CENTRAL NERVOUS CONTROL OF CARDIAC ACTIVITY* (*PART II*)†

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HYPOTHALAMIC MECHANISMS

Electrical stimulation of hypothalamus has been known to cause a discharge in the sympathetic outflow thereby increasing the arterial pressure and heart rate (33, 49, 52, 101). Sympatho-inhibitory points leading to a fall in the arterial pressure and decrease in the heart rate have also been localized in the hypothalamus (72, 73, 91). Cardiovascular effects of hypothalamic stimulation have been further studied in detail by using more refined techniques. Rosen (1961) demonstrated augmentation of cardiac contraction and heart acceleration alongwith skeletal muscle vasodilation on hypothalamic stimulation thus linking the mobilization of cardiac activity with the sympathetic vasodilator outflow (122). Rushmer's group recorded cardiac diameters, pressures in various chambers of the heart and computed heart rates before and after stimulation of the hypothalamus at the fields of Forel and demonstrated a pattern of cardiac response simulating the one achieved during muscular exercise (123, 124, 126). Folkow et al recently have been able to produce increase in cardiac output as measured by aortic flow meter alongwith the dilatation of vessels in the skeletal muscles by the electrical stimulation of the hypothalamic defence area (87). It has been further demonstrated that cardiac acceleration and cardiac augmentation can be differentially produced by stimulating the right and left posterior hypothalamus respectively thus reproducing the differential effects of right and left stellate ganglion stimulation (41, 48, 83). This is in favour of the direct projection of fibres from hypothalamic neurones to the spinal autonomic neurones for such a differentiation does not seem to have been obtained on medullary stimulation. Recording of the electrical activity of heart has shown that hypothalamic stimulation not only produces changes in heart rate but also can lead to various types of cardiac arrhythmias and changes in impulse conduction (48, 89, 111, 113, 125), and further, these effects have both vagal as well as sympathetic components (111, 113).

It is now established that the centrogenic effects on the sympathetic outflow can be quite selective with respect to different regions. For example while septal and hypothalamic stimulation leads to vasodilation in skeletal muscles, it also produces a concomitant vasoconstriction in cutaneous and splanchnic regions (84, 85, 105, 131). So far it was understood

that sympathetic discharge is a sort of mass response. These observations reflect that such a concept is erroneous, and that regional variations in sympathetic discharge are possible and perhaps are invariably employed in patterning the cardiovascular activities to suit myriads of bodily functions. This is further authenticated by the studies in which electro-neurographic activity of sympathetic nerves supplying different regions has been simultaneously recorded to see the effect of reflex or centrogenic influences on the sympathetic outflow (92, 116).

It is possible that in the animals with intact brains, stimulation of hypothalamus will also involve the excitation of pathways originating from the cortical and limbic areas like the medial forebrain bundle. Rioch and Brenner in 1938 however, were able to demonstrate general sympathetic effects by posterior hypothalamic stimulation after all descending fibres of cerebral cortical origin had degenerated (120). Hypothalamus, therefore, is in a position to affect the cardiovascular activities by virtue of its own innate mechanisms. This does not mean that hypothalamic mechanism cannot in turn be controlled by the higher parts of the forebrain. There is increasing tendency to discard the older view of dividing the hypothalamus into anterior sympatho-inhibitory or vagotonic areas and posterior sympatho-facilitatory areas as proposed by a number of authors (73, 91). It has been shown for example that the same point may have either a pressor or a depressor effect depending on the frequency of stimulation (49, 84). This is probably due to threshold differences of elements belonging to different functional groups but intermingled in the region of the electrode tip (6).

Ever since the studies of Pitts et al in 1940 it has been considered that the hypothalamus plays no role in the mediation of the stabilizing reflexes originating from the baroreceptor areas (49). Recently however some doubts have been expressed regarding this concept (42, 48). The study which is quoted most often is that of Manning (42) who found that carotid occlusion response could still be elicited after producing massive lesions in the medulla oblongata which presumably covered the whole bulbar vasomotor and cardiac centres. The carotid occlusion response disappeared after a further decerebration at the inferior collicular level in these animals. The author claimed therefore that carotid sinus reflex is possibly mediated through the supra-medullarry regions, especially the hypothalamus which he considered to be well equiped for providing a tonic drive to the cardiovascular activities. However, as yet there is no electrophysiological evidence demonstrating the projection of barostatic impulses into the hypothalamus. Preliminary studies in which Manning's experiments were repeated in our laboratory show that in the cats with massive lesions in the medulla oblongata, the carotid occlusion response could still be obtained after the neuraxis was completely transected just posterior to the mammillary bodies. This means that essentially it is not the hypothalamus which is important for maintaining or mediating the baroreflexes but it is the whole of brainstem (including the mesencephalon) reticular formation which provides the basic tone to the cardiac and vascular muscle (fig. 1).

