SOME ASPECTS OF THE PHYSIOLOGY AND PHARMACOLOGY OF THE RETICULAR FORMATION

A Review

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The reticular formation of the central nervous system has been known, for a long time, as an ill-defined structural organisation of the brain with still more ill-defined functional implications. Phylogenetically, it is more extensive in the brains of the primitive phyla where it serves adequately in integrating various afferents with visceral and motor functions in the absence of a well-developed cortex (9). Embryologically, it is that mass of cells in the brain stem that is not utilised in the formation of specialized and demarcated cell-masses as the nuclei of cranial nerves, the sensory relay nuclei and the motor roots. In the mammalian brains it practically covers the whole of the central brain stem leaving aside the ascending and descending tracts, the nuclei associated with them and the motor relay stations (119).

During the last two decades attention was particularly directed towards the reticular formation (R.F.) by a number of eminent workers in the fields of neurophysiology and neuropharmacology and its unique role in the execution and maintenance of the integrative behaviour and functions of the higher nervous activity like 'attention' and 'consciousness' was gradually being elucidated. Since then the R.F. has come to be figured prominently, and justifiably so, in a vast majority of the extensive and elegant experimental works on the various aspects of the physiology and pharmacology of the central nervous system (C.N.S.)

The reticular neurons vary very much in size and in the length of their processes. Branching collaterals from the axons along with prolific multidirectional dendritic ramifications establish polysynaptic connections with multitudes of neurons both rostrally and caudally, the neurons themselves being entangled and enmeshed in the web of their criss-crossing processes; hence the name (4). Adjacent neurons even do not all have the same connections (39).

In the background of these profuse to and fro connections, with almost all other parts of the CNS (1, 37, 52, 132, 145, 148, 149, 150, 158, 170), a functional and also partly topographical

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The following abbreviations are used in the text :

R.F.=reticular formation; ARAS=ascending reticular activiating system; DTPS=diffuse thalamo-cortica projection system; EEG=electroencephalogram (—graphic); ECoG=electrocorticogram.=LSD d-lysergic acid diethylamide.

consideration of the R.F. suggests a not well-demarcated division into two systems, a descending and an ascending reticular system. It is also pertinent to note that morphological data indicate a definite distinction between the medial and lateral regions of the R.F.; the lateral area appears to be more adapted to serve 'receptive' and 'associative' functions while the medial area seems to be concerned with 'effector' functions *i.e.*, primarily involved in modulating actions of the spinal cord or on higher structures (36).

The Descending Reticular System : Almost all motor activities involve some modulation of the segmental reflex patterns by inter-and supra-segmental influences, chiefly from the bulbar R.F. (54), that may again be under a cortical control (2). These reticular neurons exert both inhibitory (124) and facilitatory (138) influences upon the spinal motoneurons (115, 133). The exclusively inhibitory interneurons of Renshaw (139) are homologous to this system. The facilitatory counterpart of this system extends more rostrally upto the thalamus (138).

The Ascending Reticular System : The R.F., the tegmentum of midbrain and the related midline and intralaminar nuclei of the thalamus that are considered to be the cephalic extension of the R.F., are all implicated in transporting an influx of afferent impulses to the cortex besides the main sensorium arriving via the classical lemniscal pathways. Bremer's 'cerveaux isole' experiments (31, 32) showed that exclusion of these reticular areas caused a loss of wakefulness and coma. Magoun, Morruzzi and other coworkers (120, 131) employing electrophysiological techniques explained later that exclusion of the R.F. specifically, rather than a blockade of the sensory impulses conveyed by the lemniscal systems, is responsible for the coma. Since these areas have been subsequently shown to be involved in conveying 'arousing' informations to the brain and in maintaining wakefulness, irrespective and virtually independent of the sensory modalities normally being transported, these were loosely designated with the rather functional term of the 'Ascending Reticular Activating System' (ARAS) (28, 120). This system is essentially comprises of two components, the midbrain R.F. proper and the diffuse thalamo-cortical projection system arising from the thalamic counterpart of the R.F. (89, 160) and is believed to be the head way for a corticopetal conduction of the whole reticular system (92). But some workers believe that the activating system does not depend upon the DTPS for its conduction rostrally and may use an extra-thalamic pathway to the cortex not involving any interneurons (35, 107); they would rather prefer to use the term ARAS to mean the midbrain R.F. only.

It is very intriguing to note, in this context, that the brain stem R.F. is supposed to harbour not only an ascending activating system but also an ascending deactivating mechanism, if not a system by itself (50). But this functional dichotomy, though in line with some Russian observations, has not so far gained popularity.

