SPECIAL ARTICLE

THE RETICULAR FORMATION

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THE NATURE OF THE RETICULAR ACTIVATING SYSTEM

The Reticular Activating System Defined. Allen6 considered the "formatio reticularis" as that mass of cells in the brain stem and spinal cord that is not utilized in the formation of motor-root or sensory-relay nuclei. In primitive phyla, this cellular mass represents the bulk of the entire central nervous system, but vertebrates, in which encephalization is highly developed, exhibit a marked expansion of reticular formation of the brain stem coincident with the appearance of cerebellar and cerebral hemisphere.57 In its expansion, the reticular formation displaces sensory and motor neural structures laterally, surrounds or partially surrounds thalamic nuclei and becomes modified into such derivative masses as nucleus ruber, substantia nigra, subthalamus and other brain-stem elements.6

The continuum represented by the spinoreticular mass of interneurons is well illustrated by Abbie and Adey's4 diagram of the nervous system of the frog (Fig. 1). The reticulothalamic portion of this neural mass begins in the bulb a little above the decussation of the pyramids and extends cephalad into the septal nuclei. Closely interrelated in function, hence considered as part of the reticular activating system, are the reticular formation, central grey, subthalamus, hypothalamus, and midline and intralaminar thalamic nuclei. At present, it is fruitless to review more extensively the cytoarchitecture of the reticular system for, while nearly a hundred nuclear masses have been identified in the reticular formation itself,64 these collections of cells, with few exceptions, do not appear to represent functional units. It is appropriate to mention, however, that a distinction between caudal or reticular and rostral or thalamic portions of the reticular activating system is probably justified.

THE RETICULAR FORMATION

In the past decade there has developed one of the greatest booms in the history of neurology. The wastelands of the reticular formation, badly neglected except for an occasional enlightened glance since the time of Cajal, first became an active frontier in 1947 with the observations of Magoun and Rhines58 and of Moruzzi and Magoun.61 Subsequently, a huge literature has contributed such vast information about this centrally located brain-stem structure that it is almost impossible to keep up with its development. At the

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recent Ford Symposium, Sir Geoffrey Jefferson compared the reticular formation to a huge corporation which expands by buying up all its competitors: structures like the cerebellum, basal ganglia and hypothalamus seem to be disappearing successively into it. He added, perhaps a little wistfully, that the cerebral cortex now seemed to be considered by many only as a conveniently shaped object upon which to rest electrodes.

This meteoric rise in popularity of the reticular formation is justified for doubtless it is essential to, if not identical with, the vitally important in-
The diagram of the nervous system shows the reticular formation in black. Primary sensory conduction is indicated by lines C-D for somatic sensation and by lines C'-D' for audition. Lines A-B and A'-B' indicate unspecific conduction in reticular formation through midline thalamic nuclei to diffuse cortical loci. Oscilloscope records indicate potentials evoked at designated site from auditory (left column) or sciatic (right column) stimulation. Notice prolonged latency (Lat.) and peak time (Pk.) for potentials evoked in reticular formation. (From French et al.23)

Integrating structure that Wilder Penfield has proposed and called the "centrencephalic" system. Nuclear masses and fiber tracts in this small area relay and convey neural influences basic to the state of conscious awareness which enables man to react appropriately in his environment. Because of the importance of these brain-stem influences, it is considered appropriate to review them periodically and such an undertaking is attempted herein. This review will attempt only to epitomize a longer study published elsewhere24 concerning the nature and function of the central brain stem known as the reticular activating system.

Sensory Inputs. Knowledge concerning the primary sensory systems is well established and a part of neurological orthodoxy. Each of these systems, from specific receptor through laterally situated lemniscal pathway to localized cortical receiving zone, is sensitive to a single modality of sensation and single shock stimuli are rapidly conducted throughout their extent.
whether or not the subject is conscious. By contrast, the reticular activating system is responsive to stimuli applied to all sensory systems: a single electrode in the reticular formation or intralaminar nucleus of the thalamus, for example, will record alike (Fig. 2) pulses applied to sciatic, vestibular, auditory, and optic nerves (convergence). Moreover, identical neurons conduct these potentials of diverse origin since cells at a recording site in the reticular formation will not respond to a stimulus applied to one source immediately after they have been discharged from excitation of another system (interaction). These sensory potentials are known to reach the reticular activating system by direct connection with individual systems or through collateral branches from each primary conduction pathway throughout the extent of the brain stem.

