Morphology of the Experimental Epileptic Focus*

L. E. WESTRUM, M.D.,† L. E. WHITE, JR., M.D., AND A. A. WARD, JR., M.D.
Division of Neurosurgery, University of Washington School of Medicine, Seattle, Washington

The clinical syndrome of epilepsy forms one of the historic cornerstones of neurosurgery. Although numerous reports are available dealing with the clinical phenomenon and its physiological substrate,1,10,27,28,31,34,45-48 morphological studies of epileptic foci have been relatively infrequent.23,29-31,46 Furthermore, the morphological data available do not provide a basis for distinguishing epileptogenic cortex histologically.

It is generally agreed that the epileptic "spike" is one of the most characteristic electrographic signs of the epileptic discharge. Such spikes and sharp waves are thought to represent the summation of electrical activity generated in graded-response membranes which include dendritic membrane.5,4,38,43-45 Associated with these abnormalities of graded-response membrane at the focus, the all-or-none membrane of the soma or proximal axon has been shown, by microelectrode studies, to generate autonomous high-frequency bursts in varying patterns.46 It has been postulated that this electrically hyperactive condition may be caused by a relatively persistent depolarized dendritic membrane.46 This activity has certain similarities to the discharges generated by crustacean stretch receptors as a consequence of mechanical distortion of their dendrites.11 On this basis, the hypothesis was advanced that mechanical distortion of the dendritic arborizations of neurons in the cortical scar might be the basis for the epileptic discharge.44,46 This study was designed to test this hypothesis from a morphological point of view.

Method

Eight adult Macaca mulatta monkeys were rendered epileptic by the sterile intracortical injection of alumina cream by a modification of the Kopelloff technique,23-46 since this experimental preparation appears to approximate most closely human focal epilepsy.44 Under Nembutal anesthesia, a 2 × 2-in. craniotomy was carried out exposing the sensorimotor cortex. The alumina cream was injected intracortically with a 25 or 27 gauge needle, the area was rinsed with saline and was covered with a patch of polyethylene film to minimize adhesions. The craniotomy was closed in the standard fashion. Recovery from anesthesia was uneventful in all animals and they were followed postoperatively with careful clinical observations and serial electroencephalograms. Spontaneous activity of seizures occurred in 4 to 6 weeks with characteristic electroencephalographic findings of a focal epileptogenic lesion in the region of injection. Following the establishment of the pattern of the seizures, a bilateral craniotomy was carried out under Nembutal anesthesia and the epileptogenic focus was localized discretely by electrocorticography. An 8-channel Grass electroencephalograph with either wick or silver-ball electrodes was employed (Fig. 1). The external landmarks of the electrographic focus were noted carefully for future orientation and a 1 cc. block of cortex containing the focus was excised and placed immediately in freshly prepared fixative for histologic processing. A similar block was excised from the contralateral homotopic area as a control and processed in the same fashion.

Histological Technique. A previously standardized Cox modification of the Golgi method of heavy-metal impregnation was used in this study.5,12 This consisted of fixation of both the experimental and control tissues in a mixture of 20 parts 5 per cent potassium dichromate, 20 parts 5 per cent mercuric chloride, 16 parts 5 per cent potassium chromate and 40 parts water. After 1½ to 2 months the blocks were dehydrated through graded alcohol to ether-alcohol and embedded in celloidin. The blocks were cut serially on a sliding Reichert microtome at 100 μ, black-
Fig. 1. Examples of electroencephalographic localization on 2 animals, including placement of electrodes. Hatched line includes area removed for Golgi evaluation. (a) Discrete focus with reversal of phase at electrode 4. (b) Large focus with maximum potential and reversal of phase common to electrodes 13 and 15.

Results

Control Observations

Regardless of minor variations in technique, fresh Golgi preparations of adult cerebral cortex yielded a consistent picture of cortical elements described previously by many authors29,34,41 (Figs. 2–6). In general, a very intricate system of cell bodies and their processes is arranged in a stratified pattern, illustrative of classical layering of the cerebral cortex. The majority of these neuronal elements are pyramidal in type. In the present study, special attention will be drawn to the processes or dendrites of these pyramidal cells.

The cortical pyramidal neuron is endowed