Hypothalamic stimulation, however, does influence the baroreceptor reflexes. Hilton (96, 97) and Gebber and Snyder (90) believe that the carotid sinus reflexes are completely inhibited when hypothalamic defence area is stimulated. Support for

this concept has also come from the studies on human beings demonstrating inhibition of baro-

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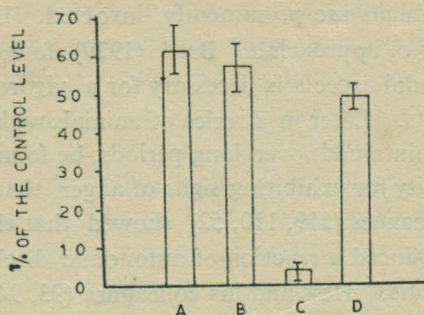
RESPONSE

RISE IN MEAN
ARTERIAL PRESSURE

Fig. 1

Bilateral carotid occlusion responses in cats anaesthetized with alpha-chloralose (50 mg/kg body weight)

A. *Controls : intact preparations.*
B. *Preparations with massive lesions in the bulbar region.*
C. *Same as B above but neuraxis sectioned below the level of inferior colliculi.*
D. *Same as B above but neuraxis sectioned caudal to the mammillary bodies.*

receptor reflexes during sustained voluntary muscle contraction (88, 104). The hypothesis that such a useful mechanism becomes redundant during muscular exercise seems highly implausible. Robinson *et al* (121) have demonstrated the continuous sensitivity of baroreceptors during muscular exercise in human beings. Besides, Swedish workers from Folkow's laboratory have recently demonstrated that although bradycardiac component of the carotid sinus hypertension is inhibited on hypothalamic stimulation, quite a fair amount of vascular dilatation as obtained on such a stimulation is secondary to the raised arterial pressure acting through the baroreceptor area (81, 102). They believe therefore that in all these cases where the cardiovascular activities are mobilized by the action of higher regions of the brain primarily to provide a larger flow of blood, the carotid sinus reflex does operate thus bringing about a synergism with the sympathetic vasodilator outflow. Evidently the purpose of hypothalamic control is more in line with achieving adjustments of different parameters of cardiovascular activities so as to meet the tissue needs in a particular response of the animal as a whole than just to produce an enhancement or inhibition of the sympathetic outflow.

Confirming such an approach are also the studies of Hilton and Joels (1965) with respect to chemoreceptor reflexes in which they found that reflex hyperpnea and vasodilation elicited by chemoreceptor activation is facilitated when the hypothalamic defence area is stimulated (98). Hypothalamic participation in the chemoreflexes was earlier observed by Bizzi et al (74).

Role of hypothalamus in the control of cardiovascular activities can be further elucidated in the light of its involvement in diverse neural activities which result in the expression of various types of precisely determined, though complex behaviour patterns such as expression of emotions, responses to heat or cold stress, alimentary behaviour and sexual activities. In all these instances somatic, autonomic and hormonal components are welded together in a purposeful manner. In several situations, specially in the expression of emotions and temperature regulation, cardiovascular adjustments are prominently involved. Evidence for these concepts has been derived from a variety of approaches. Bard (1929) found that the integrity of hypothalamus especially in its caudal aspects is necessary for a vigorous expression of anger which occurs in freshly decorticate cats. Later in a series of animals with various types of surgically created brain deficits and maintained over long periods, he found that chronic mesencephalic preparation has a far less capacity for exhibiting signs of anger than the hypothalamic animal (70, 71). Ranson and his colleagues (119, 110, 52) showed that electrical stimulation of points in the lateral hypothalamus produced a reaction of autonomic discharge which was quite similar to "sham rage" of decorticate cats. Hess and his colleagues (93, 94, 95) demonstrated a large number of behaviour patterns of stimulation of different points in the hypothalamus. Included among these were also the ones which are indistinguishable from the defensive reaction typically elaborated by normal animals when they are confronted with hostile situation. From none of these studies, a precise description of cardiovascular changes which accompany these emotional reactions was made available. In the "sham rage" behaviour of Bard's decorticate cats notable rises in arterial pressure and heart rate alongwith erection of hair, sweating, pupillary dilatation retraction of nictitating membrane and medullodrenal secretion, all signifying an enhanced sympathetic discharge, however, were observed.

