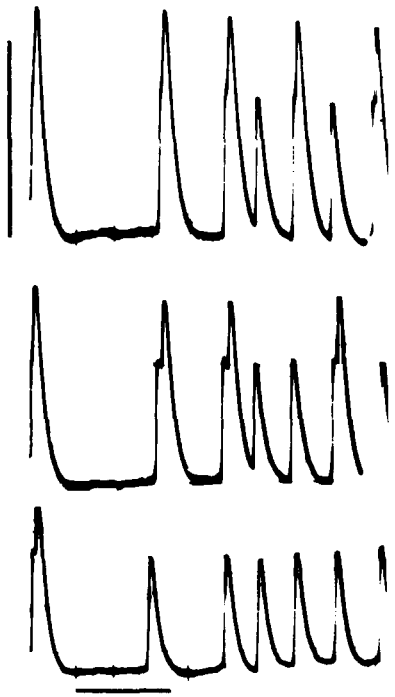

FIG. 3. Burst in a deteriorating bursting neuron at the beginning, in the middle, and at the end (top to bottom) of the short recording period. Only part of the burst is shown. The increasing notching (widening of the A-B break) and absence of the higher second B part of the spike toward the end of recording indicates progressive failure of the somadendritic (B) spike to invade the cell body. The first spike in each burst is the most resistant to the failure. Membrane potential 20 mv. Calibration 5 mv, 5 msec.

writer. During recording sessions, the EEG was recorded unipolarly from the sagittal implanted electrode (Fig. 1) relative to ground. The recording sites relative to the chamber were defined by polar coordinates (radius and angle) with respect to the center of the bone-fixed adaptor. Unit activity in the cat was recorded from the center of the focus using a concentric micropipette which was advanced out of the penicillin pipette. The recording micropipettes were filled with 1.5 molar potassium citrate and had a tip resistance of about 20 Megohms. A Bioelectric P1 electrometer amplifier with input capacitance neutralization amplified the cellular potentials which were recorded on FM tape. Most unit recordings were regarded as quasi-intracellular (action potentials about 10 mv, membrane potential 20 mv). Firing patterns of one bursting cell were analyzed and displayed with a LINC-8 computer using programs developed by Calvin (4).

RESULTS

Topography of Bursting Units in the Alumina Focus. Units firing in high-frequency bursts were recorded in all layers of the cortex. Most frequently they were found at a depth of 3–4 mm below the surface (Fig. 1). Some uncertainty is introduced into these measurements, as the electrode tracks did not run strictly perpendicular to the cortical layers. Normal and bursting units were found in both precentral and postcentral cortex in all monkeys. In one animal with generalized convulsions, the greatest number of bursting units were found in a small area in the precentral gyrus, near the most sagittal injection site (Fig. 1). The location of the central fissure was confirmed postmortem in this monkey. In the remaining animals the bursting units found were scattered over a larger area and less frequently.

Types of Bursts in the Alumina Focus. Most bursts were short and consisted of ten or less action potentials. Others were of intermediate length while one unit fired in extremely long bursts of about 250 msec duration with up to 70 action potentials (Fig. 2A, B). Most bursts had a "long first interspike interval" (6). This interval between the first and second spike coincided in some instances with a small afterhyperpolarization following the first action potential (Fig. 2A, F). Other cells exhibited a small depolarizing potential between first and second spikes (Fig. 2I). The ensuing high frequency part of the burst usually appeared on a small membrane depolarizing shift (Fig. 2E, F, G, I). In the longer bursts this transient depolarization gave way to a slight hyperpolarization (Fig. 2A, B) concomitant with a gradual decrease in firing rate. In most cases the burst was followed by a transient hyperpolarization which in some instances was very prominent (Fig. 2F). Some units exhibited sporadic spontaneous firing while others showed no signs of spike generation other than in bursts. Even in intracellular recordings in which membrane potentials were 40 mv (Fig. 2G, H), no postsynaptic potentials were observed. There was virtually no difference in duration, amplitude, or shape of action potentials occurring singly or in bursts. No prepotentials preceded the action potentials, which were almost always followed by slow afterpotentials. Figure 2F illustrates

