TREMOR AT REST FROM TEGMENTAL LESIONS IN THE CAT*†

WILLIAM W. KAELBER, M.D.

(Iowa City, La.)

A review of the significant experimental work done with primates in the production of postural (static) tremor has recently been presented by Poirier (1) together with observations and anatomical correlations from his own work. A discussion of various hypotheses derived from these findings indicates that, with the possible exception of some lesions described by Mettler and Whittier (2), tremor at rest may sometimes be produced by destruction of various portions of the ventromedial tegmentum of the midbrain and/or rostral pons dorsal to the substantia nigra. Conversely, stimulation of the medial reticular formation, from a level just rostral to the red nucleus and extending to the pyramidal decussation can produce a rest-type tremor, according to Jenkner and Ward (3). In addition, Folkerts and Spiegel (4) found in the cat, that tremor produced by primary stimulation of the rostral pontine tegmentum just dorsal to the lateral part of the medial lemniscus became more regular and of larger amplitude following certain lesions of the mesencephalic tegmentum on the corresponding side.

The present report concerns the production of tremor at rest in the cat by some mesencephalic lesions.

METHODS

Under Nembutal anesthesia bilateral electrolytic lesions were made in the mesencephalon of 40 cats using a direct current of 3 ma for 60 seconds. The number of coagulations per side was varied from 4 to 2 in attempts to determine the smallest area that could be destroyed and still obtain a tremor. In any given animal all of the lesions were produced during one operation.

Postoperatively tremor, persisting beyond 7 days, was considered a significantly positive result, thereby reducing to some extent the influence of factors such as edema and increased neuronal irritability. If tremor was then still present, the animals were examined daily by placing them supine in a V-shaped wooden trough. If tremor was not present by the 7th day, it has been the author's experience that one never developed after that time, since animals without tremor were studied over the same time interval and under the same conditions as the others. There were no animals in this series that could not be examined by the procedure described above. Only the activity of the hind limbs was taken into consideration because, as noted elsewhere (Kaelber and Hamel (5)), tremor produced by lesions or drugs, in contradistinction to stimulation (4), is poorly developed in the cat's forelimbs. Findings meeting the above criteria were obtained in 11 animals.

Electromyograms were obtained in some cases using either surface or needle electrodes inserted into the quadriceps and hamstring muscles and were in no way different from those illustrated in a previous report (5). Because of contemplated degeneration studies, which subsequently did not contribute to further clarification of the problem, the animals were killed by the 24th day. The brains were removed after perfusion with 10 per cent formal saline, and alternate microscopic sections stained by Nissl and Weil techniques.

* From the Departments of Anatomy and Neurology, State University of Iowa.
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RESULTS

Physiological Observations: The tremor occurred only at rest, was of large amplitude, appeared to be alternating, with an estimated frequency of about 6 per second, and was virtually indistinguishable from that produced in other cats by the tremor-producing drug, Tremorine*. Electromyographic analysis of the tremor rate and rhythm, however, revealed “waxing and waning” activity of 1 to 2 per second and primarily co-contraction of opposing muscle groups (fig. 1).

* The drug Tremorine was kindly furnished by Dr. G. M. Everett of Abbott Laboratories.
The general physical status of these animals was excellent. They ate ravenously, often with considerable increase in weight, in contrast to animals having tremor following lesions in the region of the olfactory tubercle. The latter showed anorexia, required feeding by hand, and died after 1 month or more apparently from inanition (5). Except for the tremor no other aberrations of motor function were observed. The absence of any ataxic movements was especially notable since they might well have been anticipated considering the location of the lesions in Figure 2. A number of the present cats showed no decrease in the tremor at the 24th day.

Anatomical Observations: Figures 2 and 3 are photomicrographs showing the largest and smallest effective lesions in 2 cats. Considered as a whole, they involved the rostral half of the midbrain tegmentum, in particular an area occupied by the central tegmental tract and nucleus mesencephalicus profundus. Since the smaller lesion was effective in 5 animals, it would seem reasonable to describe its boundaries more fully, for greater destruction evidently is not essential to the production of tremor.

