4. F. Z. Meerson, M. Ya. Maizelis, V. B. Malkin, et al., Dokl. Akad. Nauk SSSR, 73, 227 (1969).
5. F. Z. Meerson, E. S. Solomatina, Yu. I. Vikhlyaev, et al., Zh. Vyssh. Nervn. Deyat, No. 4, 751 (1973).
6. D. B. Cheek, H. E. Graystone, and R. D. Rowe, Am. J. Physiol., 217, 642 (1969).
7. E. A. Petropoulos, A. Vernadaxis, and P. S. Timiras, Fed. Proc., 28, 1001 (1969).
8. P. S. Timiras and D. E. Wooley, Fed. Proc., 25, 1312 (1966).

THALAMIC INHIBITION OF LOCOMOTION INDUCED BY MESENCEPHALIC STIMULATION

A. P. Berdashkevich, M. G. Sirota, and M. L. Shik

UDC 612.76-06-[612.826.4+612.826.5

By stimulation of a region of the thalamus with its center corresponding to Horsley–Clarke coordinates A7, L2, H2, locomotion of the lightly anesthetized cat with an intact brain can be inhibited, whether evoked by stimulation of the subthalamic or of the mesencephalic "locomotor" region.

KEY WORDS: *locomotion; mesencephalon; thalamus.*

In the intact, lightly anesthetized cat locomotion can be induced by stimulation of certain "locomotor" regions of the subthalamus (LRS) [3] or mesencephalon (LRM) [2]. Locomotion evoked by stimulation of LRS can be inhibited by stimulation of nonspecific nuclei of the thalamus (T) [4].

The object of this investigation was to discover whether locomotion evoked from LRM can be suppressed by thalamic stimulation. This problem could not be solved previously because the mechanisms of thalamic inhibition of locomotion evoked from LRS are unknown and the role of LRS in the control of locomotion differs from that of LRM [1, 2, 3].

EXPERIMENTAL METHOD

The cat was anesthetized (with ether in seven, pentobarbital in five experiments) and its head fixed in a stereotaxic apparatus. The animal's limbs were placed on the belt of a treadmill [3]. The dorsal surface of the skull was exposed and two holes drilled in it through which, after incision of the dura, electrodes were inserted into T (Horsley–Clarke coordinates A7, L2, H2), into LRM (P2, L4, HO), and LRS (A8, L2.5, H3) (the centers of the corresponding regions are indicated). In ten experiments electrodes were inserted into all three regions, in two experiments into T and into LRM only. The electrode was inserted perpendicularly into T, but anteriorly at an angle of 40° into LRM in order to avoid the tentorium cerebelli [2, 6]. The electrode was inserted into LRS anteriorly at an angle of 15°. All electrodes were located ipsilaterally. Each electrode consisted of tungsten wire 20 μ in diameter with glass insulation.

Monopolar stimulation with square pulses of negative polarity was used. The duration of each stimulus was 0.5 msec and their frequency 40-80/sec. To evoke locomotion a current (usually 30-100 μA for LRM and 50-150 μA for LRS) inducing walking or slow trotting was applied, and for thalamic stimulation a maximal current (usually 150-250 μA) too low to induce motor responses in the resting animal was used.

Laboratory of Physiology of Movements, Institute for Problems in Information Transmission, Academy of Sciences of the USSR, Moscow. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 8, pp. 903-906, August, 1976. Original article submitted January 30, 1976.