PHYSIOLOGICAL CONSIDERATIONS OF THE RETICULAR FORMATION

The brainstem R.F. represents a most important integrating structure, if not the 'master control mechanism' of the C.N.S. The 'vital centres' are located in it; it regulates the body temperature and the neuroendocrine control functions of the hypothalamus; it is essential in

'arousal' and wakefulness; it influences the motor function in phasic and tonic muscular activity; it exerts an 'editing' action on the reception, conduction, relay and final integration of all sensory inflow, to the degree that some will be perceived while others be rejected or blocked; and finally, there is the role it plays in 'attention' and 'consciousness' (60).

The multineuronal and polysynaptic complex of the R.F. provides a 'reverberating circuit' (40) for a constant background neuronal activity of an integrational character that happens to be essential for attention and consciousness. Penfield (135) has coined the term "centrencephalon" for the whole system that serves as the supreme integrator, while others ascribe this role to the DTPS (87, 89, 94).

In addition, the R.F. may play the part of a modulator of the activities of the paleocortex and rhinencephalon that are believed to be concerned with the genesis and display of emotions (118).

The Ascending Reticular Activating System (ARAS) and Arousal : Magoun (123) observed that direct electrical stimulation of the brain stem R.F. induced electroencephalographical (EEG) changes identical with that of arousing from sleep or of alerting to attention. This was later confirmed by other workers and the effect variously designated as 'activation' or 'desynchronization' or 'EEG-arousal', all of these terms being much used in subsequent literature. [The term, 'behavioural arousal', coined and added to the neurophysiological vocabulary, means differently as the name implies. The areas included the R.F. proper, the tegmentum, the subthalamus, dorsal hypothalamus and ventromedial thalamus. But these are not the only ones. A typical behavioural or EEG-arousal, similar to that obtained on stimulation of the brain stem R.F., can be elicited with low intensity stimulation from an extensive but well-defined area of the telencephalon.] These areas may be termed as 'telencephalic arousal' areas (98). This arousal is likely to be mediated through the brain stem and thalamic R.F. Physiological and anatomical evidence for an intimate relationship between these telencephalic regions and the brain stem or thalamic reticular areas have been published (55, 61, 75). However, arousal reaction in rabbits is not exclusively restricted to the reticular system (127).

According to Bremer (34), stimulation of the R.F. produces only a facilitatory effect on the cortex; cortical excitation and not inhibition is the underlying feature of desynchronization of the EEG as elicited by reticular activity. This is corroborated by others (53) while Kogan (109) believes that desynchronization of the EEG may both accompany excitation and inhibition of certain observed activity; it is a sign of neurons at work irrespective of this work being excitatory or inhibitory in nature.

The role in consciousness : Various peripheral sensory somatic stimuli and special sensory stimuli reach the cortex rapidly *via* the laterally situated lemniscal pathways; but while in transit they, simultaneously, evoke impulses in the tegmentum and the midline structures of the brain stem which reach the frontal associational cortex. The former (lemniscal pathways)

exhibit rapid conduction, segregation according to sensory modalities, discrete cortical jection and conduct sensory informations contributing to the perception, localisation and q titative discrimination of stimuli. But the latter (medially placed) pathways show a slower of conduction, common transport for all modalities and distribution to wide areas of corte a diffuse thalamo-cortical projection system (DTPS); these are concerned with the initiation maintenance of the conscious state, thus providing a necessary background of neural act without which no integrative sensorimotor and adaptive behaviour is possible (63, 65). lation of the central pathways of the R.F. in cats produces akinesis and hypersomnia and EEG shows hypersynchrony as in deep sleep (62, 113), as also brain lesions in man (But interruption of the lemniscal pathways at midbrain level leaves the cat wakeful and the E shows typical desynchrony; if asleep, it can still be aroused by sensory and auditory sti (128, 129). However, destruction of midbrain arousal area is also reported to be followe a gradual return to alertness (114, 159).

In identifying and localising the mechanism that maintains the tonic activity exerte the midbrain R.F. on the EEG, it has been observed after serial transactions that the cri site lies in the upper pontine region. The neurons exerting the activating influence lie in region and are independent of the sensory inflow from the olfactory and optic ne (130). But there is evidence that olfactory arousal is possible even in 'encephale is preparations (8).