Dorsally the lesions extended to the lateral angle of the periaqueductal gray, with slight encroachment upon the latter and involved the medial portions of the tectospinal tracts. Medioventrally they bordered the medial longitudinal fasciculus, and extended into the dorso-lateral edge of the magnocellular portion of the red nucleus. Ventrally and ventrolaterally their periphery was just dorsal to the substantia nigra and bordered the medial lemniscus. Throughout, they interrupted the crossed and uncrossed fibers of the ascending limb of the brachium conjunctivum.

![Fig. 2. Section through mesencephalon showing the largest bilateral lesions in the tegmentum that could produce a tremor. Weil stain.](image)
Fig. 3. Section through the mesencephalon of another animal showing the smallest lesions in the tegmental region that were capable of causing tremor. Weil stain.

Figure 4 shows lesions which closely resemble those of Figure 3, but no tremor developed; similar lesions with negative results were found in other animals. The remaining group within the 29 showing no tremor had lesions with a rather characteristic distribution. They were slightly rostral, and notably dorsal to those previously described. Figure 5 shows the dorsal “shift” of such lesions; the plane of sectioning is such that the rostral extent is obscured, but it closely corresponds to the mesodiencephalic junction. In terms of dorsoventral topography about two-thirds to three-quarters of the midbrain tectum was destroyed, whereas two-thirds of the tegmentum was spared.

DISCUSSION

It is possible, although not as yet demonstrated by degeneration technics, that certain anatomical connections common to both cat and monkey have been disrupted. These are nigrofugal pathways, which, according to Folkerts and Spiegel (4) are thought to effect inhibition of tegmental reticular formation neurons via the substantia nigra. Interference with tegmentospinal tracts, which are thought to arise from the nucleus mesencephalicus profundus and form part of an inhibitory rubro-tegmento-spinal system (1), may create an additional source of deranged function among systems which normally operate to maintain “homeostasis” of discharge patterns.
Fig. 4. Section through midbrain of a third animal which sustained lesions very similar to those seen in Figure 3, but in whom no tremor developed. Weil stain.

Fig. 5. Section close to meso-diencephalic junction. Lesions are more dorsal in position as compared to the others. No tremor appeared in this group. Weil stain.

There is no ready explanation for failure of tremor to develop after lesions similar to those found in positive cases; extensive anatomical analysis of the two groups did not reveal any significant structural differences. However, it seems to be highly significant that such a situation can occur, and that it is in accord with pathological observations on human material wherein comparable destruction in the same structure(s) may be associated with a Parkinsonian tremor in one case and none in another (Meyers, 6). This would also be in accord with Meyer's (7) concept that conditions of this sort cannot be adequately
explained by a "structure bound" theory, wherein a one-to-one relationship is assumed to exist between damage to a structure and the physiological manifestation(s) that follow.

The effect of temporally spaced lesions, as described by Adametz (8), could be relevant to this problem, but has not been studied. Judging from the variability in size and location of effective lesions in animals reported by others (1, 9, 10, 11) one gains the impression that a rather delicate balance must exist between reciprocally related systems. In such cases anatomy can only be correlated with physiology in a general manner. In this connection it might be noted that tremor at rest has been produced in this laboratory by lesions implicating various portions of the H-fields and/or subthalamic nucleus (bilaterally (Kaelber et al. (12))), but further attempts to isolate specific systems by anatomical analysis merely created imponderable variables.

The study of Folkerts and Spiegel (4) concerning tremor in the cat resulting from stimulation of the caudal midbrain and rostral pontine tegmentum, wherein secondary unilateral lesions of the substantia nigra and red nucleus (and adjacent structures) were followed by an increase in the regularity and amplitude of tremor upon stimulation, appears significant. Two of their animals had lesions which in part involved the same tegmental structures affected bilaterally in the cats reported here. Those authors suggested that, when inhibitory impulses originating from these rostral midbrain areas were eliminated by their lesions, increased excitability of tremorogenic zones situated at more caudal levels ensued.

