Thalamic Inhibition of the Myotatic Reflex in Man*

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DURING the evolution of subcortical surgery in the treatment of parkinsonism, it has become increasingly apparent that some of the most effective therapeutic lesions are those placed in the vicinity of the nucleus ventralis lateralis of the thalamus. Stereotactic techniques of various types have been devised which now provide more than adequate mechanical accuracy. However, similar accuracy in the geographical definition of the subcortical target has not been forthcoming. It is known that the use of bony landmarks as points of reference is highly unreliable. Anatomical studies are now available which demonstrate that greater reliability can be achieved by utilizing the anterior and posterior commissures as the points of reference. But the biological variation from one brain to another has also been shown to be sufficiently great that discrete placement of an electrode in the exact center of a subcortical target such as the nucleus ventralis lateralis (V.L.) is not possible on the basis of stereotactic coordinates alone. These problems of spatial indetermination led Bailey¹ in 1957 to emphasize the importance of finding "physiological methods of checking the point of the needle." Unfortunately, discrete physiological motor functions which can be assigned to V.L. have not been demonstrated until relatively recently.

It is now known that inhibition of the knee jerk² and of the muscle-spindle discharge¹¹ of the hind limb can be evoked by stimulation of the contralateral ventrolateral nucleus of the thalamus in the cat. This inhibition is felt to be a reflection of the inhibition of that fraction of the motor system referred to as the gamma efferent system¹,⁹,¹¹ which innervates the muscle spindles. This system is schematized in Fig. 1. It will be noted that the muscle spindle is a stretch receptor which lies in parallel with the striated muscle fibers. Each spindle is composed of a central sensory element which is sensitive to stretch and two polar contractile elements which are innervated by the gamma efferent fibers. Activation of these small gamma efferent fibers causes contraction of the polar elements of the spindle increasing the stretch on the equatorial annulo-spiral ending and making it more sensitive to stretch. When sufficient stretch is applied to the entire mass of muscle to activate the annulo-spiral sensing element, a volley of impulses is transmitted back to the cord over fast-conducting fibers in the dorsal root which terminate monosynaptically on the alpha motoneuron in the anterior horn. This feed-back loop appears to play an essential role in motor movement. The spindle registers the difference in length between the main mass of muscle and itself, whereupon the servo loop

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acts to reduce this difference. Steady voluntary or postural contraction is a result of its tonic innervation and consequent facilitation of the alpha motoneuron via this servo loop. When the entire mass of muscle is stretched suddenly, a volley of impulses is transmitted back to the cord exciting the anterior horn cells which in turn produce contraction of the mass of striated muscle. This is the basis of the myotatic reflex of which the knee jerk is an example. Since Stern and Ward\(^1\) have shown that stimulation of V.L. in the cat produced consistently inhibition of the afferent discharge of the contralateral spindle, activation of V.L. in the human should depress or abolish the contralateral knee jerk. This phenomenon might thus be utilized to provide physiological identification that the tip of the stereotactically placed electrode lies within the nucleus ventralis lateralis of the thalamus.

Observations of the effect of stimulation of V.L. upon myotatic reflexes in the unanesthetized human would also provide essential physiological data. The experiments of Stern and Ward\(^1\) on cats were carried out using barbiturate anesthesia. Because barbiturates are known to profoundly alter supraspinal mechanisms of motor control,\(^9\) it was feared that the physiological validity of the data reported in the cat might be subject to serious question.\(^1\) Since there are almost insurmountable technical difficulties in studying the gamma system in the unanesthetized animal, confirmation of these findings in the unanesthetized human would be highly desirable. Since we have been placing an electrode into V.L. for several years in the course of operations for parkinsonism, electrical stimulation of this thalamic nucleus is carried out easily. This opportunity has been utilized to study the role of the nucleus ventralis lateralis in modulating the activity of the muscle spindle in unanesthetized humans. It was also hoped that physiological confirmation of the target would result in the production of thalamic lesions which would be more effective in reducing the motor disability in these patients.