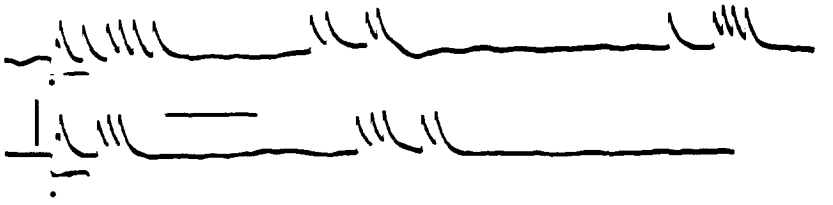

FIG. 4. Continuous recording from unit in chronic focus during two consecutive pyramidal-tract stimuli. After a latency of about 1 msec a whole burst was elicited in each case. Calibrations: 5 mv, 20 msec.

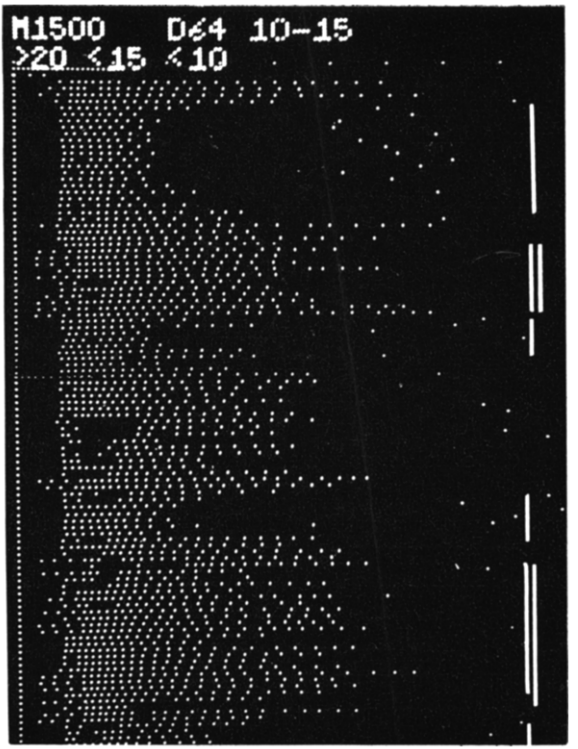

FIG. 5. Dot raster display of consecutive bursts aligned on the first spike; same unit as Fig. 2C. Each dot represents one spike. The display shows periods of short bursts (bar), which recurred with short interburst intervals, and periods (double bar) when the long-first-interval was replaced by several smaller intervals. Note progressive increase of interspike intervals toward end of bursts. The dots at the top are 10 msec apart.

slight variations in two consecutive "double burst." Each double burst consists of two segments separated by 40 msec. A pause of 450 msec separated the two sets of bursts (not shown). The two bursts look almost identical, except for one spike (dot) which changed position from the second to the first segment. All bursts in Fig. 2A–I show a uniform pattern with long first or second intervals.

In some instances a second "premature" action potential arose on the declining phase of a preceding spike, the two spikes being less than 1 msec apart (dots in Figs. 2B and 10B). This brief interval between the normal and the succeeding premature spike remained constant. Such a "fixed coupling" was observed in a number of units. It is probably significant that the sum of the short interval preceding the premature spike and the long interval following it is twice as long as the regular interspike interval.

