CHAPTER TWENTY-ONE

SPECIFIC POSTNATAL THREATS TO BRAIN DEVELOPMENT: DENDRITIC CHANGES

Madge E. Scheibl and Arnold B. Scheibl

Our approach to the problem of brain damage in infancy and childhood is a bit different from that of some of the other contributors to this book. For we have had the opportunity to see what are presumed to be remote consequences, structural and behavioral, in a series of patients who have come to surgery in middle life with various patterns of intractable partial epilepsy. (8, 12) The seizure equivalent states and the electrical storms which have been shown to accompany them have been found characteristically associated with the temporal lobes of these patients (17) slightly more than half of whom have histories of difficult and prolonged deliveries or infantile febrile convulsions.

We shall describe some of the morphologic changes which we have found in the hippocampi of approximately 40 individuals, mostly young adults with clinical seizures. In the context of this book we consider them as possible models of pathology, resulting from brain damage of one sort or another, suffered in infancy or childhood. However, as we shall show, we are not convinced that these patterns of temporal lobe pathology and disordered cortical functions stand solely as monuments to discrete insults to the brain, whether genetic, traumatic, or infectious in early life. The question raised alternatively is whether these may signal, instead, an active and continuing process in which previously uninvolved neurons become involved in the degenerative sequence, culminating in cell death.

This paper is based largely on the study of Golgi impregnated specimens of temporal neocortex and archicortex. Although the limitations of the method for quantitative neurobiology are well known, its compensating features, especially the panoramic view it affords of the nerve cell in its neuropilic environment, more than compensate for this deficiency. The dendritic systems of neurons turn out to be extraordinarily sensitive indices of pathology, and it is these elements more than any other which are susceptible to visualization with the Golgi techniques. When used in conjunction with the electron microscope, the combination promotes optimal opportunity for the critical structural study of the neuron and its setting.

S. R. Berenberg (ed.), *Brain*  
© Martinus Nijhoff, The Hague, Netherlands 1977
Our observations are based on material from two sources: a) surgical specimens removed from patients with temporal lobe epilepsy ($n = 32$) (8, 12), and formalin preserved material originally obtained at autopsy and located with the help of the Medical Center computer ($n = 8$). All of the former patient group are alive and being followed periodically. They represent a fairly homogeneous group, medically still in their young or middle years and, so far as we know, not suffering from other medical diseases of great consequence. The latter patient group are more disparate, showing a wide range of diagnosed pathology at death, and identified primarily on the basis of a shared diagnosis of clinical seizures. Since six of these eight patients were less than 18 years of age at death, it is not surprising that congenital or genetic disease was found in the majority of them.

The range of dendritic change which we have observed is great and includes, at one end of the spectrum, minimal spine loss (or non-formation) and nodule formation on portions of a single dendrite in the dendritic domain of one neuron, to extensive deteriorative changes in the total dendritic domains of cell ensembles, culminating in complete disappearance of groups of neurons, often with glial replacement. In one or two cases of brain defective epileptic children we have seen what look like outgrowths of very small supernumerary dendrites or extraordinary hyperplastic spine systems growing from both cell body and dendrite. While we can only guess at the significance of these small structures, they serve to emphasize the protean nature of dendritic response to pathogenic stimuli.

The most frequent and obvious change which we have seen in our series of resected hippocampi is an apparent diminution or loss of dendrite spines and an increasing irregularity of dendrite silhouette. Various stages of such changes appear in figure 1, which also indicates that patchy loss of spines may appear anywhere along apical or basilar dendrites in either terminal or more central position along the shaft. In most cases spine loss is accompanied by the appearance of series of nodules scattered along the course of the dendrite producing a “string-of-beads” type of deformity.

We have previously discussed the possible significance of these phenomena, (12) emphasizing that absence of spines and appearance of nodules may in themselves have no pathologic significance, depending on the circumstances.

For instance, spines are characteristically lost from the cell body and proximal segment of apical dendrite of most cortical pyramidal cells during the immediate prenatal or perinatal period in most mammals. (11) The majority