Cerebral Inputs. Evidence linking the cerebral cortex with the reticular activating system is now available from anatomic and physiologic investigations. These cortical reticular pathways arise in discrete, well-localized areas in the sensorimotor region, frontal and occipital oculomotor fields, cingulate gyrus, orbital surface, superior temporal gyrus and tip and entorhinal cortex (Fig. 3). Comparable to evoked sensory signals, responses elicited by excitation of each of these loci ("corticoreticular loci") are recorded throughout the extent of the reticular activating system, converge upon single electrode placements and interact, not only with signals from other corticoreticular loci but with shocks applied to sensory systems as well. This responsiveness to stimuli from such diverse sources is responsible for use of the terms "diffuse" or "unspecific" in describing the reticular activating system.

**Fig. 3.** The diagram of the monkey brain indicates cortical loci (hatched areas) which connect with reticular activating system (stippled areas). These "corticoreticular" loci are intimately related functionally with the reticular formation.
Other Reticular Activating System Inputs. Additional pathways of excitation of the reticular activating system are known to traverse the cerebellum, particularly its vermal and perivermal regions.\(^{15}\) The superior cerebellar peduncle would appear to be implicated in transporting cerebelloreticular influences which are directed cephalically while fastigio- reticular impulses through the uncinate fasciculus contribute largely to caudally oriented brain-stem mechanisms. Vestibular structures, formerly thought to function independently through the vestibulospinal tracts, are known to exert their major influence by way of reticulospinal pathways.\(^{32}\) Similar concepts are proposed currently for the basal ganglia which have been connected functionally with the reticulothalamic system.\(^{77}\)

Microelectrode Studies. Records made of responses evoked in single reticular neurons confirm and extend observations made in macroelectrode studies. Discharge of a single reticular neuron can be elicited by excitation of various sensory, cortical, cerebellar and brain-stem structures. While this convergence is widespread it is not absolute\(^{75}\) since different neurons exhibit varied but consistent responsiveness to different sources of stimulus. A single pulse appears to excite some but not all cells within the reticulothalamic system indicating, perhaps, that each stimulus elicits activity in a precise constellation of brain-stem neurons.\(^{41}\) The possibility of pattern responses such as these suggests that a degree of organization and specificity exists in the “unspecific” system as well as in primary neural structures.

Microelectrode studies indicate also that firing of single reticular cells can be inhibited by some stimuli and enhanced by others. Additionally, a unit can be made to increase or to cease firing by reversing a physiological stimulus: inverse vestibular excitation brought about by turning the head successively in both directions will elicit this response.\(^{22}\) The progressive interest being displayed in mechanisms that inhibit as well as facilitate behavioral activity is advanced by such observations as these.

Neurohumoral Excitation. The recent studies of Dell and his associates\(^{17}\) have indicated that neurons in the reticular activating system can be stimulated by the direct action upon them of physiological substances or chemical agents circulating in the blood as well as by neural inputs to the reticular activating system. Both epinephrine and acetylcholine are known to excite activity in reticular units\(^{10,17}\) and comparable responses are elicited by adrenergic and cholinergic drugs.\(^{11}\) In microelectrode studies, convergence upon single units from chemical and from electrical stimulation has been demonstrated. As will be discussed later, reticular activity elicited by neurohumoral stimuli is exerted both cephalically and caudally.

Reticular Activating System Conduction. Potentials elicited within the reticular activating system are conducted cephalically into the brain and caudally into the spinal cord. Anatomically, there is evidence to suggest that conduction in both directions occurs simultaneously as the Scheibels,\(^{74}\) using Golgi techniques, have described axons which branch, sending one main division rostrad and the other caudal. Conduction within the reticular activating system generally is slow because of multisynaptic organization.
but the versatility of this structure is indicated by the fact that it also contains larger fibers which transmit more rapidly.

