Technical Papers

Brain Waves and Unit Discharge in Cerebral Cortex

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In a previous communication in this journal (*1*) on "Charting the Sea of Brain Waves," one of the basic questions that was posed without satisfactory reply was the nature of the relationship which might exist between the slow rhythmic electrical potential oscillations that are recorded from the surface of the cerebral cortex and the action potentials of individual cortical cells. Are the slow waves of 50–100 or more msec in duration merely the smoothed envelope of hundreds or thousands of brief spikes discharging in clusters of imperfect synchrony, or do they represent an electrical phenomenon of a different order? How are the potential rhythms of the cortex that have been studied so extensively in electroencephalography related to actual discharge of individual nerve cells?

During the past year we have made a renewed attack on this problem by the use of glass micropipette electrodes, the inside diameter of which measured 1–3 μ, coupled through a cathode follower stage to a two- or three-channel amplifier oscilloscope apparatus, in order to record isolated spikes from single cortical neurons simultaneously with the slow potential oscillations. The technique was similar to that recently reported by Cragg (*2*), Amassian (*3*), and Thomas (*4*).

Cats under fairly deep Nembutal anesthesia were used. The electrical rhythms of 8–10/sec waves recorded from the surface of the cortex were found to be of practically the same form when recorded with the microelectrode as they were from gross surface electrodes on adjacent cortex. The microelectrode was then inserted into the depths of the cortex with a micromanipulator searching for the unit spike potentials which might form the elementary discharge underlying the slow waves. They were not found.

Only occasional cortical cells discharged for a time in response to the injury of penetration by the microelectrode, but prolonged searching throughout all layers of the cortex failed to pick up individual spikes bearing any relationship to the slow rhythms, and often no spikes at all could be detected in spite of continuous "spontaneous" slow waves. Then it was found that at certain depths in sensory cortex a few isolated spikes regularly appeared in response to tactile stimulation of the cat's paw, so that the microelectrodes were capable of recording action potentials from single nerve cells, but such potentials were not apparent at all or appeared only sporadically, with no relationship to the bursts of rhythmic slow waves in the absence of sensory stimuli. We then suspected the anesthesia.

When local, instead of general, anesthesia was used the picture was completely altered. Active unit spike discharges (Fig. 1) were found continuously in sensory cortex even though slow potential rhythms were less prominent. These spikes were of very short duration, measuring only 0.6–0.8 msec, and varied between 300 and 5000 μv in amplitude, usually negative in electrical sign at the tip of the microelectrode. The smaller ones appeared in the more superficial cortical layers, between 300 and 800 μ from the surface (Fig. 1 *A*), whereas the larger ones appeared deeper, between 1200 and 1800 μ (Fig. 1 *B*). In the upper layer, bursts of spikes frequently appeared on the rising phase or at the peak of each slow wave, but at times they fired off independently, without any apparent temporal relationship to the slow waves.

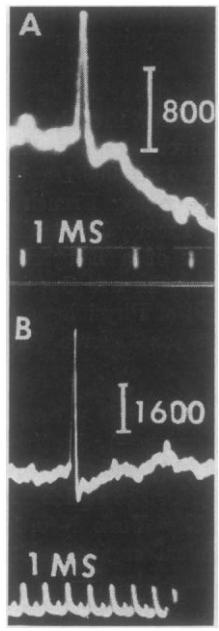

FIG. 1. Action potentials from single cortical cells in the post-sigmoid gyrus of the cat recorded by means of glass microelectrodes of 1 μ or less in diameter and recorded with a condenser-coupled amplifier oscilloscope apparatus of 0.45 sec time constant. Deflection up is electronegative at the electrode tip with reference to a diffuse lead attached to the head holder around the base of the skull. In *A* is shown a unit spike obtained from a depth of 700 μ from the surface, and in *B* is shown the larger spikes obtained at a depth of 1.8 mm from the surface, where there are larger cortical cells.

The constant voltage of these unitary spikes upon repeated discharge and their precise localization (they disappear upon movement of the electrode tip by as little as 50 μ) indicate that they represent action potentials from discharge of single cortical cells. Since they were electronegative in sign, they must have been recorded from just outside the cell membrane. Occasional high-voltage positive spikes were recorded for

brief periods of time when the electrode tip was presumably within a cell body. These were associated with injury discharge and eventual death of the cell and have not persisted long enough for study. It was found that unitary spikes of this type could be recorded only with the smaller microelectrodes, preferably of 1 μ or less. Multiple units of different amplitude were obtained with larger electrodes.

