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REVIEW ARTICLE

REVIEW OF PROF. B.K. ANAND'S SCIENTIFIC STUDY : FIFTY YEARS FOLLOWING HIS DISCOVERY OF FEEDING CENTRE

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Abstract : Prof. BK Anand the living legend, is the founder of modern neurophysiology in India. His career spanned an era that marks the beginning of Brain Research in India. His contributions to understanding of brain functions began with the epoch making discovery of lateral hypothalamic area as the 'feeding center'. Subsequently it encompasses a wider range of studies from elucidation of the intricate mechanisms underlying ingestive behaviour to hypothalamic regulation of cardiovascular, respiratory, gastrointestinal activity and regulation of various physiological functions by limbic system. The following review gives an account of the contributions made by Prof Anand and his colleagues during twenty five years of his illustrious career. The publications resulted from his studies has not only stood as a testimony to understanding of the neural control of ingestive behaviour and limbic functions but also have been a sources of a great interest to those who pursue knowledge in this field.

Key words : feeding centre lateral hypothalamic area limbic system yoga

INTRODUCTION

When asked to write an account of the work of Prof. BK Anand on the eve of 'Fifty years of discovery of feeding center', my response was to say yes immediately. Though I still enjoy the continued teaching of Prof Anand which he does without respite my realisation about his contribution to neuroscience began when I was keenly referring his studies while studying neuronal plasticity of ventromedial hypothalmic neurons under an ERATO (a national programme of Japan) project. I had the opportunity to come in close contact with him when he was invited by Prof. Masao Ito along with other living legends in Neuroscience to adore the opening ceremony of Fourth IBRO World Congress of Neuroscience in Kyoto in 1995. His remarkable career in neurophysiology spanning a period of twenty five years, stands as a monument of unstinting efforts to unravel the mystery of hypothalamus and

limbic system underlying behaviour. During this exceptionally productive career many contributions were made not only to understand neural mechanism underlying ingestive behaviour but also hypothalamic regulation of cardiovascular, respiratory, gastrointestinal activities and regulation of various physiological functions by limbic system. The much existing knowledge of neural control of ingestive behaviour to day; even the sensational discovery of new hypothalamic peptide 'orexin' finds a root in the resulting publications of Prof Anand. The review described below gives an account of the contributions made by Prof. Anand and his illustrious colleagues in the field of brain research in India.

Dr. Anand joined as Professor of Physiology at the Lady Hardinge Medical College, New Delhi, in 1949. Although he had worked as a junior and middle level teacher in Physiology since 1943, all this time he had not undertaken any research worth the name: his time being mostly devoted to teaching and besides there being no facilities and infrastructure to do research.

In 1950, he was awarded Post-Doctoral Training Fellowship by the Rockefeller Foundation for one year. As he had been personally interested to understand the functions of the Higher Nervous System, he decided to go for such training in the Department of Physiology of Yale University School of Medicine. The department was then headed by Prof J.F. Fulton, who was considered to be one of the top most neurophysiologists of the world at that time. Under his personal interest in the functioning of the various regions of the higher levels of the central nervous system, the Department had various sections and research workers studying these by using different experimental techniques.

While going there, the main objective Dr Anand had, was to learn these various experimental techniques, which will enable him to set up a neurophysiology laboratory, on return to India. However, as luck would have it, while studying the use of stereotaxic techniques, he discovered the presence of two opposing mechanisms in the hypothalamus regulating feeding behaviour, which at that time was considered to be an epoch making discovery. Till that time other workers had shown that ablation of the medial hypothalamic area of median eminence resulted in overeating leading to obesity in rats for which mechanism, no concrete suggestion was available at that moment. Dr. Anand while confirming this also demonstrated that ablation of the lateral hypothalamic area in the same region produced the opposite effect of complete "Aphagia". With further experimental evidence he designated the lateral hypothalamic area as the "Feeding Center", providing urge to eat and the medial area as the "Satiety Center" producing satiation.

So his stay of one year at the Yale was devoted not only studying the different investigative experimental techniques but also sometime on further studying the feeding behaviour.

On return to India in 1952, he seriously devoted his time to undertake various types of research. He could start the work immediately on returns, as he was able to

bring with him from USA a stereotaxic apparatus, a stimulator, an ablating apparatus and a single beam oscilloscope with its pre-amplifier.

A number of research studies and projects in the field of Neurophysiology were undertaken at first during Dr Anand's stay at the Lady Hardinge Medical College and later on at the All India Institute of Medical Sciences, New Delhi. In addition to the institutional facilities and grants, this research was supported by the establishment of "Neurophysiology Research Unit" of the Indian Council of Medical Research. Thus a 'School of Neurophysiology' probably the first of its kind in India was started, where studies were undertaken by the introduction of new experimental techniques with the objectives of study of the "Brain and Behaviour" in India. The techniques used, included the stereotaxic placement of electrodes for making local electrolytic lesions, for electrical stimulation and for recording of depth EEG, evoked potentials, and single unit potentials with microelectrodes. These also permitted the use of unanaesthetised and freely moving animals for behavioural experiments. Using these techniques the hypothalamic and limbic systems were investigated to understand their roles in the `homeostatic' regulatory mechanisms of visceral and behavioural functions. Naturally, in these studies priority was attached to understanding in more details the new physiological mechanism regulating the 'feeding behaviour'. A large number of post-graduates, research scholars and colleagues were trained in this School, some of who later on became leading contributors to neurophysiology in the country. Some of Dr Anand's most productive colleagues included especially Sheel Dua Sharma, G. S. Chinna, K. N. Sharma, S. K. Manchanda, Usha Nayar and T. Desiraju. Prof. Baldev Singh participated in all of the laboratory research. So the credit for the research studies conducted, deserved in this write up is in the words of Dr Anand, *"not of me alone, but is to be equally shared with my other colleagues"*.

