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Published in Great Britain by J. & A. Churchill, Ltd., London

PRINTED IN THE UNITED STATES OF AMERICA
Efferent Functions of the Reticular Formation

ARTHUR A. WARD, JR.
(Seattle, Washington)

The reticular formation of the higher mammals is the remnant of those structures which, in primitive forms, represented the highest levels of integrative nervous activity. Its phylogenetic antiquity is reflected in the undistinguished morphology of this portion of the brain stem, where the microscope reveals “cells of varying types and sizes separated by fiber bundles coursing in all directions.” It is thus not surprising that the efferent functions of the reticular formation encompass the primitive and basic substrates of motor activity. In higher forms, it is thus directly responsible for postural reflexes and righting reactions, and plays a critical role in phasic movement and in maintenance of muscle tone. It is the basic motor apparatus upon which is built the intricate and delicate motor performance characteristic of higher forms, even though it be susceptible to modifications and influences from the highest voluntary motor levels.

Tonic, Postural Mechanisms

The intrinsic motor functions of the mesencephalic tegmentum were first elicited with electrical stimulation by Thiele in 1905, and since that time a number of investigators have electrically stimulated the exposed cut surface of the mesencephalon and reported a “tegmental response.” However, discrete stimulation of the reticular formation in the intact animal was first carried out by Ingram et al. twenty-seven years later, using fine electrodes stereotactically placed in the brain stem of anesthetized cats. Their investigation of the “tegmental reaction” showed that it can be elicited anywhere in the reticular formation caudal to the red nucleus, and this was confirmed by Jenkner and Ward. The postural responses obtained in this fashion were studied in somewhat greater detail by Sprague and Chambers, who felt that the responses so obtained were usually reciprocal and that, although complexity of responses was observed, some topographic organization was present. Thus direct stimulation of the medial reticular formation tended to yield a postural pattern

* Aided by grants from the National Institute of Neurological Diseases and Blindness and the Office of Naval Research.
of ipsilateral flexion and contralateral extension, whereas all areas of the lateral reticular formation yielded a pattern opposite in direction.

It is apparent from all the studies that these complex postural responses can be obtained in quite similar form in decerebrate preparations, in normal anesthetized as well as awake animals with implanted electrodes, and in mammalian forms from cat to monkey. In the unanesthetized cat, the postural responses are more complex than those obtained under anesthesia or decerebration. In addition to the stereotyped postures already mentioned, these also include turning the head to the side of stimulation and righting of the forelegs and then hindquarters if the animal was lying down, followed by stepping and circling toward the side of stimulation.

It seems fairly clear that these postural responses are the consequence of activation of reticular neurons, since they may be obtained after degeneration of the pyramids, after chronic cerebellectomy, and after bilateral section of the medial longitudinal fasciculi or substantia nigra. Furthermore, the beautifully organized movements obtained by reticular stimulation in the unanesthetized animal indicate that this primitive motor system is capable of complex activity which may be somewhat less stereotyped than was once thought. Ingram and associates postulated that the tegmental reaction evoked by stimulation of the reticular formation represents a phylogenetically old motor pattern which is normally not seen in its isolated form in postnatal life. This concept is supported by the observation of Windle and Griffin that the earliest movements that can be observed in kitten embryos are bending of the neck and tonic postures analogous to the tegmental responses elicited by tegmental stimulation.

In addition to these postural responses evoked by stimulation, the reticular formation also mediates the general static reactions, which include the tonic neck reflexes and the tonic labyrinthine reflexes. The more cephalad portions of the reticular formation deal with the righting reflexes, since they are not abolished by lesions of the substantia nigra, the entire cerebellum, or the dorsal half of the midbrain. Although it was originally thought that the red nuclei were the centers for the labyrinthine and the body-righting reflexes which act upon the body, recent evidence places these outside the red nuclei in the reticular formation at the same level. Since the orientation of the human body in space is dependent, to a greater or lesser degree, on all the sensory modalities with the exception of visceral sensation and taste, it is appropriate that this function reside in the reticular formation—a primitive motor center receiving a polysensory input from all sense organs which are capable of giving information about the environment. Because of their primitive and basic nature, the vestibular and labyrinthine input plays a major role in the righting
reactions, but it is of interest that this varies widely from individual to individual. In modern high-speed travel, many of these basic mechanisms no longer result in useful adaptation, and this is particularly true of pilots of high-speed aircraft. In the human, the optic righting reflexes and the visual cues to orientation seem to have a priority, in many instances, over other forms of sensation. For this reason, visual or “contact” flying is least subject to errors. However, as soon as visual cues are lost, as when flying blind, the labyrinthine, vestibular, and proprioceptive reflexes assume major importance and may become so overwhelming that information from the plane’s instruments is partially disregarded by the pilot. Thus it is not surprising that there is good evidence indicating that the best pilots are those in whom the vestibular and labyrinthine reflexes are least active. Such individuals make rapid adjustments in response to the accurate instruments in the plane, and are not confused and only minimally hampered by false cues from other sense organs.

Torticollis

Certain of the tonic, postural responses evoked by stimulation of the reticular formation can appear under pathologic conditions in monkey and man. Following small, discrete lesions of the cephalad tegmentum in the monkey, a torticollis appears with the head and neck deviated to one side. Initially this torticollis is often minimal under resting conditions and is markedly accentuated by stress. We have postulated that these fortuitous lesions functionally denervate clusters of reticular cells in the rostral reticular formation whose function is to evoke such postures. Once denervated, they become hypersensitive to acetylcholine liberated by neighboring cells of different function. Activation of the reticular formation by stress is then postulated to release sufficient acetylcholine to activate them, and the postural movement is accentuated. In man, the administration of anticholinergic drugs in adequate dosage will often afford profound relief from these involuntary torsion spasms. Surgical interruption of the pallidofugal outflow may also modify this postural response. However, in both monkey and man, if the torticollis is of long duration, secondary mechanical changes occur in ligamentous structures and joints of the neck which minimize the improvement of posture following administration of anticholinergic drugs. Since the responsible lesion in man remains to be demonstrated, this hypothesis based on experimental observations is yet to be confirmed.

