MONOAMINE NEURONS IN TORTICOLLIS


HISTOCHEMICAL STUDY OF THE CENTRAL MONOAMINE NEURON SYSTEMS IN THE TORTICOLLIS OF CAT

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Spasmodic torticollis is a tonic and phasic involuntary contraction of neck muscles, the etiology of which is unknown. Foltz et al (3) and Mizawa (5) re-

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ported that in the case of monkeys and cats respectively, they were able to produce spasmodic torticollis by placing midbrain tegmental lesions in the medial reticular formation. With the use of the formaldehyde fluorescence histochemical method developed by Falck and Hillarp (2), monoamine (dopamine: DA, noradrenaline: NA, serotonin: 5-HT) -containing neurons can be observed in the mammalian brain (1, 4, 6). Among these monoamine neuron systems, the nigrostriatal dopaminergic system (8) is well recognized in relation to Parkinsonism. However, the functional role of DA neurons other than the substantia nigra, NA neurons and 5-HT neurons still remains to be clarified. In the present study, the Falck-Hillarp method was employed in an attempt to investigate the possibility that the central monoamine neuron systems might be involved in the experimental torticollis followed by destruction of midbrain tegmentum in the cat.

Twenty five adult cats, weighing 2.5 to 3.5 kg., were used in this study. The localization of monoamine neurons and their fiber pathways in the midbrain were studied in 9 non-treated or drug-treated (L-dopa and/or Pargyline) cats and

![Diagram](image)
Fig. 2. Torticollis produced by the destruction of midbrain medial tegmental lesion. A: Isolated rotation of the head, in which the lesioned side was up. Anisocoria (L>R) was noted. B: Lateral bending of the head to the lesioned side.
16 lesioned cats. In lesioned cats, each animal was placed in a stereotaxic apparatus under thiamylal sodium anesthesia. Electrocoagulation was produced by 4 mA of direct currents for 10 sec via a bipolar electrode which was inserted in a point ranging 5.0 to 7.0 mm in anterior plane, 1.0 to 3.0 mm in lateral plane and 0 to −4.0 mm in horizontal plane. Behavioral changes after lesioning were observed for 2 to 6 days. All 25 cats were sacrificed by pentobarbital sodium and the brains were quickly removed. The thinly dissected brains were quenched with isopentane cooled by liquid nitrogen and freeze-dried for 2 weeks. They were treated with formaldehyde fumes, embedded in paraffin in vacuo, and sectioned for observation under a Zeiss fluorescence microscope.

The distribution of DA neurons and 5-HT neurons and their fiber pathways, which are considered to be relevant to the involuntary movements, are illustrated in Fig. 1 on the basis of Snider and Niemer’s a stereotaxic atlas of the cat Brain (7). The NA neurons were found to be located in the nucleus caeruleus and subcaeruleus in the dorsolateral tegmentum of the pons and caudal midbrain. The DA neurons were in the caudal midbrain reticular formation, the compact division of the substantia nigra, the ventral tegmental area, the rostral half of the central linear nucleus, and the rostral linear nucleus. The 5-HT neurons were located in the dorsal raphe nucleus, the superior central nucleus and the caudal half of the central nucleus. The ascending monoamine fibers ran through the central gray, the central tegmental tract, the medial and lateral parts of the red nucleus, and the ventral tegmental area. The ventral tegmental area was revealed to be an area of great significance as a large number of monoamine fibers, particularly DA and 5-HT fibers, joined and ran rostrally in this area.

Behavioral changes following electrolytic lesions in the medial tegmentum of the rostral midbrain were observed in 16 cats. Torticollis was observed in 8 cats, of which seven were tonic and one was phasic in nature. The rotational component of torticollis (Fig. 2, A) was prominent, though various degrees of in lateral bending (Fig. 2, B) and leaning were noted. Circling gait was observed in 3 cats. All lesioned cats were more or less ataxic. In cats with torticollis in which there were significant retrograde changes of DA and 5-HT fibers in the ventral tegmental area as revealed by use of the Falck-Hillarp method (Fig. 3), the midbrain ventromedial tegmentum, including the ventral tegmental area, was destroyed. In cats without torticollis, lesions were found in the dorsomedial tegmentum of the rostral midbrain involving the periaqueductal gray, the interstitial nucleus of Cajal, the central tegmental tract and/or parafascicular nucleus of thalamus. In view of these findings, the possible role of the ascending DA and 5-HT fiber pathways passing through the ventral tegmental area in the control of the neck movements has to be considered.

**Fig. 3.** Photomontage of the ventral tegmental area (VTA) 4 days after lesioning. Frontal section. Strongly fluorescent monoamine axons were clearly evident ventral to the lesion. Swollen varicose fibers were observed running ventromedially to VTA. DA cells in the ventromedial part of the compact division of the substantia nigra (SNC) and paranigral nucleus (PN) appeared normal. 3N: oculomotor nerve, NR: red nucleus.
REFERENCES


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CHANGES AT THE NEUROMUSCULAR JUNCTIONS IN THE AFFECTED MUSCLES OF NEOSTIGMINE-TREATED RATS, TENOTOMIZED RATS AND A PATIENT WITH NEMALINE MYOPATHY*

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Since the original reports made in 1963 (1, 10), many cases of nemaline myopathy have been described. However, little remains known about the pathogenesis of this disease.

It has been reported by several workers that the rod-shaped structures are formed by the tenotomy of the Achilles tendon (2, 4, 7, 8).

Recently we reported that the repeated administration of neostigmine methylsulfate produces rods indistinguishable from those observed in human nemaline myopathy, and that this procedure is a new method for producing rods (6).

In this experiment, three procedures were performed to produce different kinds of muscle atrophies: denervation, tenotomy and daily administration of neostigmine. The neuromuscular junctions in each affected muscle were then observed histochemically and electronmicroscopically, and the relative amounts as well as the rate of synthesis of structural proteins in the affected muscles were

* This work was partly supported by a scientific grant from the Ministry of Education, Japan (1976).