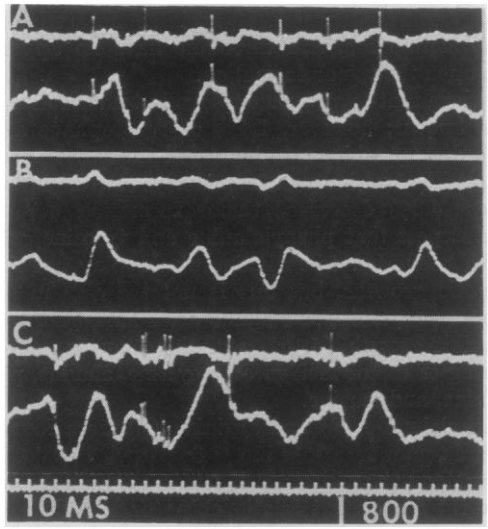

FIG. 2. Unitary spikes and slow waves recorded with a microelectrode connected to 2 amplifier oscilloscope systems for simultaneous recording with a short and a long time constant. The slow waves do not appear, therefore, in the upper tracing in each sample. Records taken at a depth of 1800 μ. *A*, a burst of slow waves and spikes in the animal without general anesthesia; *B*, taken from the same point 8 min following the intravenous administration of 50 mg Nembutal; *C*, taken 1 hr later, when the animal had recovered somewhat from the anesthesia.

Slight anoxia or Nembutal anesthesia would readily abolish the spike discharges, leaving the bursts of slow waves relatively unaffected (Fig. 2), the spikes returning with oxygen administration or by the administration of picrotoxin to counteract the effect of Nembutal. When the spikes disappeared with hypoxia or anesthesia, careful search was made through the cortex in several places in the attempt to find other units that might account for the slow waves, but only an odd sporadic unit was found. It appeared that unit discharge in the cortex had been readily suppressed with slight hypoxia or anesthesia without having much effect upon the rhythmic slow waves.

Higher voltage slow waves caused by applying strychnine or eserine and acetylcholine to the cortex were more consistently related to bursts of rapid spikes during the rising phase or negative peak of the slow wave, although even then they sometimes continued much longer at a frequency unrelated to the slow waves.

These results would seem to prove that the brain waves commonly used by the electroencephalographer as an index of cortical activity may, under certain circumstances, bear little relationship to the active discharge of individual cortical cells, at least of the type from which records can be obtained with microelectrodes. Certainly there is no support for the supposition that the slow waves result from envelopes of spike discharge.

There is also no support for the notion that the "spontaneous" rhythms of the brain are due to nerve impulses circulating in reverberating closed chains of self-re-exciting units, since the slow waves continue when unit discharge (at least as recorded with microelectrodes) is suppressed by hypoxia or anesthesia. In the depths of the cortex one may find extremely active discharge of neurons, or they may be remarkably silent, with very little reflection of these vastly different conditions upon the brain wave record obtained from the cortical surface.

Brain waves do seem to be phenomena of a different order. The most plausible hypothesis is that they represent synchronized oscillations in membrane potentials, possibly involving small interneurons and dendrites in the cortical matrix, oscillations which would have a definite effect upon neuronal excitability, but not dependent upon neuronal discharge. They would thus be classed with the so-called "synaptic" or soma potentials of the spinal cord, which are also obtained from anterior horn cells after the discharge of these cells has been suppressed by barbiturate anesthesia (*5*). Their oscillatory character is of particular interest, since it does not seem to depend upon repetitive discharge of the larger cortical cells of the type whose activity was recorded with the microelectrodes used in these studies. They may still be related to impulses circulating in the fine dendritic network of the cortex, whose unitary activity may not appear with the techniques here employed.

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Influence of Amino Acids upon Incidence of Tumors in *Tu*^{50j} Stock of *D. melanogaster*

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In a recent report Mittler (*1*) has shown that nutrition of *Drosophila melanogaster* when restricted to certain yeasts alters the penetrance of *tu*^{50j}, a second chromosome recessive mutation located near 90 that produces melanotic growths in the abdomen. Other workers, Tannenbaum (*2*) and Herskowitz and Bur-

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