Reticulocortical conduction is much slower than is transmission of impulses in the primary sensory system. Additionally, in contrast to specific pathways, reticular potentials are disseminated to widespread areas of cortex. This transport of "unspecific" influences is mediated in part by means of connections which the posterior part of the reticular activating system has with the anterior or thalamic portion of the system\textsuperscript{42,69} and probably in part by direct or extrathalamic fiber bundles.\textsuperscript{74,82}

Reticulospinal influences are conducted in fibers which course bilaterally from each side of the reticular formation and which are scattered throughout the lateral and ventral funiculi.\textsuperscript{62} Transmission of these impulses is thought to be quite rapid.\textsuperscript{29}

**ASCENDING RETICULAR INFLUENCES**

*The Arousal Response.* Two methods of assessment have been employed to study wakefulness and sleep. One method has utilized electroencephalographic techniques as a desynchronized tracing characterized by low-voltage fast activity is exhibited commonly during wakefulness and the wavy or synchronous tracing usually connotes sleep (Fig. 4). A second method of study relies upon behavioral responses of an animal to indicate its degree of wakefulness. In general, either of these methods is a reliable indicator of alertness but not invariably so. An example of paradoxical response is supplied by the atropinized animal which exhibits a hypersynchronous electroencephalogram yet is quite awake.\textsuperscript{27} Despite such disparities as this (which may relate to selective blockade of acetylcholine activation of the reticular activating system), arousal or wakefulness will be used here to imply appropriate behavioral as well as electrographic responses.

Moruzzi and Magoun\textsuperscript{61} first demonstrated that direct repetitive excitation of the reticular activating system induced arousal in the sleeping animal. Subsequently, it was adduced that electrical stimulation of a peripheral nerve or physiological excitation of a receptor system elicited arousal by energizing the reticular activating system and through it the diffuse reticulo-cortical projections: such excitation was accomplished by means of collateral inputs to the reticular activating system from primary sensory pathways.\textsuperscript{22} Wakefulness can be elicited by stimulation of all sensory systems yet some, such as somatic sensory structures, are distinctly more potent arousers than are others such as the visual system.

*Sustained Wakefulness.* Arousal is induced generally by sensory activation of the reticular activating system and doubtless continued sensory inputs contribute to maintenance of the wakeful state. While cells in the reticular formation probably are capable of firing spontaneously,\textsuperscript{17} such tonic basal activity is clearly unable at times to prevent sleep. The importance of sensory inputs in maintaining wakefulness is indicated by the fact that animals exhibit an alert electroencephalogram when the brain stem is transected up to but not beyond the sensory nucleus of the trigeminal
Fig. 4. The electroencephalographic tracings show abrupt transition from wavy record of sleep to desynchronized record of wakefulness to excitation of reticular activating system (upper tracing) and to physiological stimulus (lower tracing). (From French and King.21)

nerve.12 Similarly, an alert cat with a post-trigeminal transection will be rendered stuporous by division of the trigeminal nerves.71 Clinically, remarkable mental aberrations were displayed by volunteer subjects placed in an environment that minimized sensory contacts.39

Probably inputs from corticoreticular loci to the reticular activating system contribute also to the alert state.74 Arousal could be induced in normal, chronically prepared cats and monkeys by excitation of these zones74 (Fig. 5). Additionally, the wakeful but inattentive animal would immediately exhibit behavior suggesting that it had become alerted when comparable surface stimulation was applied. As decorticate preparations are incapable of prolonged wakefulness or of attentive behavior, it must be presumed that corticoreticular loci are requisite to the mediation of these alert states.23,76

It has been proposed that neurohumoral mechanisms contribute to sustained wakefulness. Bonvallet et al.10 suggested that arousal to noxious
Photographs of the monkey show behavioral responses of alerting (left column), cowering (middle column) and flight (right column) to stimuli of increasing intensity. Pictures in upper line were made before the stimulus was applied (PRE. ST.); those in middle two lines show behavior during stimulus (ST.) and those in lower line were taken after stimulus was stopped (POST.-ST.). Comparable results were noted from stimulation of corticoreticular loci. (From Segundo et al.38)

stimuli has a dual etiology: the initial rapid response is thought to be mediated by neural excitation of the reticular activating system while slower developing epinephrine activation serves to perpetuate arousal.