Phasic, Rhythmic Mechanisms

During the course of their investigation of movements elicited by stimulation of the reticular formation, Ingram et al. noted, as an incidental finding, rhythmic movements or tremor when stimulating the
subthalamic nucleus and the reticular formation close to the rubrospinal tract in the trapezoid body. Subsequent studies of rhythmic movements evoked by reticular stimulation in the intact animal have been reported by Jenkner and Ward in the monkey and Folkerts and Spiegel in cats. The rhythmic, alternating movements are usually more pronounced on the contralateral side of the body, although homolateral responses are present. Stimulation at more rostral levels usually evoked a rhythmic tremor limited to the face, neck, and occasionally fingers. The tremor of the face included fast, rhythmic up-and-down movements of the eyelids, alternating protrusion and retraction of the tongue, rhythmic wiggling of the ears and brows, and rhythmic contractions of the platysma muscles. At more caudal levels, all parts of the body took part in the tremor at one time or another, and these movements consisted of alternating contraction of flexor and extensor muscles at any joint. The amplitude of such movements seemed to be small at proximal joints and much greater at distal joints. The frequency of this induced tremor varied from 15 to 25/sec., slower frequencies being observed only occasionally. The frequency of the stimulating current was never lower than 60/sec.

Often such rhythmic movements were accompanied by a smaller or larger amount of tonic contraction, which occasionally overshadowed the rhythmic response, particularly when strong stimulation was used. The movements elicited by electrical stimulation thus represent only crude approximations of the postural tremor seen in paralysis agitans, although a pill-rolling rhythmic movement was occasionally evoked which appeared to be identical with the pill-rolling tremor seen after chronic lesions of the brain stem in the monkey.

The anatomic region from which such tremor-like movements can be elicited in the monkey is shown in Figure 1. It is seen that the maximum representation for such responses lies in the more medial portions of the reticular formation between the red nucleus and the nucleus of the abducens nerve. Although the lateral and ventral extent of the region yielding tremor was not exhaustively mapped in the monkey, Folkerts and Spiegel demonstrated that such a tremor could be elicited from a wide area of the tegmentum in the cat. It has been assumed that such rhythmic movements are the result of activation of reticular neurons rather than that of other fibers coursing through this region. This conclusion is fortified by the observation of Wycis et al. that degeneration of the brachium conjunctivum did not prevent or alter the characteristics of the tremor induced by stimulation of the mesencephalic reticular formation in cats.

Thus, in addition to circuits in the reticular formation which deal with tonic, postural movements, there appear to be cells embedded in this diffuse matrix whose activity is expressed by rhythmic, alternating
movements. If the reticular formation is a primitive motor system, one might anticipate that circuits would be present to mediate such rhythmic movement. Indeed, Jung has postulated that tremor represents a phylogenetically early form of movement (cf. movements of fins of fishes), which is depressed by the elaborate development of the nervous system in higher forms. Although anatomic correlates of function are far from...
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conclusive, it is of interest that the reticular pontal nucleus is of great size in birds, and one wonders whether this is related to the rhythmic flying movements which are peculiar to this genus.

Parkinsonism

Since the early descriptions of the pathology of paralysis agitans placed emphasis upon lesions in the basal ganglia, a host of unsuccessful attempts have been made to reproduce the Parkinson syndrome by experimental lesions in that region. On the basis of a serendipitous observation by Ward et al.\(^{31}\) in 1948, it was shown that bilateral electrolytic lesions at the base of the tegmentum in monkeys, extending from the red nucleus to the caudal end of the pons, were followed by a static tremor, masklike facies, sluggish movements, and poverty of emotional expression. The tremor at rest was augmented by excitement in all animals described and was seldom synchronized in several limbs. It sometimes appeared during postural adjustment in one extremity; it was uniformly abolished by active, voluntary movement. The frequency of the tremor varied from 7 to 10/sec. Extension of these studies by Peterson et al.\(^{22}\) indicated that the responsible lesion lay in the ventral tegmentum dorsal to the central part of the substantia nigra. With unilateral lesions, the tremor was present on the opposite side.

On the basis of data obtained from both lesions and stimulation of the "tremorogenic" circuits within the rostral reticular formation, Jenkner and Ward\(^{9}\) proposed the hypothesis that the lesions which produce tremor such as that seen in parkinsonism interrupt projections to those neurons in the reticular formation stimulation of which evokes rhythmic tremor. These deafferented cells subsequently become hypersensitive to acetylcholine. Activation by locally liberated acetylcholine then yields the observed tremor. For this reason, suitable anticholinergic drugs reduce the tremor in patients with parkinsonism. This hypothesis assumes that the responsible lesion interrupts those projections to cells yielding rhythmic tremor and does not involve projections to other cells of different function in the same portion of the brain stem. This may explain the fact that large lesions of the tegmentum fail to result in tremor and that the animals whose neurologic abnormalities most closely resemble human parkinsonism are those in whom the lesion is least devastating. It is well known that the tremor of human parkinsonism is exaggerated by emotional stress. Recent evidence indicates that certain circuits within the reticular formation are also involved in the stress response. This activity in neighboring cells may thus result in increased liberation of acetylcholine and accentuation of tremor, as observed.

However, it is not now entirely clear whether the concept of denervation hypersensitivity to acetylcholine is essential to this hypothesis.