Similarly, with regard to body temperature regulation, it was observed that circumscribed lesions in the anterior hypothalamus (including the preoptic area) produced a loss of the heat loss mechanism. These animals would become hyperthermic whenever exposed to high temperature in the environment. This signified a loss of the dilator control of cutaneous vessels. Lesions placed in the posterior hypothalamus on the other hand produced a loss of mechanism of heat production and heat conservation (119). Local heating in the anterior hypothalamus produced panting and sweating (110). Andersson and his colleagues confirmed these observations in the unanaesthetized goats (66). They were even able to drive the hypothalamic "heat loss" mechanism by electrical stimulation so vigorously that their goats became hypothermic (67). Relation of the centrogenic cardiac activity with respect to body temperature regulation however does not seem to be of primary importance. Perhaps the cardiac changes likely to occur in the course of such a regulation will be secondary to the vascular and respiratory changes.

Recently Abrahams et al and Hilton in a series of publications (62, 63, 96, 97) described the experiments in conscious animals elucidating a pathway extending from lateral region of preoptic areas and the hypothalamus to the periaqueductal mesencephalon stimulation of which produced a defence reaction similar in content to that reported by Hess and his colleagues

(93, 94).   Abrahams et al also measured the skeletal muscle blood flow during these reactions and concluded that muscle vasodilation forms an integral part of alerting response that occurs when these areas are stimulated (63).   Folkow and Rubinstein stimulated the lateral hypothalamic areas in conscious animals and elicited defence reaction from more basal areas of the hypothalamus but on stimulating the more rostral areas they produced eating responses. On further stimulating the same animals under anaesthetic so that the cardiovascular parameters could be recorded they found that the points which gave eating responses produced vasodilation in the G.I.T. and the points which gave defence reaction produced vasodilation in the skeletal muscles but vasoconstriction in the muscles of G.I.T. (86).   Bolme et al (76) studied the changes in blood pressure, heart rate, blood flow to hind limbs and behaviour in conscious dogs on stimulation of the sympathetic vasodilator outflow areas in hypothalamus and mesencephalon and demonstrated the rise in blood pressure, tachycardia and cholinergic vasodilation in the hind limb.   Although in a few animals rage reaction was produced, in general however, behaviour changes were relatively small and consisted of variation in alertness.   In many experiments marked circulatory responses were obtained without any apparent behavioural reactions.   These authors were unable to decide whether this vasodilator cardioaccelerator pathway is involved in specific situations like adjustments preparatory to muscular efforts in exercise and in emotional reactions or it acts more generally in circulatory homeostasis. They were however inclined to agree with Hilton (97) about the possibility of its involvement in situations preparatory to animal's muscular efforts.   The Italian school (64, 65) have recently performed some very elegant experiments in which they confronted their cats with another animal ready to go into fighting reaction on hypothalamic stimulation and observed their natural reactions alongwith the recording of cardiovascular parameters. They found that during the preparation for fighting the cats got bradycardia, decreased cardiac output, mesenteric vasoconstriction and decrease of blood flow in the iliac artery.   During actual fighting, on the other hand, there was tachycardia, increased cardiac output and variable increases in the iliac blood flow alongwith mesenteric vasoconstriction.   These authors consider therefore that the cardiovascular changes which occur during preparation for fighting are not the same as implied when cholinergic vasodilator-cardioccelerator regions of the hypothalamus are stimulated.   According to them, the cardiovascular adjustments during fighting have a huge peripheral component issuing out of metabolic changes due to skeletal muscle contraction.   This seems to be true at least in cats.   Future studies alone will be able to delineate as to which cardiovascular changes are centrally elicited and which are reflexly elicited or modified.   .