Cortex and the R.F. : Role in Attention : Corticifugal impulses reach the R.F and rious relay cell stations in the sensory pathways of the brain stem (33), exerting a tonic inhibi activity in controlling the afferent inflow of impulses from the periphery. They can mo depress or even abolish the postsynaptic corticipetal impulses originating in the brain s neurons including the R.F., while the sensory stimuli are being relayed on (73, 74, 81, 82, 1 Various anatomical studies have suggested pathways by which such influence of the cortex ca exerted on the incoming traffic of sensory impulses (83,99,166). According to many work a secondary sensory impulse may weaken or suppress the inflow of a first impulse in the pro of being relayed (66, 77, 82). In this 'switching over of attention' the R.F. plays the role a switchboard operator (169), presumably, under the command of the cortex (or may independently?)

Adrian (3) discusses the role of the cortex in perception and the physiological mecha of attention. Attention essentially means the preferential registration upon the consciousnes a particular sensory modality while other sensory channels are restricted or attenuated, a although their impulses may register on the sensory cortex electrically, they are percieved at a subthreshold conscious level. It is in studying attention that we approach most clo to the level of consciousness. "The climax of mental integration", says Sherrington, "wo seem to be attention" (157).

It appears quite probable, therefore, that the R.F., by virtue of its modulating influence over the afferent traffic of impulses, plays a major part in the control of attention. The physiological mechanism underlying habituation of the arousal reaction, *i.e.*, the tendency for a repeating stimulus to lose its arousing effect, seems to be mediated through the R.F. (76, 156).

But there is no consensus regarding this habituation of the arousal response. While most of the Western workers corroborate the finding that a reduction of primary cortical response occurs when a sensory stimulus (e.g. auditory) is repeated both at cortical and subcortical levels, especially, during conditioning (67,71, 80), some Russian workers report that no evidence was found of any habituation of electrical response to repeated stimuli at any level of the auditory pathway (72, 144).

Reticular Formation as the Editor of the sensory inflow : The role of the R.F. appears as if to be preparing not only the cortex but also the other sensory pathways to respond to a particular sensory modality only for a particular time. This may be achieved in a two-fold way: (a) by a reduction of other sensory inputs that might compete for 'attention' and by suppressing or diverting them to other labyrinthine circuits leading to oblivion, or by creating delay in their perception, and (b) by the integration of the sensory informations being attended to with the continually changing background of somatic and environmental data (28).

This distribution of 'attention' is rather difficult to comprehend, but the R.F. seems to be responsible in attaching special value to a particular sensory modality or a prepotent stimulus at one particular time. Some workers have demonstrated the prepotency of nociceptive stimuli above all others in the arousal reaction (11).

The R.F. plays a more or less similar role in the establishment of conditioned reflexes (69, 70). Gastaut reports in this context that conditioned reflexes can be formed in decorticate or decerebrate cats in striking contrast to the failure of the genesis of conditioned reflex by even a small lesion in the brain stem R.F. Hence, R.F. appears to be primarily involved in the formation of conditioned reflexes in addition to harbouring the sites for the attention, startle and orientation responses and habituation as stated above (71). Because of the convergence of impulses from many sources, the R.F. along with some limbic and diencephalic structures are essential for establishing any transcortical connections as in conditioning (93). But all workers do not agree to ascribe this role solely to the R.F. (72, 110, 144, 164).

According to Jasper (87, 89), the diencephalic component of the ARAS serves to mediate sudden brief shifts or arrests of 'attention' in response to shades of sensory stimulation or inflow, while the midbrain R.F. is responsible for the maintenance of consciousness and wakefulness by a chronic tonic activity upon the cortex. This difference in the phasic and tonic activity of the R.F. upon the cortex is of interest in explaining its role in the habituation and conditioned learning processes. Evidently, the alerting processes depend upon some form of interaction between elaborate patterns in the specific thalamocortical systems and the brain stem reticular systems (90).

In a very similar way the R.F. is involved in the instinctive behavioural activity of t brain; the reduction of the alertness and vigilance following consummation and satisfacti of the instinctual drives is brought about by a depression of the reticular activity induced by t very act of consummation of the drives (43).

PHARMACOLOGICAL PARAMETERS OF THE RETICULAR ACTIVITY

The pharmacological investigations on the activity of the reticular system probably o number those in pure electrophysiological fields both in quantity and complexity and the spa is hardly sufficient to account for all of them here.