### Methods

Electrolytic thalamotomy was carried out in a similar fashion in all of the patients included in this study. Following premedication with Phenergan, 25 mg. intramuscularly, trephination was performed in the vicinity of the coronal suture under local anesthesia. The Planisphere, a stereotactic instrument of our own design,\(^1\) was then attached to the skull. The frontal horn of the lateral ventricle was then punctured under stereotactic control and sufficient air was injected to demonstrate the anterior and posterior commissures. From these films taken in the operating room, the necessary simple calculations were made and a unipolar electrode was delivered to the target in the nucleus ventralis lateralis of thalamus based on coordinates obtained from an atlas of the human brain. The electrode was insulated except for 4 mm. at its tip. Stimulation of V.L. was carried out utilizing a Grass stimulator delivering 1 m sec. biphasic pulses at a frequency of 60 c/sec. for the observations dealing with modulation of myotatic reflexes. With the electrodes used, the threshold for inducing inhibition of the knee jerk was 3–5 V. and all of the observations reported here were a consequence of stimulation at 3–7 V. At higher voltages, spread to adjacent structures is induced. Stimulation of higher voltage (up to 18 V.) was always carried out to provide a crude index of the distance of the stimulating electrode from other structures such as the internal capsule or the nucleus ventralis posterolateralis. Thus, in the dominant hemisphere, a lesion was not carried out if blocking of speech could be obtained at 12 V. even though, at low voltages, apparent physiological confirmation of the position of the electrode in V.L. was obtained. Presumably, under these circumstances, the electrode lay in the lateral portion of V.L. and a spherical lesion could be anticipated to produce damage to adjacent fibers in the capsule.

Observations on myotatic reflexes during stimulation of V.L. were made by observing changes in the knee jerk evoked by a 1/sec. repetitive blow to the patellar tendon which was delivered manually. Only marked reduction or complete inhibition of the knee jerk temporally related to stimulation of V.L. was recorded on the protocol. If minor alterations of amplitude of the knee jerk were to be recorded, it would be necessary to evoke the knee jerk by electromechanical means and record the excursions by gauges of displacement. But this was not considered to be necessary since interest was centered only on obvious and rather dramatic changes in the reflex.

The majority of observations were carried out on patients with parkinsonism although limited data were obtained in patients with a variety of
Thalamic Inhibition of Myotatic Reflex in Man

Dyskineties including dystonia, choreo-athetosis, cerebellar tremor and torticollis. The results were the same in all diagnostic categories.

Results

Out of a much larger group of patients undergoing operation for abnormal motor movements, observations regarding the effect of electrical stimulation of V.L. upon the knee jerk were made during the course of 48 operations.

After the electrode had been introduced stereotactically to the calculated target in V.L., the contralateral knee jerk was evoked at 1/sec. Once a stable amplitude of response had been established, V.L. was stimulated electrically for 5 sec. Observations were made on the amplitude of the knee jerk during and for at least 1 min. following such activation of V.L. Unequivocal reduction or abolition of the contralateral knee jerk was obtained in 37 instances. Of this group, complete suppression of the contralateral knee jerk was observed in 15 instances and, in 5 of these, complete suppression of the knee jerk persisted for periods ranging from 4 to 21 sec. following cessation of the thalamic stimulation. Marked reduction but incomplete inhibition was evoked in 6 cases while definite but only moderate reduction in the amplitude of the knee jerk was observed in 7 cases. In 3 additional cases, inhibition of the knee jerk was obtained but concomitant tonic contraction of the leg occurred which could well have masked the reflex. In 5 instances no change in the knee jerk was observed during stimulation of what was presumed to be V.L.; in 2 instances the knee jerk appeared to be facilitated.

Since stimulation of V.L. has been shown to facilitate spinal alpha motoneurons in the cat; over a pathway involving the sensori-motor cortex, one might anticipate that active motor phenomena might also be induced by stimulation of V.L. in the conscious human. This often is the case since various fragments of the dyskinesia often can be evoked by such stimulation during operation. Such evoked motor activity appears to be related to pre-existing disease rather than any specific localization of function within V.L. In patients with choreo-athetosis, athetoid movements of the contralateral extremities usually are evoked; in patients with parkinsonism, tremor of the contralateral extremities is augmented during stimulation. Such induced motor activity appears to be evoked more commonly in the contralateral arm than in the leg. Since such motor activity obviously blocks observations upon deep reflexes, the data reported here are confined largely to the knee jerk where, at low-stimulus strengths, evoked superimposed motor activity was uncommon. Although observations of the effect of stimulation of V.L. on the contralateral biceps reflex were very limited, complete suppression of this tendon reflex in the arm was obtained in 3 instances during stimulation of V.L. In patients with parkinsonism having spontaneous tremor, driving of tremor usually was obtained during stimulation of V.L. A review of the cases reported here does not reveal any clear correlation between inhibition of the knee jerk and the degree of driving of tremor by stimulation of V.L. However, with only 1 exception, whenever driving of the spontaneous tremor was evoked by high-frequency stimulation of V.L., inhibition of the knee jerk was also observed.