Manchanda (1965) stimulated the laterel aspects of hypothalamus in conscious but restrained cats and found a good deal of overlapping between the points eliciting biting as a component of attack behaviour and chewing as a component of alimentary behaviour (112).   He was able to elicit these responses from the whole of lateral extent of hypothalamus at points medial to the int.rnal capsule.   In all his cats the attack behaviour was accompanied by marked tachycardia, rise in blood pressure, enhanced ventilation, limb movements and vigorous

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SPONTANEOUS RESPIRATION
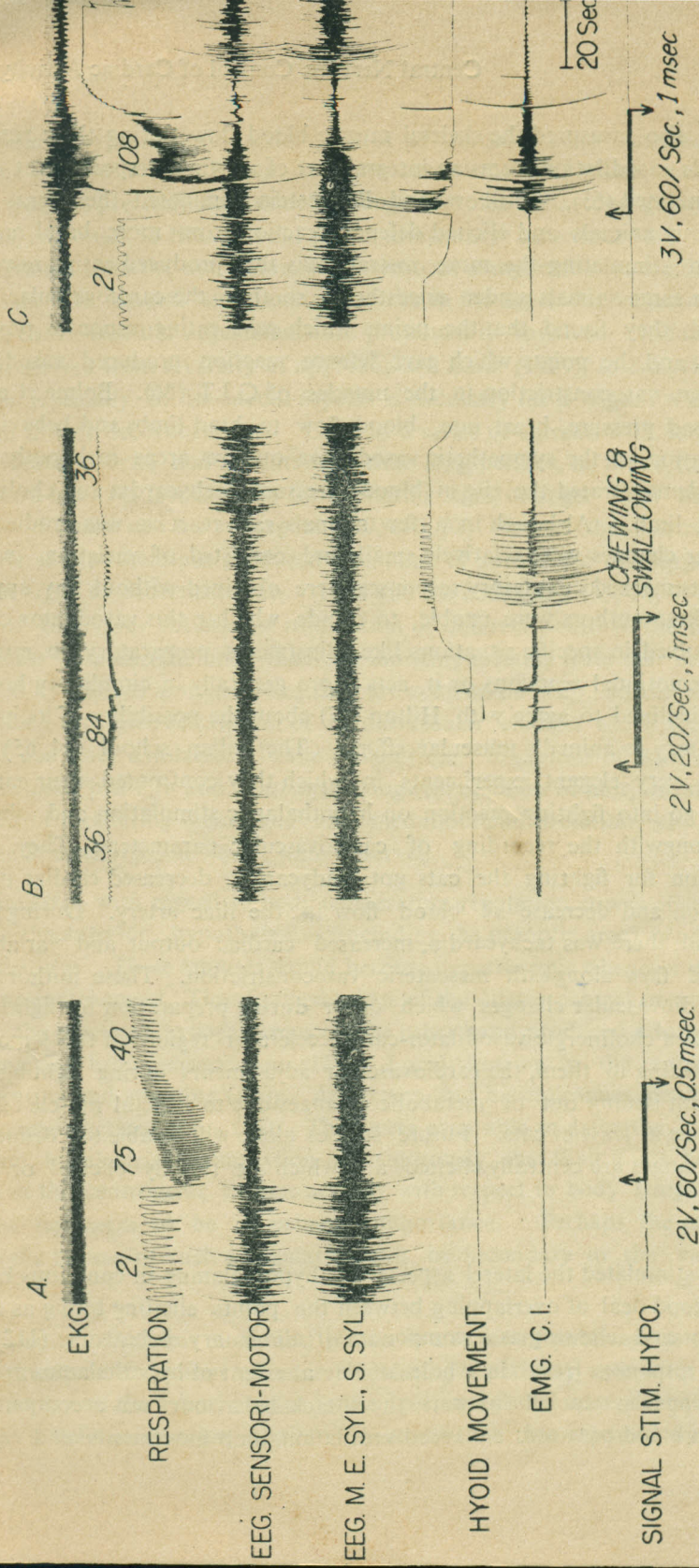## STIMULATION HYPOTHALAMUS (MID-LATERAL)

Fig. 2

Hypothalamic stimulation in an unanaesthetized but restrained cat.