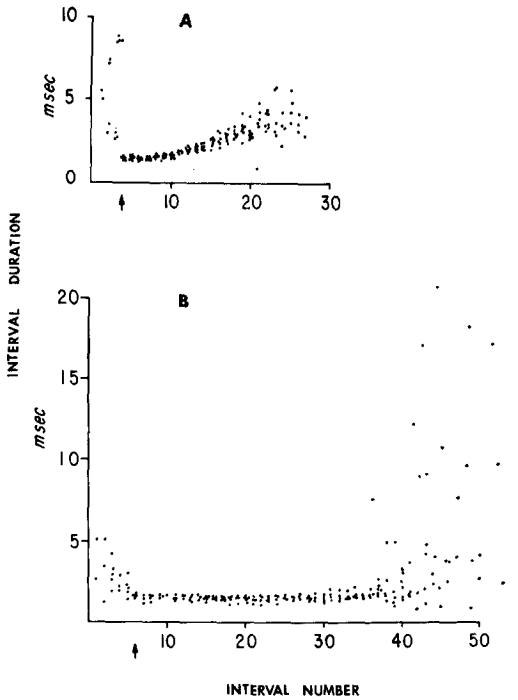

FIG. 6. Successive interspike intervals as a function of interval number. Several consecutive bursts are superimposed. Bursts are aligned to the first "shortest interval," indicated by arrow. The preceding, initial intervals are plotted to the left, the subsequent intervals to the right of arrow. Above: Chronic focus; six consecutive bursts in one neuron (same as Fig. 2C). Below: Acute focus; five consecutive bursts in one neuron (same as Fig. 9, top).

In other words, the premature action potential is followed by a complete compensatory pause during which one regular impulse is omitted without disruption of the original rhythm; thus, the timing of subsequent spikes is not reset to the premature spike. During the compensatory pause, a slight hyperpolarization developed. However, this hyperpolarization is not the timing mechanism for the compensatory pause since the succeeding spike is not generated when the membrane potential returns to the firing level but well after that (Fig. 2B, last two dots).

In one unit which was held only for a short period, the action potentials in the burst showed a clear A-B break (Fig. 3). These A-B breaks became more pronounced as the unit deteriorated. Finally the B-spike (soma-dendritic) failed completely (Fig. 3, bottom) leaving only the first B-spike, which proved the most resistant to failure.

Two units firing in short bursts were identified as pyramidal tract neu-

rons by antidromic stimulation. They responded with a complete burst to each stimulus (Fig. 4). Two units with bursts of intermediate length were not antidromically activated by pyramidal tract stimulation, even at high stimulus intensities. These were classified as nonpyramidal tract neurons. Since these four were the only cells identified by antidromic stimulation, we could not relate the length of bursts to the type of neuron.

The bursts of one unit showed intermittent changes in the pattern over a period of time. The bursts became shorter while the rate of successive bursts increased (Fig. 5, bar). At another point (Fig. 5, double bar) the long-first-interval was replaced by a more gradual initiation of the burst by two or three spikes after which the unit returned to the long-first-interval mode.

Figure 6 plots duration of successive interspike intervals as a function of interval number. When superimposed for consecutive bursts of the same unit, these plots show the increased duration and variability of the inter-

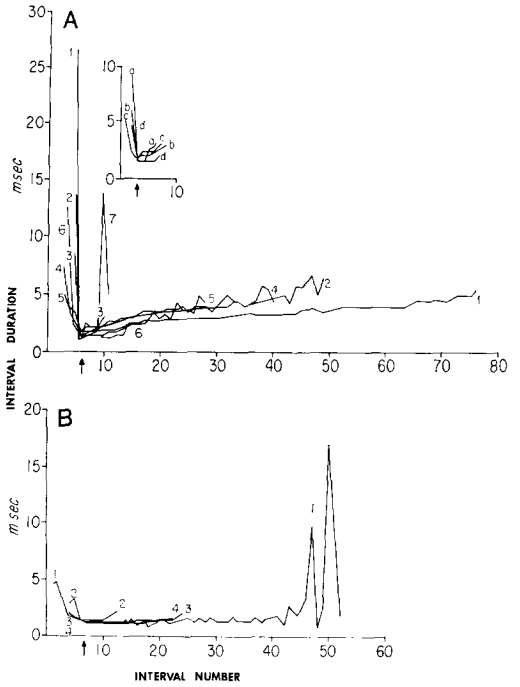

FIG. 7. Interspike interval curves of different neurons versus time. The curves are generated in the same way as plots in Fig. 6. Above: Chronic focus; bursts of seven neurons at different recording sites in different rhesus monkeys. Inset: Chronic focus; four neurons in three monkeys, taken from the literature. a: Ward (28); b and c: Wyler *et al.* (30); d: Calvin *et al.* (6). Below: Acute focus, four neurons in three cats.