Bradley suggests that considering the sites of action of drugs related to the R.F., th distinct sites seem probable :

(*i*) the reticular formation proper (upto the midbrain); the standard examples are a phetamine which stimulates it and the barbiturates which depress it ;

(*ii*) the diffuse thalamocortical projection system (DTPS) that is considered to be rostral extension of the R.F. (28, 160) and is not concerned with behavioural cha ges; atropine, benactyzine, eserine, *etc.* belong to this category;

(*iii*) the afferent collaterals entering the R.F.; examples are chlorpromazine, reserpine a LSD-25, which probably control the afferent input of impulses to the R.F.

There are at least three pharmacologically distinct types of receptors for drugs in C.N.S. One of these is certainly cholinergic in nature (in the DTPS?) (26); the second is p bably related to a catecholamine, while the third may be an indole (19, 22, 23).

For behavioural arousal adrenergic drugs are dominant and for EEG-arousal cholin gic drugs are prepotent (18, 146). Benactyzine, a central anticholinergic drug, abolishes EE arousal but not the behavioural one (17, 27).

Effects of drugs on the arousal responses : It has been demonstrated that EEG-arou can be induced by administration of acetylcholine as well as the adrenergic drugs (14, 15, 19, 42, 44, 45, 46), and since they both stimulate the R.F., presumably directly, separate bra stem mechanisms have been postulated (146). Besides the R.F., they also act upon the ceph extensions of it, *viz.* posterior hypothalamus and some of the limbic structures. It follo therefore, that either of the anticholinergic or antiadrenergic drugs can block the neuroge stimulation, mediated presumably by the R.F., for the release of the pituitary gonadotropl hormones (147).

The concept of a selective depressive action on the input side of the R.F., as outli above, may also have a bearing on the 'telencephalic arousal' areas since descending impu from some of these areas appear to converge upon the same reticular neurons as receiving s sory informations (61).

These 'telencephalic arousal' areas again are rather susceptible to anaesthetics and the arousal is readily blocked by such agents as compared to the other brainstem arousal areas (97, 155).

EEG:-and/or behavioural arousal by nociceptive stimuli and like agents has two components in it : (i) the initial rapid desynchronization by direct neural excitation of the R.F., and then, (ii) a slower adrenergic activation that tends to perpetuate arousal. This dual excitatory influences compliment each other (14).

Cholinergic drugs are known to activate the EEG and the site of action is presumably the DTPS, without behavioural correlates (13, 14, 20). Acetylcholine and eserine, given intra-arterially, definitely stimulate the R.F. and can also reduce the facilitatory/inhibitory influences of the R.F. on monosynaptic cord reflexes; though ineffective on motoneurons, these drugs often stimulate the internuncial neurons.

Although adrenaline produces a brief EEG arousal, repeated administration results in slowing and spindle activity of the EEG. Chlorpromazine abolishes the arousal but enhances the synchronizing effect (162). Noradrenaline, though endogenous, has no such effects (47).

Amphetamine induces a pregressive lowering of the threshold for both EEG and behavioural arousal by electrical or sensory stimulation. LSD-25 has little effect on electrical arousal threshold but markedly lowers the threshold for auditory arousal without altering that for the click response in the auditory cortex (19, 22). Amphetamine directly stimulates the R.F., independent of external influences (140) while under LSD-25, the preparations become more sensitive to afferent stimuli so that these are more easily aroused (19,22).

Jasper suggests (91,156) a dual arousal mechanism in operation; a prolonged tonic arousal occurs from the midbrain R.F., and a short phasic arousal follows from the DTPS. This may help in explaining the differential action of chlorpromazine on EEG-and behavioural arousal. It seems probable that direct stimulation of the R.F. or DTPS is capable of EEG-arousal, but tonic input from the sensory systems is essential for behavioural arousal. Low doses of chlorpromazine often lowers both arousal thresholds but, in higher doses a slight rise in both occurs (19). But according to other reports, chlorpromazine only slightly raises the threshold for EEG-arousal while that for behavioural arousal is raised about ten-fold, especially from thalamic stimulation; arousals from midbrain are not affected critically (20, 100, 101, 103, 104, 105).

In contrast with chlorpromazine, barbiturates depress the R.F. to the point of a subtotal impairment of attention and consciousness. These raise the thresholds to both arousals, the auditory and tactile arousals being blocked first; with higher doses direct electrical arousal is also blocked (7, 50, 51, 102, 106, 107).

There is no consensus about the action of reserpine on the R.F. It depresses diencephalic centres and also antagonizes the adrenergic activation of the medullary R.F. (10). It is also reported to inhibit afferent impulses which normally elicit sympathetic activation *via* the R.F. (153). It appears that reserpine has little effect on the EEG-or behavioural arousal, *per se*, (101, 104), though there are reports that it may actually exert an alerting influence on the R.F. while depressing the hypothalamus and making it insensitive to account for the tranquility (86).

