AN UNUSUAL LESION RESULTING FROM ELECTRODES IMPLANTED IN MONKEY BRAINS [1]

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With the use of implanted electrodes have come many important contributions to our understanding of the subcortical brain regions. The technique has been used extensively for both stimulating and recording from the subcortical regions of animals (Delgado 1955; Delgado, Roberts and Miller 1954; Gloor 1955; Kaada 1951; Ranson, Kabat and Magoun 1935; and many others). More recently, electrodes have been implanted in the brains of humans by workers such as Bickford *et al.* (1953), Delgado and Hamlin (1956), Heath *et al.* (1954) and others. The potentialities for this technique as a research tool and as an aid in diagnostic and therapeutic procedures are enormous and it is reasonable to suppose that intracerebrally implanted electrodes will be used more and more widely as time goes on. For this reason, evaluation of the technique from as many viewpoints as possible is of great importance.

In the literature we find few detailed reports of the histopathological changes due to needles implanted in the brain. Those workers who have described the tissue responses (such as Bagenstoss, Kernohan and Drapiewski 1943; Dodge *et al.* 1955; and Wilson 1926) have generally characterized them as "minimal". Delgado (1952) has described the tissue changes due to implanted multilead electrodes as "limited gliosis", and later (1955) as "mechanical destruction along the needle tract with some hemorrhage, in general very small, and a brain reaction with leukocytic infiltration and glial proliferation around the needle tract".

A most careful analysis of the tissue responses to multilead electrodes (of the type described by Delgado 1952) implanted in the brains of cats has been made by Collias and Manuelidis (in press). The cats were sacrificed at various intervals after implantation so that the progress of the lesion from the acute to the six-months stage could be observed. Areas of demyelinization were noted at distances of no more than 0.5 mm. from the track of the electrode.[2] The greatest extent of the lesion was found in the gray matter where microglial proliferation (but not gitter cells) was seen at a distance of 3 mm. from the track.

In the course of experiments involving stimulation of the limbic system in monkeys, multilead electrodes of the type described by Delgado (1952, 1955) were implanted in various parts of the brains of six animals. The operations proceeded normally and the post-operative behavior of the animals and their reactions in the experimental situation gave us no cause to suspect an unusual lesion. However, histological study of the brains of two of the animals revealed lesions of a type and extent which we have not seen described elsewhere.

In one monkey (fig. 1) where the electrode had been in place for 18 days, there was extensive uni-

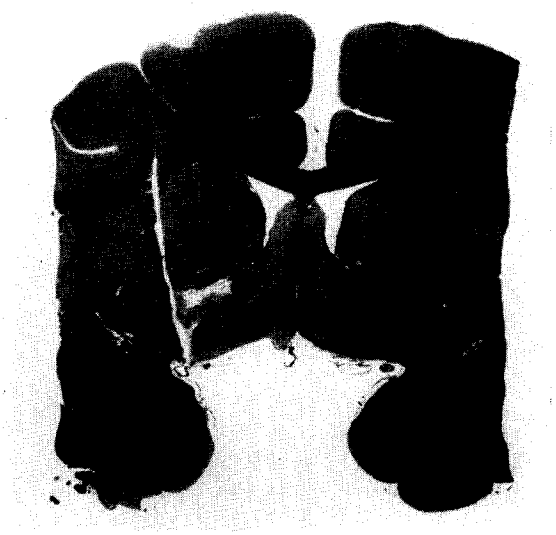

Fig. 1

lateral destruction of the anterior commissure. One can see the area of destruction extending medially for a distance of about 5 mm. from the electrode track. On the lateral side of the track and in the contralateral limb of the anterior commissure, the fibers are generally intact, although some evidence of demyelinization (confirmed in a section stained for myelin) is visible.

Examination under higher power showed the area of complete necrosis with liquefaction and cavity

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2 Delgado (in press) noted some instances of partial demyelinization "extending for several millimeters".

formation. Around the edges of this cavity were seen many swollen, fat-laden gitter cells. At various places around the periphery of the lesion, capillary and some fibroblastic proliferation were evident. At some points outside the zone of mesenchymal and fibroblastic proliferation accumulations of swollen, pale astrocytes were seen.

In the other monkey, where the electrode had been in place for 71 days, a similar lesion (extending unilaterally for about 8 mm. from the electrode track) was seen in the corpus callosum. Although other electrodes had traversed the corpus callosum and the anterior commissure in this and other studies, no other instances of this type of lesion were seen. However, Foley, in a personal communication to Manuelidis, has reported similar findings in one human patient.