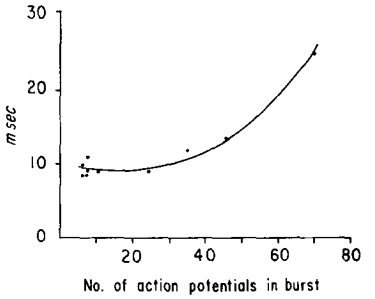

FIG. 8. Chronic focus. Relationship between length of bursts expressed in number of spikes and duration of the first interval. Each point represents one cell.

spike intervals at the beginning and toward the end of the bursts (Fig. 6A). The shortest intervals show virtually no variability at all. In this stereotyped part of the burst, the interspike intervals of about 1.5 msec are close to the maximum firing rate. The limits provided by the maximal firing rate may explain the absence of variability.

Comparison of bursts of different focal units in three monkeys shows some uniformity of the timing pattern in spite of the varying length of the bursts (Fig. 7A). All bursts in Fig. 2A–I exhibit the pattern of Fig. 7A. The bursts in Fig. 2J, L, M, which do not have long-first-intervals fit the pattern when the first spike was aligned with the arrow in Fig. 7A. In burst L, however, the progressive increase in interval duration is much

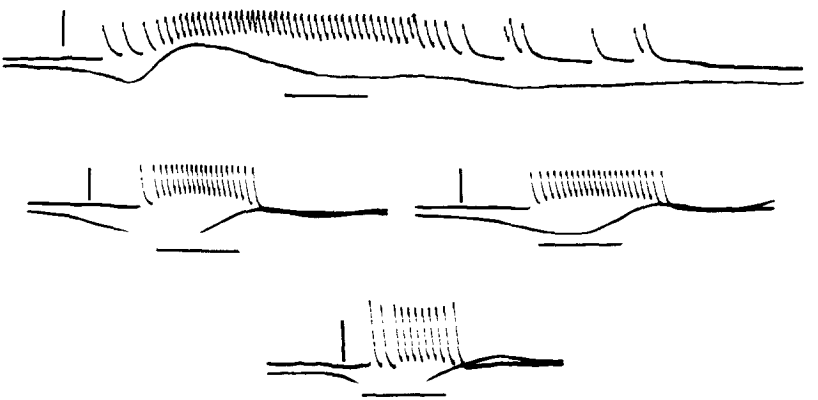

FIG. 9. Center of the acute penicillin focus. Bursts in four cortical neurons in three cats. Simultaneous recordings of local paroxysmal EEG discharges. Note the more symmetrical shape of bursts in contrast to bursts of the chronic focus (Fig. 2). Calibration: Top and middle row 20 mv and 1 mv (EEG), bottom 10 mv and 1 mv. Same time scale (20 msec) in all recordings. Membrane potential in top and middle row 30–35 mv; in bottom row 20 mv.