The muscle relaxants do not affect the ARAS but depress the descending reticulospinal pathways; it is uncertain whether they act only on the spinal interneurons or on some brain stem neurons as well. Meprobamate, being a tranquillizer, may have some action on the R.F. (51, 79, 107, 108).

Morphine and related compounds usually depress the EEG-arousal elicited by peripheral or reticular stimulation, induce a sleep-like EEG and abolishes attention response (68, 161); but they are poor blockers of arousal as they fail to block arousal by persistent pain (86), suggesting that the site of action may be elsewhere. They increase the excitability and recruiting response of the DTPS and activity of hippocampus; levallorphan antagonizes all of these actions of morphine and congeners and may induce an EEG-arousal by itself (68). Apomorphine also induces EEG-arousal but differently (38).

Anaesthetics and the Reticular Formation : A state of anaesthesia does not necessitate the prevention of sensory impulses from reaching the cortex; in fact, sometimes they may be recorded in augmented form (28,64). Barbiturates seem to have a differential depressant action on the subcortical inhibitory system, resulting in an augmentation of the secondary response in the non-specific sensory system (58). Primary sense-linked response seem to be resistant to the anaesthetics (hence augmented Forbes response); but ARAS responses are more vulnerable which need have to be functioning and would thus determine whether incoming sensory impulses receive the integrative elaboration necessary for an 'awareness' of them (29). Anaesthetics block the RF at a time when conduction continues in the leminscal pathways though some blockade in the latter may occur later with changes in the interneuronal circuits (30, 64).

The close similarity between the comatose behavioural response following the ablation of the R.F. and drug-induced anaesthesia led to the belief that anaesthesia is brought about by a reversible depression of the R.F. selectively (107, 121, 122). These agents supposedly exert a blocking effect upon synaptic transmission preferentially than upon nerve conduction. As the R.F. is a multineuronal polysynaptic system, it will hence be far more susceptible to the action of the anaesthetics than the oligo-synaptic classical sensory pathways (7, 30, 64, 111, 152). But failure of the interneuron depressants to affect reticular arousal fails to support this concept (106, 107).

While a rapid repetitive stimulation of the R. F. fails to activate EEG in anaesthetised animals , the recruiting responses elicited by stimulation of the DTPS at 6 -12 c.p.s. are, para-

doxically, enhanced by barbiturates although ether blocks this as well as the EEG - arousal (95,107).

Besides blocking arousal, anaesthetics seriously modify caudally directed functions of the R. F., especially on the spinal reflex activities. The easy blocking of the 'telencephalic arousal' has already been cited (97,155).

Psychotropic drugs : Desynchrony of the EEG has long been associated with wakefulness while synchrony is equated with sleep or narcosis. Some drugs, however, complicate the picture. For example, atropinized animals appear awake and alert, yet exhibit quite a synchronized EEG, while eserine desynchronizes ECoG without any alerting (22,26, 27, 134,171). By contrast, reserpine induces drowsiness and inattentiveness without altering or even inducing, in high doses the low voltage fast EEG, characteristic of desynchrony / arousal (27,105,169). Mephenesin depresses the arousal and recruitment by stimulation of the DTPS but does not affect the arousal from the midbrain R.F. (107). The action of chlorpromazine on arousal has already been cited (19,20,100,101,103,104,105).

Desynchronizing effects of the R.F. on the EEG are not fully unspecific arousal response. Not all stimuli that induce desynchronization work through the same system. Arousal by pain and food stimuli, for example, may be mediated in the R. F. by different chemical mediators. Chlorpromazine blocks the former but not the latter which is blocked by adrenaline (6).

It seems quite unlikely that phenothiazines, in general, act by direct depression of the ARAS although it has been suggested so, *prima facie*, by many workers from the evidence that chlorpromazine treated animals are less responsive to peripheral arousing stimuli (17,24,25,41,78,117, 140,162,). The microelectrode studies of Bradley (21) indicate a more specific depressive action of chlorpromazine on the sensory inflow to the R.F., although the primary sensory input is not interfered with. On the contrary, it may also seem possible that the primary reticular input might be increased by these drugs as seen in the enhancement of the evoked activity from peripheral nerve and intrareticular stimulation as well as by the increased inhibition on responses in the auditory system (101). Thus these drugs might enhance the caudally directed inhibitory influences of the R. F. exerted upon the afferent conduction of the sensory modalities; they augment the activity of the filtering servo - mechanisms of the ARAS and so reduce the inflow of information to the cortex (104). This inhibition coupled with the depressed cephalic influence upon the arousal response would give rise to the observed " tranquility" (60).