It was hoped that there might be a correlation between the degree of clinical improvement and the placement of a lesion at a thalamic site where activation induced inhibition of the gamma system and the knee jerk. The clinical results following operation in the 5 patients in whom stimulation of V.L. failed to inhibit the knee jerk were not as satisfactory as those instances in which this physiological confirmation of the target in V.L. had been obtained. However, 1 patient of this group demonstrated no inhibition of the knee jerk during stimulation of V.L. but such stimulation did evoke marked driving of tremor (as noted above) and this patient showed dramatic clinical improvement following operation. If one excludes this case from the group, the remaining 4 patients
showed minimal but disappointing clinical improvement which might indicate that inadequate lesions of V.L. had been made. However, the number of cases is insufficient to draw valid conclusions. Furthermore, the area of destruction usually is somewhat larger than the population of neurons activated by the stimulating current. Of the entire group, it would appear that the degree of parkinsonian disability was related more directly to the clinical result than the adequacy of the thalamic lesion. It has been reported widely that superior improvement does not occur in patients with advanced parkinsonism and this has been the case in this series as well. It is of some interest that the over-all results were appreciably better in this group of 48 patients than in a previous group of over 100 cases in which no attempts were made to obtain physiological confirmation of the target. Since the same surgeon (A.A.W.) carried out all the procedures in both series, this improvement in results may, however, be only a consequence of better selection of patients as well as a host of other factors.

Discussion

The myotatic reflex, as it is understood today, is dependent upon the balanced functions of the alpha and gamma motor systems. The tonic gamma activity determines the sensitivity of the muscle spindle to deformation of stretching. When the muscle is stretched, as by tendon tap, the annulo-spiral ending of the spindle is stretched and discharges an afferent barrage to the spinal cord. Monosynaptic activation of the homonymous anterior horn cell (alpha motoneuron) occurs and the muscle contracts. The magnitude of the myotatic reflex is then dependent on three factors: the amount of muscle stretching; the tonic gamma efferent discharge that sets the sensitivity of the spindle to applied stretching; and the responsiveness of the alpha anterior horn cells that innervate the main mass of muscle. Both the alpha and gamma anterior horn cells are subject to supraspinal, intersegmental and intrasegmental modulating influences. We have shown previously that stimulation of the contralateral ventrolateral nucleus of the thalamus in the cat inhibits profoundly the hind-limb muscle-spindle discharge. Since these experiments were carried out under barbiturate anesthesia which is known to alter supraspinal mechanisms of motor control, it was feared that the physiological validity of these experimental observations was subject to serious question. Since stimulation of V.L. in the conscious human also can completely inhibit the contralateral knee jerk, it would appear that the data obtained in the cat are not artifacts of anesthesia and its physiological validity is confirmed. Since the inhibition of the contralateral myotatic reflex in the human induced by stimulation of V.L. was obtained in a variety of patients, it is assumed that this inhibition is not a consequence of a specific process of disease but is a normal physiological function of the intact nucleus ventralis lateralis. Complete confirmation of this assumption requires that this observation be made in the human with no evidence of any disease of the central nervous system and this observation has not been made. As in the cat, with higher intensities of stimulation the inhibition of the knee jerk may outlast the 5-sec. period of stimulation by many sec. The requisite parameters of stimulation of V. L. to induce inhibition of the tendon jerk were not investigated systematically but the response did not appear to be particularly sensitive to the frequency of stimulation. Inhibition was obtained at stimulating frequencies ranging from 30–150/sec. although 60/sec. were used most commonly.

In many of the patients, inhibition of the contralateral knee jerk was not evoked by stimulation at the initial locus of placement of the electrode at a point calculated to be the center of V.L. by the stereotactic coordinates. Often readjustment of position of the tip of the electrode by as little as 1 mm. would then permit the inhibitory response to be evoked. With the known biological variation of the limits of this thalamic nucleus in the human, one might postulate that the initial placement of the electrode lay outside
the confines of the target. However, this thalamic nucleus is a relatively large structure while the geographical area yielding this inhibitory response was often quite restricted. This would lead us to postulate that there may be functional localization within V.L. and that not all the neurons have the catholic properties of both inhibiting the gamma loop and also facilitating the alpha system. In retrospect there may be data to support this assumption from the experiments on the cat in which it was stated that “movement of the electrode less than 2 mm. would abolish the inhibition.” These data were utilized to support the conclusion that the phenomenon was a consequence of local stimulation of V.L. rather than spread of current to adjacent circuits. However, the ventrolateral nucleus even in the cat occupies a volume of close to 18 mm.³, and such minor alterations of the position of the electrode should not abolish the physiological response to stimulation if all of the neurons in that nucleus possess the same function. The observations in the cat were based on histological verification of the position of the tip of the electrode while the opportunity for such verification in the clinical series reported here has not yet presented itself. Thus the observations in the human indicate that this inhibitory response can be obtained only from a relatively restricted volume of neuronal tissue in the region of the calculated position of V.L. and that this region is appreciably smaller than the anatomical volume of this thalamic nucleus. The concept that there may be functional subdivisions within V.L. is not novel. Hassler et al.⁵ have presented several lines of data to indicate that there is both morphological and physiological evidence for subdivisions within this thalamic nucleus. The observations reported here, although of a different type, would be consistent with such a concept of functional subdivisions within the nucleus ventralis lateralis.