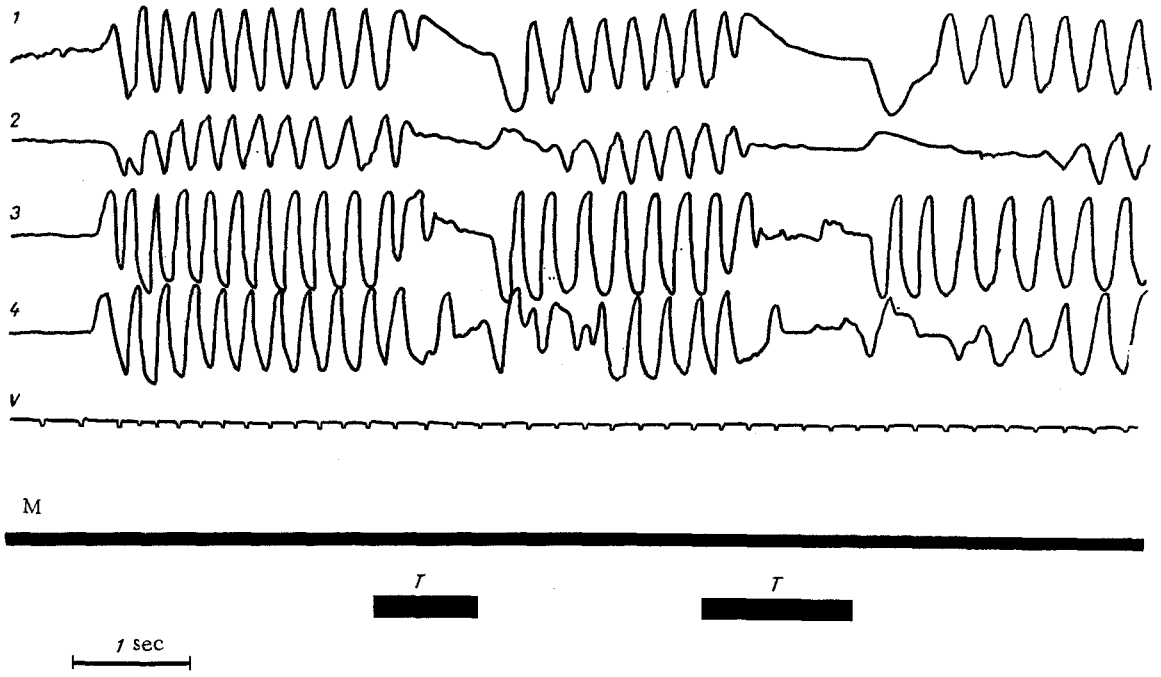

Fig. 1. Thalamic inhibition of locomotion induced by stimulation of LRM. 1, 2, 3, 4) longitudinal movements of limbs: 1, 2) left and right forelimbs; 3, 4) left and right hind limbs. Upward deviation of curve corresponds to forward transfer of limb. V) Marker of velocity of motion of treadmill belt, interval between adjacent markers corresponds to displacement of belt through 0.5 m. M) Stimulation of LRM (50 μA); T) thalamic stimulation (200 μA). Time marker 1 sec.

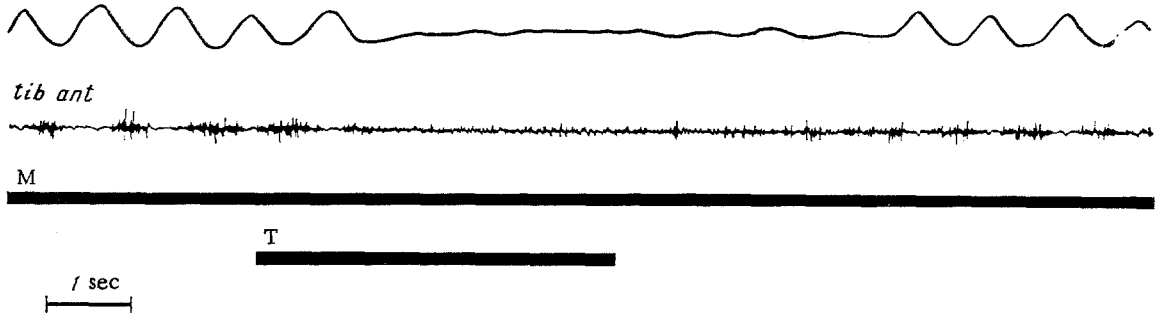

Fig. 2. Stepping movements of left hind limb and EMG of tibialis anterior muscle of that limb during stimulation of LRM (M) and T. Legend as in Fig. 1.

Longitudinal movements of the limbs were recorded by potentiometric transducers [3] on an Alvar electroencephalograph. In two experiments electromyograms (EMG) of the limb muscles also were recorded through copper wires sutured in them.

At the end of the experiment a direct current was passed through each electrode. The brain was fixed in formalin. Electrolytic markers were located in sections, 60 μ in thickness, cut on a freezing microtome. The sections were photographed and the location of the markers identified by reference to a stereotaxic atlas [7].

EXPERIMENTAL RESULTS AND DISCUSSION

The same thalamic stimulation which abolished spontaneous locomotion (observed during rotation of the treadmill belt, when the anesthesia became too light) or locomotion induced by stimulation of LRS, also abolished locomotion evoked by stimulation of LRM. Throughout the experiment an attempt was made to maintain anesthesia at a depth which would eliminate spontaneous stepping and it would not arise in response to motion of the treadmill belt, but pinching would still evoke flexion of the limb. In five experiments during thalamic stimulation the stepping movements of all four limbs ceased during locomotion induced by stimu-

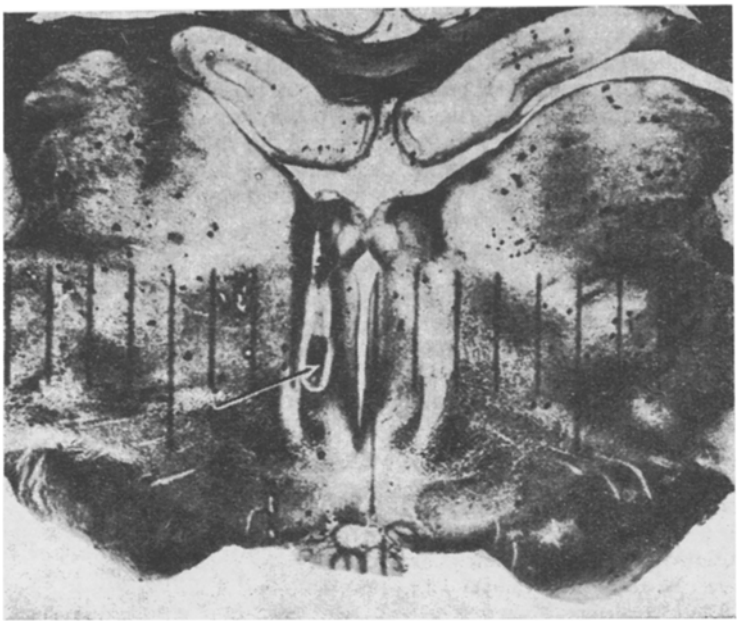

Fig. 3. Electrolytic injury in thalamic point (marked by arrow), stimulation of which inhibited induced locomotion.