The present experiment suggests that mesencephalic lesions, showing a variability similar to that found in primates, can produce a tremor akin to that described as static or resting in the cat. This tremor, as judged by available evidence, most of it physiological, seems to be associated with disruption of inhibitory pathways from the substantia nigra to reticular tegmental neurons, and of tectospinal tracts. The variable locations from which such effects can be produced implies that under normal conditions there exists a fine "bias" on the discharge patterns of suprasegmental structures, probably extending as far forward as the basal forebrain. This can be altered by dissociation of the proper sequential firing of inhibitory and facilitatory neurons, effecting either an asynchronous discharge of ventral horn cells, resulting in tremor activity which is 180 degrees out of phase in opposing muscle groups, or a hypersynchronous discharge of these cells, so that co-contraction of agonists and antagonists occurs. Such a condition has been referred to by Cordeau and associates (11).

Relevant to the foregoing discussion is a recent study by Adey, Buehwald and Lindsley (13) concerning amygdaloid or pallidial influences, or both, on unit firing patterns in the rostral mesencephalic tegmentum particularly when stimulation of the former structures was paired with ascending peripheral volleys. According to them, sciatic stimuli paired with amygdaloid or pallidal shocks often converted a sustained high rate of mesencephalic unit firing, that was initially produced by the peripheral stimulus alone, into a rhythmic series of high frequency discharges. These findings would be compatible with the suggestion pre-
viously made, that some control of the "bias" on suprasegmental discharge patterns may emanate from certain so-called rhinencephalic areas (basal forebrain). They could also be related to previous observations by Kaelber and Hamel (5) concerning the production of rest-type tremor in the cat following bilateral destruction of the olfactory tubercle. These lesions also involved portions of the anterior amygdaloid area, globus pallidus, putamen, and nuclei and fibers of the diagonal band of Broca.

SUMMARY

Bilateral electrolytic lesions were made in the mesencephalon of 40 cats, and in particular many involved the central tegmental tract and nucleus mesencephalicus profundus. The postoperative manifestation of an alternating tremor at rest in 11 of these animals led to further studies of this phenomenon. Electromyographically, tremor was composed of co-contraction of opposing muscle groups with a frequency of 1 to 2 per second. Although the animals were sacrificed by the twenty-fourth day, tremor was still prominent in most. The lesions, compared with those produced in primates by others, also implicated nigrofugal and rubro-tegmento-spinal systems, whose actions are thought to be inhibitory for neurons of the tegmental portion of the reticular formation.

REFERENCES

ANNOUNCEMENTS

At a meeting of a Planning Committee in Vienna on June 19, 1963 arrangements were made for the Vth International Congress of Neuropathology, to be held in Zürich August 30-September 3, 1965. The President is Professor Lüthy of Zürich. Previous Honorary Presidents were reelected, and Dr. Webb Haymaker and Professor Dorothy S. Russell were added to this group. Major themes are: 1. The Pathology of Coma and Post-Comatose States (Chairman—Dr. Erna Christensen, Denmark). 2. Genetically Induced Metabolic Diseases of the Central Nervous System, with subtheme Kuru and Diseases on Guam (Chairman, Dr. R. M. Norman, Great Britain). 3. Iatrogenic Modifications of Infections and Intoxications, with subtheme Immunopathology (Chairman, Dr. Abner Wolf, United States). The minor themes are Histochemical and Biochemical Topography; Pathology of Aging; Neuromuscular Diseases; Embryo-Foetopathy. There will also be sessions devoted to free papers. Further information can be obtained from Dr. Orville T. Bailey, Chairman, U. S. Delegation, 912 South Wood Street, Chicago, Illinois 60612. Dates and Places of International Congresses in 1965:

August 23-28 International Congress of Neurosurgery, Copenhagen, Denmark
August 30-September 3 International Congress of Neuropathology, Zürich, Switzerland
September 6-10 International Congress of Neurology, Vienna, Austria

MEETING OF THE BRAZILIAN ACADEMY OF NEUROLOGY

The Brazilian Academy of Neurology will hold the First Brazilian Congress of Neurology, at the Faculty of Medicine in Ribeirão Preto, on July 1964.

The subjects of the Congress will be: Pain physiopathogenesis, neuralgia in cancer, and cervico-cranial neuralgias, not including the Vth and IXth nerves neuralgia, Nervous System and Chaga's Disease, and Teaching of Neurology.

The Congress Committee would appreciate receiving contributions from Neurologists. Details can be obtained from the Secretary, Dr. Paulo Pinto Pupo, Caixa Postal 5496, São Paulo, Brazil.