*Induced Sleep.* Hess42 has reported that sleep is induced in cats by pro-
longed slow stimulation of the midline thalamic nuclei. These observations indicate a significant difference in the physiological characteristics exhibited by the caudal and thalamic portions of the reticular activating system. Direct excitation of both loci with rapidly repetitive shocks induces immediate arousal. The application of slower pulses (5–10 c./sec.) to the reticular formation elicits only wakefulness while comparable excitation of the thalamic activating system induces diffuse electrocortical synchrony ("the recruiting response"). This synchronous response, presumably conducted by the same neurons that conveyed the more rapid desynchronizing influence, is comparable to the electroencephalographic rhythm of sleep. Apparently, therefore, the sleep induction reported by Hess is elicited when the thalamic portion of the reticular activating system is driven at a rate comparable to slow frequencies observed during sleep. Confirming this proposal are the observations of Akimoto et al. who induced sleep in dogs by stimulating the diffuse thalamic system with 5 c./sec. pulses while 30–90 c./sec. bursts to the same region awakened the animals.

Anesthesia and Stupor. Some years ago it was proposed that transections of the brain stem at the collicular level produced coma because they deafferentiated the brain. Now it is clear that the unconsciousness of decerebration results specifically from blockade of "unspecific" corticipetal influences rather than from total cerebral deafferentiation. Electrolytic lesions confined to the reticular activating system of cats and monkeys will induce permanent coma while laterally placed brain-stem lesions which divide the long sensory pathways but spare the reticular activating system permit a continuation of the wakeful state.

Reversible blockade of cephalic conduction in the reticular activating system by the administration of soporific drugs is known to account in large part for the induction of the anesthetic state. In Fig. 6 it can be seen that potentials evoked in the medial lemniscus by sciatic stimulation are unchanged during anesthesia while responses in the reticular activating system are obliterated by the drug. Comparable blockade has been shown to account for the temporary stupor of concussion. By contrast, excitant drugs such as amphetamine and epinephrine augment activity within the reticular activating system. Evidence is still fragmentary and somewhat conflicting concerning the action of "mood altering" drugs and "tranquilizers" but it is agreed that much of their effect results from altered function of the reticular activating system.

Mental and Emotional Stability. In 1937 Papez proposed that circuits from rhinencephalon through fornix, hypothalamus, thalamus, cingulate cortex and back to rhinencephalon were important pathways in the mediation of emotional behavior. More recent information linking the rhinencephalon functionally with the reticular system promises to contribute importantly to understanding of emotional problems and mental disorder. It has been demonstrated that electroencephalographic arousal is manifested in the rhinencephalon by the appearance of synchronous waves rather than by a desynchronized tracing and waves comparable to these have been re-
corded in the temporal regions of children and psychopathic adults. Doubtless rhinencephalic-reticular links participate importantly in disturbed mental states as well as in temporal lobe epilepsy.

**DESCENDING RETICULAR INFLUENCES**

The main reticulothalamic influences which are expressed caudally are exerted upon the three principal divisions of nervous system function. The vital contribution of brain-stem structures to autonomic control and to neuromuscular function has been subjected to decades of investigation. More recent observations have indicated that the reticular system exerts powerful controls over sensory receptor and conduction systems.

*Neuromuscular Modulation.* The classical truncation experiments of Sherrington and Magnus indicated that, as transections were progressively lowered from the intercollicular level, spasticity became increasingly severe until the region of the vestibular nuclei was reached. Medullary transection below these structures terminated extensor rigidity and substituted instead a flaccid state. For this reason it was proposed that vestibulospinal facilitation accounted for the spasticity of decerebration.

*Fig. 6.* The diagram on the right indicates recording sites in the medial lemniscus (ML) and in reticular activating system (RAS) to stimuli applied to a peripheral nerve. The records on the left show the potentials evoked in these two brain-stem areas before, during, and after the administration of ether to the monkey. Note that potentials recorded in the medial lemniscus are uninfluenced by the anesthetic agent while those recorded in the reticular activating system disappear soon after the application of ether only to return after termination of the anesthetic. (From French and King.)
In 1932, Allen⁴ suggested alternatively: "... it might be explained that the section below Deiters' nucleus eliminated all or practically all of the connections of the formatio reticularis of the brain stem." Magoun and Rhines⁵ later confirmed the correctness of this proposal. They were able to elicit inhibition of reflex and cortically induced movements by excitation of the medullary reticular formation and observed facilitation of these same responses by stimulating centrally located pontomesencephalic structures. Other observations suggested that stimulation of cortical "suppressor strips"⁶ evoked motor inhibition by virtue of corticoreticular connections with the medullary inhibitory center.⁷ Presumably, then, exclusion of these inhibitory corticoreticular inputs through decerebration enfeebled suppression and left unopposed augmenting reticulospinal influences. Infravestibular transection not only eliminated augmenting influences expressed by way of Deitersospinal pathways, but also amputated reticular facilitatory structures leaving intact only reticulospinal inhibition.