Since stimulation of the contralateral V.L. facilitates the alpha system of motoneurons in the spinal cord of the non-narcotized cat¹² it might be anticipated that stimulation of this thalamic mass in the human would evoke activation of certain motor mechanisms. In patients with parkinsonism it is recognized widely that thalamic stimulation may augment the tremor. In other cases semipurpose movements of the contralateral arm may be evoked while, as in other forms of dyskinesia, the athetotic or dystonic movements may be augmented. Such motor activity induced by stimulation of V.L. occurs primarily in the contralateral arm and to a much lesser degree in the leg, which may be related to the heavier long-tract projections to the cervical enlargement. Since it is difficult or impossible to monitor myotatic reflexes in the presence of superimposed motor activity of this type, the majority of the observations reported here were undertaken on the knee jerk. When inhibition of the knee jerk was obtained during stimulation of V.L., stimulating currents near threshold proved to be the most effective, possibly because superimposed motor contractions of the leg were rare under these conditions. If stimulation of V.L. in the human facilitates the alpha motoneuron of the anterior horn (as occurs in the experimental animal) modest inhibition of the muscle spindle and a reduction of its monosynaptic afferent barrage on the motoneuron might well result in no change in the peripheral myotatic reflex since these two actions are in opposite directions. It is thus somewhat surprising that such dramatic and complete inhibition of the knee jerk was ever obtained. One must infer that the flaccidity of the muscle spindle induced by stimulation of V.L. outweighs the increased responsiveness of the alpha anterior horn cells. Then, when the muscle is stretched, inadequate tension is exerted upon the spindle to excite the monosynaptic myotatic reflex.

It has been postulated previously¹¹,¹² that the rigidity, akinesia, and the tremor of parkinsonism result from an alteration of normal alpha-gamma motor balance with a depression of gamma activity and an augmentation of alpha activity. These observations lend support to the hypothesis that the efficacy of thalamotomy in the treatment of Parkinson’s disease is a result of partial de-
struction of alpha facilitatory and gamma inhibitory centers thereby restoring an alpha-gamma balance which approximates normal more closely. It follows from these assumptions that, since the degree and character of alpha-gamma imbalance will be somewhat different in every patient with parkinsonism, the magnitude and possibly the location of the surgical lesion should be tailored individually for each patient. If the disease-produced imbalance of these motor circuits is minor, a small lesion might be anticipated to have more dramatic consequences than in those cases in which gross imbalance of the circuits is present. Clinical experience would tend to at least partially substantiate this view since the mechanical lesion produced by simple insertion of the electrode will result occasionally in striking improvement of rigidity and bradykinesia. However marked tremor of large amplitude appears to be relieved rarely without a lesion of appreciable magnitude.

In addition to the physiological insight provided by these observations, it would appear that this physiological consequence of stimulation of V.L. can be utilized as a method of checking the point of the needle to provide the additional accuracy which cannot be obtained from purely geographical or anatomical sources alone. It would appear that stereotactic maps can provide the surgeon with measurements by which he can place an electrode or other instrument into some part of V.L. in essentially every brain. With the documented variability of the limits of this thalamic nucleus, only very rarely will such measurements place the stereotactically introduced electrode in the geographical center of the target. It is only by the utilization of physiological clues that this final precise localization can be achieved. Such clues include not only the consequences of stimulation upon the motor system, but also electrical events induced in cortex such as the augmenting response. Once confirmation of the position of the electrode in V.L. is obtained in any of these ways, some index of its position with respect to surrounding structures can also be obtained by stimula-

tion of higher intensity that can activate such structures by spread of current. In this fashion it is possible to estimate the proximity of the electrode to such structures as the internal capsule, nucleus ventralis posterolateralis of thalamus and (with less assurance) medial thalamic structures. Since most techniques utilized for the production of thalamic lesions do not permit appreciable sculpturing of the shape of the lesion and usually result in circular or ovoid areas of damage, it is highly desirable that the instrument be placed centrally within V.L. to prevent significant extension of the lesion into adjacent structures. The utilization of such physiological techniques can thus provide appreciable help of a most practical nature to the surgeon and, hopefully, increase the therapeutic effectiveness of the surgical procedure.

Summary

1. Electrical stimulation of the ventrolateral nucleus of the thalamus in the unanesthetized patient evoked inhibition of the contralateral knee jerk.

2. This inhibition of the myotatic reflex is assumed to be secondary to inhibition of the gamma efferent neuron in the cord and a consequent reduction of the afferent discharge of the spindle.

3. Utilization of such physiological clues may assist in more precise production of thalamic lesions in patients with parkinsonism or other dyskinesias.

References


13. WARD, A. A., Jr., and STERN, J. Unpublished data.