A. Note the marked increase in the rate and depth of respiration and equally marked desynchronization of the EEG activity of cortex. The animal was alert and its pupils dilated. Heart rate as calculated from EKG tracing increased from a basal level of 110/minute to 130 per minute during stimulation.

B. Stimulation of the same point as in A. Already desynchronized cortical activity became more desynchronized during stimulation. No change in the depth of respiration was noticed although the respiratory rate increased markedly. Pupils were not dilated. The heart rate did not show any significant change. At the end of stimulation chewing, intermittantly interrupted by swallows appeared which is reflected on tracings indicating hyoid bone movements and EMG of the inferior pharyngeal constrictor.

C. Stimulation of the same point as in A and B but with strengthened parameters. Vigorous biting along with the forelimb movements started immediately with the onset of stimulation. Marked electrocortical desynchronization, respiratory augmentation and pupillary dilatation was noticed.

biting alongwith foamy salivation and pupillary dilatation (Fig. 2).   This reaction was accompanied by marked cerebral activation as recorded electroencephalographically.   These studies showed that hypothalamus is the main integrating centre both for autonomic and somatic activities and welds them into purposeful behaviour patterns in response to sensory inputs of various origins.

LIMBIC AND NEOCORTICAL REGIONS

Limbic areas of the cortex have profound influence on the cardiovascular activities. Changes in heart rate, arterial pressure and blood flow have been demonstrated on stimulation of these regions in a number of animal species including man (3, 32, 80, 128, 78, 109, 106, 118). The limbic regions are intimately related to hypothalamus via the fornix system, stria terminalis and medial forebrain bundle with profuse reciprocal connections (115).   The hypothalamus thus seems to be a sort of link station between the limbic system and mesencephalon.   MacLean (106, 107, 109) divides the limbic system into two subsystems.   One comprises amygdala, hippocampus and related structures and is considered to be "primarily concerned with behaviour that pertains to survival mechanisms involved in feeding and in activities such as searching, fighting and defence required for obtaining food".   The other consisting of cingulate cortex, fornix and septum is supposed to be concerned with the activities associated with preservation of the species and therefore is involved in the elicitation of grooming reactions and sexual manifestations including search for the mate, copulation, penile erections and ejaculations.   Both systems alongwith their respective olfactory inputs coalesce in the hypothalamus.   In as much as these structures are involved in governing such basic animal behaviour, cardiovascular activities induced from these regions will be a part and parcel of their behavioural manifestations.

So far, however, limbic stimulations in the anaesthetised animal, have produced only non-specific, generalized, and variable changes in the cardiovascular parameters.   This is partly due to the lack of technology employed for recording of cardiovascular parameters in freely behaving animals, and partly due to the fact that organization of neural activities at these levels is rather complex generating a vast multitude of behaviours.   MacLean et al (109), however, have been able to produce very localized circulatory effects in the form of penile erections on stimulation of points located in the system and its connections in the hypothalamus in unanaesthetized squirrel monkeys.

Various autonomic responses such as galvanic skin resistance, salivation, pupillary dilatation, respiration and heart rate can also be conditioned (69, 114).   Cardiovascular responses have been conditioned to various types of stimuli like pain, food, sound and light (53, 23).   Although cardioacceleration as a conditioned response has been known to occur since long, it is only recently that increase of cardiac output has been demonstrated as a conditional response in the monkeys by Smith and Stebbens (127).   These monkeys could differentiate between a conditioned light stimulus and an unconditioned light stimulus.   Such conditioning is purely of central nervous origin and is not a result of the activity of skeletal musculature which often accompanies a conditioned autonomic response because cardiovascular condi-

tioning was still obtainable after curarization of the animals (75,129). These studies show that besides the limbic regions which are primarily concerned with animalistic urges, other cortical regions too have an important role in determining the cardiovascular activities. The interplay of learning behaviour and the instinctual behaviour is demonstrated by an interesting experiment in which massive neuronal discharge produced on stimulation of hippocampus and spreading throughout the limbic regions could block the conditioned cardiac reflexes in cats (108).