Originally, it was felt that inhibitory and facilitatory influences exerted by brain-stem stimulation upon segmental motor responses were nonreciprocal, affecting opposing flexor and extensor muscle groups alike.⁸ Subsequent observations confirmed the existence of reticular stimulus sites inducing nonreciprocal responses but described, additionally, more numerous loci, excitation of which elicited reciprocal responses.⁹ Presumably, nonreciprocal brain-stem activity contributes to tonic mechanism and to stabilization of joints during activity, while reciprocal loci obviously meditate movement.

Reticulopetal inputs exert a critical measure of control over the motor-modulating function of the reticular formation. The validity of proposals based upon the existence of "suppressor strip" has been challenged as originally enunciated⁵⁹,⁷⁸ and these concepts now require modification. The "strip" areas, however, must contribute to motor control, for each one (8s, 4s, 2s, 18s, 24s) resides in or near a region described herein as a "corticoreticular" locus. Stimulation of some of these loci—the sensorimotor cortex, the frontal and occipital eye fields—elicit frank motor response, while excitation of other corticoreticular loci—cingulate gyrus, orbital surface—are said to inhibit motor activity.⁶⁷,⁷⁹ It appears now that both facilitatory and inhibitory influences can emanate from some if not all of the corticoreticular loci.⁵¹ The nature of the induced response doubtless depends on the type of stimulus applied and upon the local state of excitability displayed by responding cell populations.⁵¹

Reticulopetal inputs from other sources are important also in controlling motor activity. Midline and perivermal areas of cerebellum are known to exert both augmenting and suppressing influences upon reticulospinal mechanisms.⁶³,⁸⁰ The vestibule not only supplies appropriate facilitatory or inhibitory impulses to the reticular formation depending upon the nature of the physiological stimulus delivered but tonically energizes it, for section of the vestibular nerves results in diminution of the spinal myotatic reflex.⁵² Spinal afferent inputs appear to supply similar reticulospinal en-
ergies as the relatively normal posture of the decerebrate frog is destroyed by posterior root section.¹

The role of the basal ganglia in supporting reticulospinal motor activity is more obscure than is the contribution of any of the other structures mentioned. Both facilitatory⁴⁸ and inhibitory⁴⁹ properties have been assigned to these nuclear masses and probably either response can be elicited alternatively. Pallidospinal pathways have not been defined and it is probable that influences of the basal ganglia upon spinal motor mechanisms are exerted by way of the reticular system.

*The Nature of Suprasegmental Influences.* The reticular system appears to be able to act upon spinal motor (alpha) neurons through which muscular contraction is elicited or upon small efferent (gamma) neurons which connect with proprioceptor organs, the muscle spindles. The former influences are exerted primarily through internuncial satellite cells⁴⁹ and some of these interneurons appear to inhibit rather than enhance the excitatory state of the alpha neuron.⁶⁷

It has been suggested that the rapidly conducting reticulospinal tracts set the stage for stimuli transported over the slower pyramidal tracts.⁵⁴ Whether or not this proposed relationship exists, pyramidal and reticulospinal functions doubtless are closely integrated. The reticular system exerts its influences cephalically as well as caudally and conceivably could act on spinal centers through the corticospinal tracts. Confirming this possibility is the observation that unit discharges which are synchronous with cortical waves elicited by stimulation of the reticular activating system can be recorded in the pyramid.⁸⁸ Moreover, the pyramidal tract apparently delivers its stimuli upon alpha neuron satellite cells in much the same way as do reticulospinal fibers.⁸⁸ These interrelationships and interdependencies have prompted one proposal that "... the now classical dissociation of pyramidal and extrapyramidal control of muscle is largely an artifact. Both mechanisms are found intermixed in the cerebral cortex and the reticular formation and localized in the cerebellum."⁸¹

Reticular control over gamma efferent activity, hence over the stretch receptor organ, has been recently established⁵⁵ and through such reticulospinal modulation, the myotatic reflex can be enhanced or inhibited. The importance of this control is suggested by Eldred et al.¹⁹ who estimated recently that "... the range of bias at the command of the supraspinal centres is adequate to cover the whole physiological range of movement."