The pathogenesis of these lesions is difficult to establish. They are obviously different from the lesions seen after mechanical interruption of nerve fibers as they extend on only one side of the electrode track, whereas we would expect degeneration due to interruption of fibers in a commissural area to appear bilaterally. We have no evidence that the lesions were due to faulty operative technique or to agents other than the electrode. The tissue reaction is not that found in the presence of a bacterial abcess.

It is known that edema may cause necrosis of the tissue, especially when the edema fluid has a high protein content (Jacob 1940). However, the unilateral distribution of the lesion again makes this explanation unlikely in the present case. Furthermore, the amount of edema reported in chronically implanted electrodes (Collias and Manuelidis, in press) is moderate.

Although no thrombosed vessels were found in the neighborhood of these lesions, it is conceivable that occlusion of a vessel could have caused the degeneration.

In evaluating these lesions, we should emphasize the fact that they are apparently rare, and that, at least in our monkeys, they were accompanied by no obvious behavioral changes. However, the possibility of encountering lesions (apparently due to the presence of electrodes) which are greater than the "minimal" lesions generally reported in the literature, should be borne in mind by those using implanted electrodes in both human and animal studies.

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REFERENCES

BAGENSTOSS, A. H., KERNOHAN, J. W. and DRAPIEWSKI, J. F. The healing process in wounds of the brain. *Amer. J. clin. Pathol.*, **1943**, *13*: 333-348.

BICKFORD, R. G., UIHLEIN, A. and PETERSEN, M. C. Electrical rhythms recorded from the depth of the frontal lobes during operations on psychotic patients. *Proc. Staff Meet. Mayo Clin.*, **1953**, *28*: 135-143.

COLLIAS, J. C. and MANUELIDIS, E. E. Histopathological changes produced by implanted electrodes in cat brains. *J. Neurosurg.*, in press.

DELGADO, J. M. R. Permanent implantation of multilead electrodes in the brain. *Yale J. Biol. Med.*, **1952**, *24*: 351-358.

DELGADO, J. M. R. Cerebral structures involved in transmission and elaboration of noxious stimulation. *J. Neurophysiol.*, **1955**, *18*: 261-276.

DELGADO, J. M. R. Evaluation of permanent implantation of electrodes within the brain. *EEG Clin. Neurophysiol.*, **1955**, *7*: 637-644.

DELGADO, J. M. R. Chronic emplacement of intracerebral electrodes. *Proc., Symp. Brain Stim.*, Univ. of Houston, **1957**. In press.

DELGADO, J. M. R. and HAMLIN, H. Surface and depth electrography of the frontal lobes in conscious patients. *EEG Clin. Neurophysiol.*, **1956**, *8*: 371-384.

DELGADO, J. M. R., ROBERTS, W. W. and MILLER, N. E. Learning motivated by electrical stimulation of the brain. *Amer. J. Physiol.*, **1954**, *179*: 587-593.

DODGE, H. W., JR., PETERSEN, M. C., SEM-JACOBSEN, C. W., SAYRE, G. P. and BICKFORD, R. G. The paucity of demonstrable brain damage following intracerebral electrography. Report of a case. *Proc. Staff Meet. Mayo Clin.*, **1955**, *30*: 215-221.

GLOOR, P. Studies on the connections of the amygdaloid nucleus in the cat. Parts I and II. *EEG Clin. Neurophysiol.*, **1955**, *7*: 223-264.

HEATH, R. G. *et al. Studies in Schizophrenia.* Cambridge, Harvard Univ. Press, **1954**, 619 pp.

JACOB, H. Ueber diffuse Markdestruction in gefolge eines Hirnödema. *Z. ges. Neurol. Psychiat.*, **1940**, *168*: 382-395.

KAADA, B. R. Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of "rhinencephalic" and other structures in primates, cat and dog. *Acta Physiol. scand.*, *24*, supp. 83, **1951**, 285 pp.

RANSON, S. W., KABAT, H. and MAGOUN, H. W. Autonomic responses to electrical stimulation of the hypothalamus, preoptic region, and septum. *Arch. Neurol. Psychiat.*, Chicago, **1935**, *33*: 467-477.

WILSON, R. B. Brain repair. *Arch. Neurol. Psychiat.*, Chicago, **1926**, *15*: 75-84.

Reference: BURSTEN, B. An unusual lesion resulting from electrodes implanted in monkey brains. *EEG Clin. Neurophysiol.*, **1957**, *9*: 544-545.