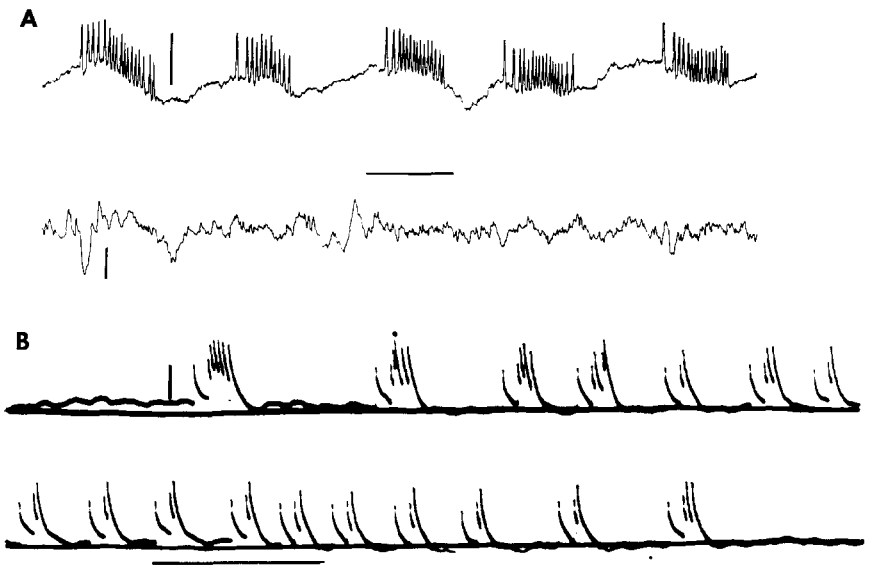

FIG. 10. Groups of bursts in a neuron of the chronic focus. Above: Groups of bursts separated by quiet periods; each spike represents one burst. Inkwriter recording. The simultaneous EEG shows intermittent slow waves. Calibration: 5 mv and 100 μv, 1 sec. Below: Continuous recording of the fourth cycle in the above recording at larger scale. Calibration: 2 mv, 100 msec; EEG: 500 μv.

more pronounced than in the rest of the bursts (Fig. 7A). In burst K (Fig. 2) the interspike intervals do not show the usual progressive increase and are fairly stable at about 4 msec.

We already noted that the duration of successive bursts in one unit could vary in time even though the long-first-interval stayed fairly stable. The maximum burst duration occurred when bursts recurred infrequently. Plotting the duration of the long-first-interval versus the maximum duration of the bursts for different units, we found a monotonic relationship (Fig. 8). The cells with the longest bursts also exhibited the longest first intervals.

Bursts in the Penicillin Focus. In the penicillin focus bursts occur closely time-locked to the surface paroxysmal potential. Most units were recorded at a depth of about 2 mm. The aim was to record trains of action potentials. We did not attempt to record from the cell soma.

In contrast to the recordings from the cell body (13, 14), the presumed axonal recordings showed long trains of action potentials riding on a membrane-depolarizing shift more prominent than in the alumina focus (Fig. 9) but less prominent than in the recordings from the cell body. Consistent long-first-intervals were not seen; instead, successive intervals became shorter as the firing frequency increased (Fig. 6B). A period of "shortest

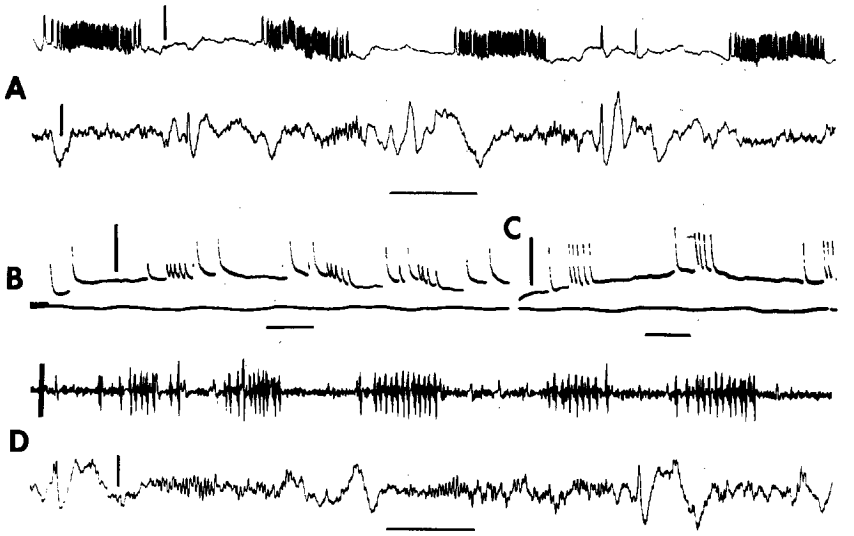

FIG. 11. Simultaneous groups of bursts in two neurons of the chronic focus. A: Groups of bursts and simultaneous EEG. Each spike in the top trace represents one doublet of the large unit. The small unit is not discernable in this recording. Sharp-slow-wave complexes coincide with quiet periods in the unit recording. Calibration: 10 mv and 100 μv, 1 sec. B and C: The two units at larger scale. The large unit fires in doublets; the small has a long first interval. C shows the small unit after isolation; flat trace below is EEG. Calibration: 2 mv and 500 μv, 20 msec. D: Groups of bursts after isolation of the smaller unit and simultaneous EEG recording; each spike represents one burst. A.C. recording to eliminate large pulsation artifacts. Calibration: 2 mv and 100 μv, 1 sec.