*Spasticity.* Spasticity results when the balance of facilitation and inhibition in reticulospinal output is disturbed in favor of facilitation. Such imbalance is induced by destruction of reticular inputs suggesting that, normally, reticulo-petal influences are tonically inhibitory in nature. Spasticity is induced in animals when reticular inputs from the motor cortex, cerebellar vermis and striatum are destroyed: the effect is transient when these areas are removed individually and most extensive when all are eliminated together or successively.⁴⁹ Clearly, some of these reticular inputs serve to energize loci in the brain stem which contribute to reciprocal as well as nonreciprocal
activity, as loss of phasic movement is a prominent feature in spasticity. These effects are subject to marked phylogenetic variation for normal-appearing postures are retained in lower orders with the bulk of the brain removed while, in primates, severe disturbances result from cortical resection alone.

The spasticity of decerebration apparently results from tonic facilitatory inputs to the spinal cord, largely from suprasegmental levels, rather than from simple release of inhibitory control. As such suprasegmental influences are impossible in explaining the slowly developing spasticity of paraplegia, additional contributing factors must be sought. It may be proposed that a factor of release exists after spinal transection, for facilitatory influences residing in the spinal homologue of the reticular system are freed from suprasegmental inhibition (cf. Schiff-Sherrington phenomenon)\(^{126}\).\(^5\) Additionally, “short-circuiting” and diffusion of conduction potentials doubtless occur at the site of transection;\(^{73}\) such artificial synapses have been demonstrated experimentally, in spinal cord\(^{48}\) as well as in peripheral nerve.\(^{36}\) Finally, ephaptic excitation\(^7\) (non-synaptic excitation of one cell by its neighbor) may be enhanced in paraplegia.

Tremor. Tremor comparable to the disturbance of parkinsonism is induced in animals by making lesions in the reticular formation\(^{85}\) (although opinion\(^{14}\) has been expressed that such lesions induce tremor by interfering

![Oscilloscope records of the monosynaptic reflex are shown.](image)
with cerebellofugal pathways). As similar tremors can be elicited by stimulation of the reticular formation, and as these tremors are opposed by anticholinergic drugs, it has been proposed that brain-stem lesions may cause cells in the reticular activating system to become hyperactive through sensitivity of degeneration. This proposal implies that such hyperactivity in the reticular formation can exert a rhythmic discharge in spinal motor neurons and there is reason to believe that it can. Lloyd and Kleyntjens et al. have demonstrated that a reticular stimulus exerts a waxing-and-waning rather than sustained effect upon alpha neuron activity and such synchrony could doubtless be amplified by disordered brain-stem function (Fig. 7).

While abnormal reticular influences inducing tremor probably are conveyed directly to the spinal cord, transport through cortical relay may be involved additionally. Cortical reverberations traversing the reticular system may contribute to normal movement and some theories, notably that of Bucy, consider these pathways implicated in the genesis of tremor (Fig. 8). Improvement induced by surgical attack upon pallidothalamic or corticospinal tracts would support this concept. Contrastingly it has been suggested that tremor results from direct reticulospinal defects but becomes apparent only against a background of tonic pyramidal activity. This tonic influence would be eliminated by corticospinal division.

![Diagram](image-url)

**Fig. 8.** This familiar diagram illustrates Bucy's proposal concerning cortico-reentrant pathways which may be disturbed in patients with tremor. It is probable now that the reticular formation should be added to the diagram. (From Bucy.)
This diagram of the cat brain illustrates the centrifugal influences which the reticular system (RF) exerts upon sensory inputs to the brain. The black arrows designate inhibitory responses which have been observed in spinal and brain-stem nuclear masses, in the thalamus and in the olfactory bulb. The hatched arrow indicates both facilitatory and inhibitory responses which have been described in the optic system. Arrows with heavy stippling illustrate comparablemodulating influences which can be elicited by a cortical and cerebellar stimulation. (From Hernández-Peón. 46)

noted that the rate (10 c./sec.), regularity and time sequence of parkinsonian movements parallel at least one natural cortical rhythm, the alpha rhythm. Following brain-stem lesions such rhythmic influences, normally excluded from spinal neurons, might find restrictive barriers gone.