However, some authors, though not in obvious disagreement with Bradley's contention that the effect of Chlorpromazine is mainly attributable to a depression of afferent input of impulses to the R.F. seem to prefer some modifications or supplementations of the view. For instance, the behavioural effect of chlorpromazine may be due to a reduction of some aspects of stimulus control over behaviour (48,49); the drugs might interfere with the release of some transmitters at the afferent collaterals thus affecting input (137), or due to some other factors (168).

The net effect of reserpine on the R. F. has been assessed to be negligible ; it does not depress the R. F. at midbrain level, but does so at thalamocortical level according to some workers (126). A depression of the bulbar reticular activity even after midcollicular decerebration has been reported (12) and has been offered as the basis of the hypotensive and probably, the tranquillizing action of reserpine.

Chlorpromazine, reserpine, meprobamate, hydroxyzine, benactyzine, *etc*, induce a more or less marked state of synchronization of the EEG; but the EEG blocking of the arousal reaction by electrical or sensory stimulation is abolished or depressed by these drugs; except benactyzine all others inhibit the motor alarm reaction following electrical stimulation of the R.F. or, at least reduce it (17).

In accounting for the tranquillizing effect of these drugs, one must consider their actions on the rhinencephalic structures besides the R.F. proper. The particular type of EEG —arousal recorded from the hippocampus, the entorhinal area and the amygdala in response to peripheral, reticular and thalamic stimulation are blocked by low doses of chlorpromazine and reserpine that have only slightly depressive effect on the arousal in neocortex (76, 102, 103). A cholinergic mechanism may be involved in hippocampal arousal (116).

Of the emotional reactions, at least, fear and anger have been produced in man by stimulation of the amygdala (36). It has been suggested that the 'fear-producing' and 'arousal' areas of the hypothalamus and brain stem R.F. are the principal sites of action of tranquillizing drugs since the relief of fear, anxiety and tension is their characteristic clinical effect. But such areas also exist above the brain stem level, especially within the limbic structures (88, 154).

All of the variety of agents which have the common property of altering the perceptive experience in man (e.g. mood elevators, LSD-25, 5-HT, adrenochrome, cocaine, atropine, morphine etc.) have important structural similarities, including an indole-like linkage in their chemimical structures (112). This might point to the possiblities of receptors, probably located in the R.F. LSD-25 and amphetamine may facilitate or actually stiumulate the R.F., though acting at different sites. The direct action of adrenaline on the R.F. is depressant and synaptic inhibitor (125). Leake (112) feels that the excitant action of adrenaline on the brain, as reported earlier (15, 42, 45, 47), may be secondary to the proprioceptive feedbacks from its peripheral actions into the brain stem R.F.

The effects of LSD-25 are susceptible to spinal section *i.e.*, if the sensory input is interrupted, there will be no effect of LSD-25 (22). But, Purpura suggests (136) that the desynchronizing effect of LSD-25 upon ECoG may not be specifically mediated by the ARAS, but rather occurs within the cortex itself.

Antiparkinson Drugs : It is relevant to note that a number of workers have investigated into the Parkinsonism like syndromes from a different angle altogether, implicating the interesting possibility that the R.F. might be affected. Experimental lesions in the midbrain

R.F. may produce tremors or such abnormal motor movements (96, 163, 166); tremors might be produced by a direct stiumlation of the midbrain tegmentum (57). Furthermore, there exists an interesting correlation between the ability of certain drugs to control tremors (e.g., atropine, scopolamine benztropine, caramiphen etc.) and to block alerting response from the R.F., so much so that the ability to prevent alerting reaction may be used as a screening test for antiparkinson drugs. (85, 141). Parkinsonism like extrapyramidal toxic symptoms exhibited by most of the tranquillizers may be due to a chemical lesion effect on the R.F. (143), or its excitation (167). The fact that antiparkinson drugs are anticholinergic in nature points strongly to the possibility of a cholinergic mechanism being involved in the activity of mesodiencephalic reticular formation (142 b).

In locating the sites of action of centrally acting drugs, the R.F. is being often implicated. Furthermore, drugs are being used increasingly in elaborating the physiological significance of the R.F. as in conditioning and behaviour. This will be accounted for in a subsequent review.

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