intervals" occurred in the middle of the burst, which lasted much longer than in a burst of comparable duration in the alumina focus. Compared to the alumina bursts, the penicillin bursts appear to be "forced" into the short intervals over a much longer period of time and the terminal decline in frequency is much more rapid. In this way the interval plot of penicillin bursts has a more "symmetrical" appearance in contrast to the "asymmetry" of the alumina bursts. That these features are consistent in different neurons is shown by the superposition of their interval plots (Fig. 7B).

Movement-related Groups of Bursts in the Alumina Focus. In some neurons of the alumina focus bursts were observed to recur in groups. These groups were related to fairly regular, involuntary movements induced by Sernylan. In one neuron such a cycle of bursts was observed for about 40 sec (Fig. 10). The bursts occurred in trains separated by quiet periods of 1–1.2 sec (Fig. 10A). A single cycle, composed of active phase plus quiet period, lasted a little less than 2 sec; these recurred at about 35 cycles/min. The groups of bursts rode on slow depolarizing waves of about

3–4 mv amplitude. Within the trains the interburst intervals became as short at 20 msec and the number of spikes per burst was reduced to three (Fig. 10B). The long-first-interval remained remarkably constant.

In another recording session, the activity of two neurons was recorded by the same microelectrode (Fig. 11). The larger unit showed doublets of action potentials, while the smaller fired in distinct bursts (Fig. 11B). The cycles of active and quiet periods of the two units were recurring in a correlated manner at about 25 cycles/min (Fig. 11A). Thus, in the quiet period, neither unit was active. The two spikes in the doublet were about 9 msec apart. Many bursting units had an interval of about the same duration between the first and second spike. Therefore, it is possible that the doublets are bursts reduced to two spikes (30). Toward the end of the recording, the microelectrode was advanced until the "large" unit was lost and the "small" isolated (Fig. 11C, D). The cyclic unit activity was observed for about 10 min. It is very interesting that in this case the trains of bursts started in temporal relationship to the slow wave activity before the EEG became desynchronized (Fig. 11A) whereas paroxysmal surface potentials occurred during the quiet periods. The relationship is not consistent in Fig. 10.

DISCUSSION

Most units were recorded in deep cortical layers (3–4 mm) even if one takes into account that the electrode tracks ran at an angle to the layers. In the macaque the transition of layer VI to the underlying white matter starts at about 2.7 mm in area 4 (26). Our findings parallel the observations of Enomoto and Ajmone Marsan (8) in the penicillin focus in which most bursting units were found in layer VI of the cat cortex. We assume that our recordings are either from axons or from neurons in deep layers and only to a smaller extent from more superficial structures.

Our recordings in the cortical penicillin focus of cats showed predominantly high-frequency trains of spikes superimposed on relatively small depolarizing shifts and no spike inactivation, whereas other intracellular recordings from cell bodies as reported by Matsumoto and Ajmone Marsan (13, 14) show large membrane depolarizing shifts with rapid inactivation of spike generation.

These considerations suggest that in the chronic and acute focus the bursts are generated in the axons fairly remote from the cell bodies, as proposed by Dichter and Spencer (7). In fact, during penetrations we saw quite a number of cells with postsynaptic potentials ("synaptic noise") in which propagated discharges were completely absent. These cells were found more superficially than the bursts. For all these reasons, we classify our burst recordings as axonal.

Compared to usual intracellular recordings, the spike amplitude in most bursts is smaller. These small spikes exhibit a very slow decay that seems to summate temporally (Fig. 2A–I). Tasaki *et al.* (25) and Segundo *et al.* (22) found such spikes in units of the lateral geniculate nucleus and the medullary reticular nuclei of cats. As possible explanations they suggested cell damage, electrotonically attenuated spikes generated at some distance, peculiar but normal dendritic action potentials. Among these alteratives Segundo *et al.* (22) found cell damage the most unlikely in stable recordings. The possible dendritic origin is an alternative to our concept of presumed axonal recordings.