lation of LRM (Fig. 1). In the remaining seven experiments the stepping movements were performed by only three or even two limbs. The limb performing stepping movements during stimulation of LRM did not necessarily participate in stepping induced by stimulation of LRS, and vice versa. In some experiments thalamic stimulation abolished stepping in not all four limbs (sometimes in only one). If, however, stepping of one particular limb was inhibited by thalamic stimulation this was usually observed during locomotion evoked both from LRS and from LRM.

Stopping of the limbs during thalamic stimulation took place usually during one or two stepping cycles, but sometimes one limb stopped only 2-3 sec after another limb stopped. In that case the order in which the stepping movements of the different limbs ceased was independent of whether locomotion was induced by stimulation of LRS or LRM. Displacement of the electrode in T by 1-2 mm (from H3 to H1) could lead to a different distribution of the inhibitory effect.

The limbs undergoing inhibition became flaccid and were carried passively backward by the moving treadmill belt. On inhibition of the stepping movements of the limbs the amplitude of the EMG fell sharply in the case of both the extensor (gastrocnemius) and flexor (tibialis anterior) and the cyclic pattern of the EMG disappeared (Fig. 2). On the cessation of thalamic stimulation the normal character of the EMG and stepping movements were restored usually at once or after only 2-4 sec (during continuing stimulation of LRM). However, sometimes after strong thalamic stimulation the stepping was not renewed for several tens of seconds. The duration of the inhibitory effect after the cessation of thalamic stimulation depended on the relative strength of stimulation of T and LRM (LRS). During stimulation of LRM (LRS) of the same strength, rapid recovery of locomotion inhibited by weak thalamic stimulation and an inhibitory aftereffect for 10-20 sec after strong thalamic stimulation could be observed.

The inhibition of locomotion induced by stimulation of LRM or LRS was also observed during thalamic stimulation in animals from which the cerebral cortex had been removed bilaterally in the region of the cruciate fissure by suction. The location of the inhibitory point in T is shown in Fig. 3.

The "incomplete" locomotion in many experiments forced us to restrict our experiments, because of the difficulty of the work, to anesthetized cats with an intact brain. Deep anesthesia did not permit locomotion to be induced, and when light anesthesia was used the animal became uncontrollable, supported itself by its limbs on the moving treadmill belt, or ran spontaneously. The strength of stimulation of LRM required to induce locomotion was

usually higher in these experiments than in experiments on "mesencephalic" cats. In three experiments fentanyl was injected and this stabilized the animal's state somewhat.

Stimulation of the thalamic region discovered by Grossman [4] led to inhibition of locomotion induced by stimulation not only of LRS [4], but also of LRM. It can therefore be postulated that T exerts its action not on LRS, and not on LRM, but on some other structure which controls or mediates the locomotor effects of both LRS and LRM. Probably descending influences play the main role in the inhibitory effect of thalamic stimulation, for inhibition was observed also after bilateral extirpation of the cortex in the region of the cruciate fissure. However, the structures mediating the inhibitory effect of thalamic stimulation still remain unknown. The "point of application" of the inhibitory effect likewise has not been established: it could be structures of the hind brain activating automatized spinal stepping; automatized spinal stepping itself, or even the motor nuclei of the spinal cord.

The region of T, stimulation of which stopped locomotion, coincides to some extent with the region (nucleus parafascicularis) whose stimulation makes locomotion of the unanesthetized cat with unrestricted movements controllable (compare Fig. 3 and Fig. 4 in [2]). Stimulation of LRM in animals with destructive lesions in T enables locomotion to be obtained without complication by side effects, and its intensity can be controlled under chronic experimental conditions. This may confirm the hypothesis expressed previously [2] to the effect that this region of T is not only responsible for the response of "nociceptive" type [5], but also participates in voluntary inhibitory control of locomotion.

LITERATURE CITED

1. G. N. Orlovskii, Biofizika, 14, 1095 (1969).
2. M. G. Sirota and M. L. Shik, Fiziol. Zh. SSSR, 59, 1314 (1973).
3. M. L. Shik, F. V. Severin and G. N. Orlovskii, Biofizika, 11, 659 (1966).
4. R. G. Grossman, J. Neurophysiol., 21, 85 (1958).
5. C. L. Mitchei and W. W. Kaelber, Arch. Neurol., 17, 653 (1967).
6. J. M. Siegel, Physiol. Behav., 13, 715 (1974).
7. R. S. Snider and W. T. Niemer, A Stereotaxic Atlas of the Cat Brain, Univ. Chicago Press, Chicago (1962).
8. W. H. Waller, J. Neurophysiol., 3, 300 (1940).