Hoff and his colleagues over a number of years have published reports in which arterial pressure, heart rate changes, and blood flow changes in renal and skeletal muscle circulations have been produced by stimulation of the cortical motor areas (28, 99, 100, 29). Although no strict localization of pressor or depressor points was obtainable, they were uniformly able to show vasodilation in the skeletal muscles and vasoconstriction in the renal circulation. As a matter of fact these authors were able to produce a permanent damage to the kidney in the form of lower nephron necrosis by producing repeated ischaemia on cortical stimulation in their chronic preparations. Swedish group of workers have explored in detail the nervous pathway involved in cholinergic sympathetic vasodilator outflow and have shown that the innervation has a central representation which originates in the motor cortex, and possesses relay stations in the hypothalamus and in the tectum. The descending fibres, according to them bypass the bulbar cardiovascular areas and continue in the spinal cord close to the lateral columns in the lateral fasciculus (82, 76, 84, 130, 131). As has been discussed while dealing with the hypothalamic mechanisms, opinions differ with regard to the physiological significance of this system.

Cerebral cortex can also affect the cardiovascular system independent of the hypothalamic mediation. Wall and Davis (58) elicited changes in blood pressure and heart rate by stimulation of Rolandic area and temporal cortex which were not affected by hypothalamic destruction, but were abolished by the section of pyramids. Possibly the pathway goes direct to the pyramids via the internal capsule. Landau (103) stimulated the medullary pyramids in the decerebrate cats and obtained changes in cardiovascular parameters alongwith other autonomic responses. These changes were obtainable even after neuromuscular blocking by curarization. Delgado (80, 79) has summed up his studies on cortical stimulation by stating that the cortical areas with cardiovascular functions are located in the anterior half of the brain and include the tip of frontal lobe, the orbital cortex, the motor and premotor cortex, the hidden motor areas, the anterior part of the temporal lobe, the insula and the cingulate gyrus, and is firmly of the view that contrary to earlier concepts quite specific and selective effects on heart and blood vessels can be obtained by stimulation of discrete cortical points in unanaesthetized cats and monkeys independent of changes in the electrical activity of the brain or changes in other systems signifying the possibility of direct cortical representation of individual parameters of cardiovascular system.

Apart from the studies in which various cortical regions were stimulated to obtain cardiovascular responses, there are other studies in which selected cortical ablations produce

cardiovascular effects. Thus it is known that paralysis of cerebral origin is accompanied by vasomotor changes in the human beings (77). In the cat and dog removal of sensorimotor area of one hemisphere caused vasodilation in the opposite paws. These vessels did not constrict as efficiently in response to cold as those on the ipsilateral side. It seems however that the response varies with the species for in the monkeys the response obtained was opposite to that in cats (6, 117). Perhaps these regions of the cortex have a role to play in the regulation of body temperature. Further, it has been reported that frontal lobe lesions can lead to the production of gastric ulcer by causing intense vasoconstriction (68).

ROLE OF CEREBELLUM

Stimulation and ablation studies of cerebellum have revealed marked cerebellar influences on the cardiovascular parameters. The literature has been reviewed by Dow and Moruzzi (132). Rasheed et al (133) recently proposed that cerebellar autonomic influences may be operating at various levels of the neuraxis i.e. limbic-hypothalamic, or brainstem level depending upon the complexity of the response elicited on cerebellar stimulation. Manchanda et al (134) from the same laboratory have further suggested that the cerebellar involvement in cardiovascular regulation is more in terms of the patterning of a response in its temporal aspects than in the supply of a background facilitatory or inhibitory tone to the autonomic nerves. What precisely is the role of cerebellum is not yet clear. Nevertheless the view is gaining ground that for any conceptual scheme of the CNS regulation of cardiovascular activities, the part played by the cerebellum must also be taken into account.

CONCLUSIONS

Whitteridge (61) while discussing the cardiovascular reflexes initiated from afferent sites other than the cardiovascular system itself stated that "......although we all disclaim teleological thinking, in fact we all think in terms of purpose even when we may invoke the higher teleology and ask : How does this reflex aid in the preservation of the constancy of internal environment ?" No doubt such an approach has provided a rich harvest in interpreting the results of experiments performed on anaesthetized animals.