Synaptic mechanisms cannot easily account for the stereotyped coupling of the premature spike to the preceding one and the omission of the next regular spike (Fig. 2B). Therefore, in our opinion, fixed coupling is an indication that these neurons are genuine pacemaker cells. The phenomenon can be explained by the following model: A train of spikes is generated at a site outside the cell body such as Ranvier node or dendrite. During the burst a spike generator (cell body?), ectopic in relation to the train generator, is triggered by the preceding spike, and generates the premature action potential. The latter abolishes the next regular spike by invading the train generator. In this model two assumptions are important: One, that the train generator must have a very long refractory period after the invasion (more than 1 msec), in order to account for the long compensatory pause, and two, that the ectopic generator is not invaded completely by the preceding spike or else it would be refractory and not able to generate the spike prematurely.

Penicillin Versus Alumina Bursts. Bursts in the acute and chronic focus tend to be different. However, one has to bear in mind that different species of animals were involved in these experiments.

Different bursting units in foci in different macaques seem to follow the same patterns of discharge (Fig. 7A and inset). The dominant feature in many of these bursts is the long-first-interval which is absent in the unit firing of the acute focus. Instead, there is a more gradual build-up of high frequency discharges. This and the relatively long period of "shortest intervals" in the penicillin bursts give them the appearance of symmetry (Fig. 6B, 7B, 9). This symmetry has not been reported in previous recordings from the penicillin focus; however no analysis of the interspike intervals has been done in these studies (8, 12). However, a mathematical analysis of interspike interval distributions with bursts from the cortical penicillin focus in cats has been reported by Sherwin (23). By inspection, most bursts illustrated in Figs. 2 and 3 of that study fit the symmetrical scheme described here. But some of his units are of the asymmetrical type. Our own recordings show that bursts in the alumina focus may be very

close to the pattern of penicillin bursts (Fig. 2N). Therefore, the specific burst pattern in each type of focus should be regarded as predominant rather than exclusive feature.

A recent study by Ishijima (12) compared the acute penicillin and the chronic alumina focus. In contrast to the acute focus the author found only a few units in the chronic focus which showed a high-frequency burst pattern. As others reported (1, 21) he did not find a consistent relationship between bursts and surface paroxysms. Prince and Futamachi (20) stressed that intensity of epileptogenesis as measured by the amplitude of cellular depolarizing shifts and surface potentials is much higher in the penicillin focus. This is consistent with our findings.

Maynard (16) pointed out that in a "simple neural system, neurons that discharge within the same temporal pattern are usually highly interconnected synaptically; they have almost no functional connections with other contiguous elements . . . which discharge within a different pattern." Applied to the focus this may mean that there is an imbalance of connections: units would be highly interconnected within the focus but poorly to the surrounding. In the acute focus no changes in distribution of synapses are likely to occur. But penicillin may produce a facilitation of excitatory synaptic coupling within the preexisting connections (3) or may enhance electrotonic coupling, both of which would account for the high degree of synchronicity of unit and surface discharges.

In the chronic focus, axon and terminal degeneration has been demonstrated (11) and partial deafferentation suggested by loss of dendritic spines (29). The relatively poor correlation between unit and surface activity may indicate that intrafocal connections are less developed than in the acute focus or that the focus is organized into a large number of subfoci.

Groups of Bursts Related to Movements. In a number of units, recurrent groups of bursts related to involuntary movements (see p. 507) were observed. Other investigators did not mention this type of activity in the chronic focus. Therefore we attribute it to the Sernylan with which one animal was treated before each recording session. The observed cyclic occurrence of bursts could be a phenomenon endogenous to the focus, like the cycling that Prince (17) found in the penicillin focus. In this case a spread of the cyclic activity from the focus to the contralateral side must be postulated in order to explain the bilateral rhythmic muscle activity. An alternative is that the bursting units follow or respond to an extrafocally generated scheme of rhythmic activity which may or may not be related to epileptic activity.

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