Control of Sensory Conduction. Since Granit and Kaada's 35 original observation in 1953, additional studies have indicated that the reticular system exerts extensive control over most, if not all, sensory pathways of the nervous system. Both facilitatory 34 and inhibitory 39 effects have been elicited although suppression appears to predominate. These controls, mediated by centrifugal fibers, have been demonstrated in cutaneous receptors, 47 muscle spindles, 35 cochlea, 28 retina 44 and olfactory bulb. 44 Reticular stimulation is known to modify afferent conduction particularly at relay nuclei: synaptic inhibition has been described in the dorsal root, 28 posterior column nuclei, 38 spinal V ganglia, 41 specific thalamic relays 46 and even in the reticular formation itself 4 (Fig. 9). That the entire reticular activating system contributes to this phenomenon is indicated by the fact that comparable effects are elicited whether the stimulus is applied to the reticular system or its corticifugal inputs. 4, 38

These phenomena would appear to explain the mechanisms utilized by animals and man in accepting certain stimuli and rejecting others. Certainly chaos would result if the nervous system was forced to recognize the overwhelming barrage of signals to which it is constantly exposed. Failure of this mechanism, indeed, may contribute importantly to mental disease. Additionally, functional disorders, such as the elusive trigeminal neuralgia, might well result from faulty receptive mechanisms. 47
**Autonomic Control.** For the sake of completeness only, brief mention is made of the fact that numerous "centers" implicated in cardiovascular, respiratory, visceromotor, metabolic and temperature-regulating controls as well as with other autonomic mechanisms, coexist in brain stem with the reticular activating system. There is reason to believe, moreover, that these mechanisms are inseparable functionally from those relating to arousal, movement, sensation, etc. A stimulus from a single electrode placed in the bulbar reticular formation, for example, will elicit simultaneously changes in blood pressure, respiratory rate and reflex activity. Polyphasic responses comparable to those resulting from stimulation of reticular formation are elicited by excitation of corticoreticular loci. Such integrating mechanisms as these underlie the mediation of pattern responses which are implicit in all levels of nervous system function but are most highly developed in cortical-centrencephalic systems.

**SUMMARY**

It has been possible to review here only in the most abbreviated manner the nature and function of the reticular activating system. The central brain-stem masses comprising this system are derivatives of a phylogenetically ancient column of spinocerebral neurons which are interposed between sensory nuclei and motor cells. Vertebrate encephalization has resulted in tremendous expansion of the rostral end of this structure and magnified extensively the ramifications of its function. Implicit in the mediation of these manifold functions of the reticular activating system are its interconnections with spinal cord, cerebral cortex, basal ganglia, cerebellum and vestibular nuclei and its response to humoral excitation.

Coextensive within the reticular activating system are systems which appear to exert influences that are oriented rostrally and others that are directed caudally. Principal among influences directed cephalically is that mediated by a diffusely projecting system of neurons which subserves arousal, sustained wakefulness and all the mental attributes of conscious awareness. Caudally oriented mechanisms include those that modulate muscle tone and movement, that control sensory inputs to nervous system, and that mediate processes of visceral regulation. Interference with cephalically directed influences results in mental disturbances, coma and the anesthetic state. Defects in caudally directed activity induce spasticity, tremor, and disturbances in motion as well as faculty preceptive phenomena.

The divisions of nervous system function enumerated above are entirely artificial and made purely for purposes of description. The evidence indicates rather that these several activities are so interdependent as to be inseparable since stimulation never elicits changes in one area of reticular function without inducing related change in all others. The reticular activating system, therefore, must be considered the great integrating mechanism of the brain without which unity of response to complex environmental stimuli is impossible. Investigation of its functions can be expected to extend knowledge concerning the intricacies of normal behavior. Doubtless in its dysfunction will be found the seeds of many nervous and mental disorders that currently plague man's understanding.
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