A prominent aim of the conscious animal however is to generate dynamic activity to meet the challenges of survival in the external environment. For this purpose the animal mobilizes its resources, somatic as well as visceral, to elaborate behaviour patterns best suitable for its survival in a particular situation in the external environment. All behaviours whether employed for defence against an enemy or against extremes of climate, for food intake or for sexual performance can be broken down into simpler reflexes for analysis. Elaboration of these behaviours of a conscious animal is a function of the higher nervous regions which integrate the somatic and visceral reflexes in appropriate temporal and spatial orders to evolve a particular behaviour. It is in this respect that while interpreting our stimulus-response observations, we may as well pose another question : How does this reflex or response
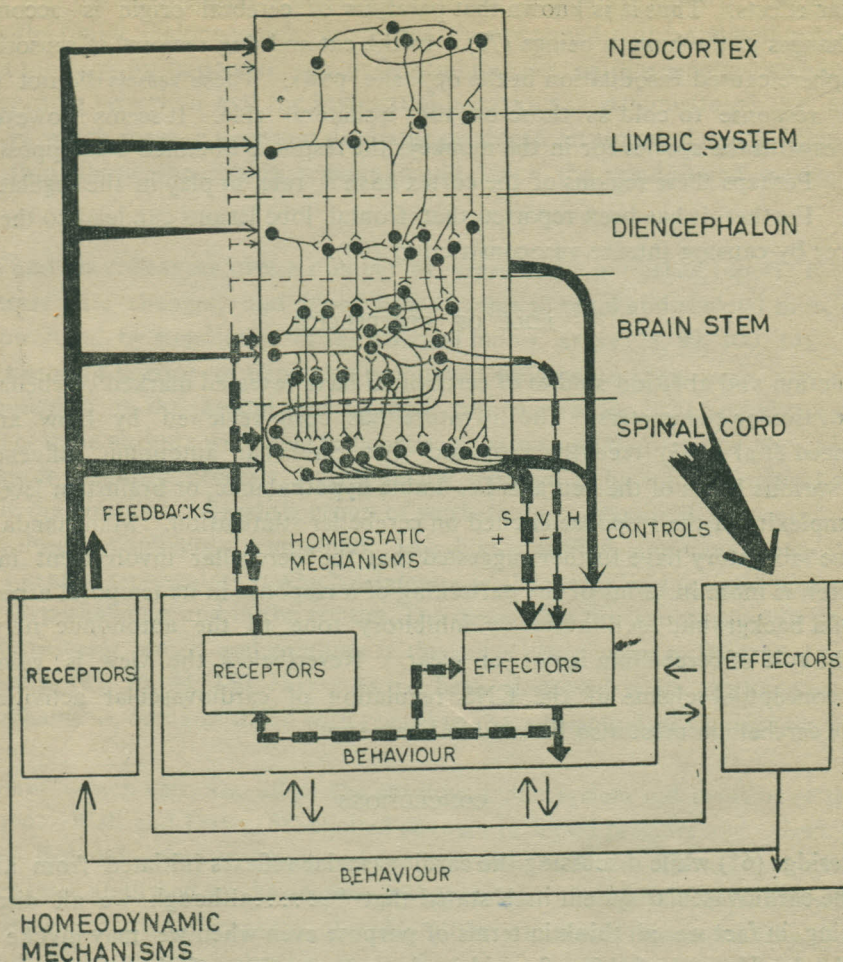
Fig. 3

Diagram of the conceptual model proposed for the central nervous regulation of cardiovascular activities. Two feedback regulatory circuits are shown. The inner circuit is private to the cardiovascular system and aims at stabilizing its behaviour. These reflexes seem to be mediated at various levels in the reticular formation of spinal cord and brainstem. Possibly integration of cardiovascular activities with other autonomically controled visceral activities like respiration, GIT motility and secretion, etc. required for stabilized conditions of rest also occurs at this level.

The outer circuit depicts the control of cardiovascular regulation through the feedback from receptors located at sites other than the cardiovasculr system. These inputs are known to feed in at different levels of the CNS. Nature of the cardiovascular response resulting from these sensory inputs will vary according to the behaviour pattern elaborated depending upon the level of CNS involved. In general the effects of these inputs may be predicted as opposite to those of the stabilizing inputs. Future studies may however demonstrate that the interplay between different components of mobilizing inputs ad those of stabilizing inputs possesses a wide range of complexity.

(S : Sympathetic, V : Vagus, H : Hormons. Arrows indicate direction of the flow of information. Filled circles represent neurones at various levels)

aid in the elaboration of behaviour for survival in the external environment? Such an approach to analysis will be particularly beneficial with respect to those visceral reflexes or responses which are initiated from higher regions of CNS or from sites other than those which belong to the system expressing the viscerum's activity. The concept of Central Nervous Regulation of Cardiovascular Activities which is being put forward here, therefore, is based on two types of reflexes. One type includes those reflexes which are private to the system and aid in the stabilization of the system's behaviour itself.   The other type of reflexes are initiated from receptor sites located in other systems of the body and aim at producing disturbances in the system's behaviour (cardiovascular system, in the present context) primarily to mobilize the cardiovascular activities in favour of their own respective systems (fig. 3).

Behaviour of the cardiovascular system is effected by controls on heart's activity and on the blood vessels in different parallel-coupled circulatory beds exercised through the vagus and sympathetic nerves and the secretions of endocrine organs.   The aim of the sensory input emanating from the reflexogenic areas of the cardiovascular system is to produce reflexes which maintain the behaviour of the system expressed in terms of volume of blood flow and perfusion pressure in these circulatory beds as required under conditions of outward inactivity or rest.   Existing evidence shows that the neuronal substratum supplied by the reticular formation in the spinal cord and brainstem has got sufficient versatility to regulate the performance of these reflexes.   Conditions of rest and inactivity are almost similar to what is obtained in a stable anaesthetized preparation.   Literature is full of such preparations in which closed loops of the stabilizing reflexes have been experimentally opened to see the effect of artificially created behaviour disturbances on the activity of receptors, CNS centres and effectors, essentially substantiating this concept.

Sensory input from receptor sites located in systems other than the cardiovascular, will operate at different levels of the central nervous heirarchy depending on the complexity of the response it is supposed to generate.   For example the cardiovascular mobilization which accompanies the musculoskeletal response employed in defence reaction at the site of an enemy is essentially the outcome of integrating mechanisms at the level of hypothalamic and limbic regions of brain.   Clearly, only rudiments of such behaviors are elicitable when these regions of CNS are excited in anaesthetized preparations.   Nevertheless, in the relative paucity of studies on conscious animals which is mainly due to the lack of efficient recording techniques in such animals, it will be profitable to analyse these responses in light of animal's total behaviour expected at that moment.

Evidence has been quoted in this article for the presence of at least three pathways which can possibly be used for the mobilization of cardiovascular activities : (1) A direct corticospinal pathway traversing through the medullary pyramids, (2) A cortico-hypothalamotectal pathway bypassing the classical bulbar cardiovascular centres, and (3) the pathway involving the so called cardiovascular centres of the bulbar reticular formation.   It cannot yet be said if all the three pathways participate in stabilizing the system's behaviour.

Perhaps mediation of the stabilizing reflexes is mainly the concern of the pathways involving bulbar and brainstem reticular formation.   Feedback information for continuation in appropriate grading or for cessation of the mobilization activity, it may be logical to speculate, would come from the same type of receptors which initiated the process of mobilization. Knowledge about the mechanisms which integrate the activity of 'cardiovascular neurones' with the neuronal activity concerned with other systems so as to elaborate the total behaviour of the body in any one situation is just rudimentary to say the least.

At the level of bulbar and brainstem reticular formation, however, there is a huge overlap of sensory information from a multitude of receptors of visceral as well as somatic origin. It is possible therefore that the reference level for the cardiovascular homeostasis is a function not merely of feedbacks from the cardiovascular areas but may also be effectively influenced by the sensory inputs from other systems.

Lastly, though the conceptual model of cardiovascular regulation presented in figure 3 is derived from the existing experimental evidence, a review of scientific literature will bring to light a large number of unfilled gaps in this concept which are not mentioned in this article. In that case an important purpose of this review will be served. Besides, it is this author's opinion that the concept given in this model is an important step towards the understanding of cardiovascular regulation in light of the total body function which, we do not have to speculate, is to survive.

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