A reader may point out two deficiencies in this write up. Firstly, that there were various similar studies being, carried out during that period at various centres in other countries also and there is no mention of them in this. Secondly, many other studies have been carried out on these mechanisms even after 1973 with experimental techniques some confirming the conclusions given here, while some others providing a different concept of these functions. Here is quoted an often repeated statement of Dr Anand that, *"Observations made from any experiment are never wrong, it is the conclusions drawn from the same which may change"*. Anyway, these omissions have been intentional as the whole objective of this write up was to highlight only the studies carried out by Dr Anand and his colleagues, in his laboratories under his guidance and direction.

RESEARCH

As stated earlier Dr Anand's interest and career in research began only when he went for training in the discipline of Neurophysiology to Yale University in USA in the year 1950. His year's stay there was utilised in carrying out a small project leading to the discovery of the presence of

Feeding" and "Satiety" centres in the hypothalamus. In addition he devoted many time in mostly learning the various experimental techniques employed for the study of CNS. This training allowed him to use some of these techniques and experimental procedures for the valid research studies undertaken by him and his colleagues on his return to India.

Some of the more important research from Dr Anand's laboratory is summarised as follow:

During a period of some 20 years, they studied the functional importance of those regions of the brain, collectively designated as the "limbic system". It is a system that regulates various autonomic, visceral, endocrine and behavioural functions of the individual, and thereby maintains normal "homeostatic" conditions in the body including the constancy of the "milieu interiuer" (1-7). Keeping this in view, the limbic system has also been designated as the "visceral brain". The hypothalamus, being the effector organ of this system, came to be gradual recognition of the functional importance of those areas in the brain which subserve autonomic functions, because they form the structural background, not only of emotional expression, but also of effective and motivated behaviour in the broadest sense. This recognition can be considered as a landmark in the history of medical science.

Although Dr Anand's Research Unit have analyzed various patterns of regulation from the Limbic System of the brain and the maintenance of homeostatic conditions in the body, it has concentrated its interest on the regulation of one such function i.e. feeding bevaviour, which is vital, because it maintains energy balance in the body.

(1) NERVOUS REGULATION OF FEEDING BEHAVIOUR

Innate behaviour of feeding is genetically fixed and is characteristic of the species. The 'motivated' behaviour of feeding depends upon the opposed 'drives' of hunger and satiation, which are elicited and reduced directly by changes in the internal environment and are thus "homeostatic" in nature (8). Most basic motivational forces on drives depend upon central nervous regulation state; this is true also of feeding behaviour (9).

(i) Maintenance of Energy Balance

Energy balance is brought about by adjustment of four important variables; food intake, stored energy, work, and heat production. All these variables are controlled by central nervous mechanisms similar to those that regulate other visceral and endocrinal activities, so as to achieve constancy of the milieu interieur (10,11).

In maintaining a proper equilibrium, food intake has to be integrated with the other three variables, i.e. work done, heat produced, and energy stored. Ordinarily, the energy stored in the fat depots of the body does not change appreciably over long periods, and body temperature is maintained at normal levels by adjusting the heat loss to heat production. In such situations food intake (energy intake) is adjusted mainly to the metabolic activity of the body (energy utilisation) which results in work and heat

production. Therefore, it is essential that the central nervous mechanisms that regulate food intake should obtain precise information about the other three variables, which are also controlled through adjoining areas in the central nervous system. Information about both energy intake and energy utilisation is provided to the hypothalamic mechanisms related to feeding. The hypothalamus also provides an important regulatory mechanism adjusting heat loss from the body to heat production, the latter being further dependent on energy utilisation resulting in work.

It is thus apparent that the hypothalamic mechanisms, which regulate food intake, play the most important role in maintaining energy balance. Their activity is influenced through feedback of information about energy utilisation, and is further modulated through needs of the body for maintenance of body temperature.

If the regulatory mechanisms are able to integrate all of these activities, food intake will be precisely balanced with work done and heat produced, and so there will not be either a surplus work and deficiency of energy for extra storage depletion of body stores. Thus, body weight may be maintained at constant levels over long period of time. Cowgil has nicely summed up this situation by stating that under a variety of circumstances, and on a variety of diets, "animals eat for calories".

(ii) Central Nervous Mechanisms Related to Feeding

Hunger, appetite and satiety phenomena associated with food intake, were previously regarded as problems in the physiology of digestion. However, a large number of experimental studies have brought out that these are mostly dependent on the functional activity of the central nervous system.

Whereas early during the present century hunger was scheduled to have a "peripheral" origin, dependent upon rhythmic gastric hunger contractions, evidence gradually accumulated against this "peripheral" theory. For example, feeding persists even after the operation on the stomach, including nearly complete removal of the organ. Similarly, denervation of the stomach in human subjects does not alter the appetite.

(a) Hypothalamic Mechanisms

Attention began to focus on the hypothalamic region as a possible regulator of food intake when Hetherington and Ranson in 1940 were able to induce obesity in rats by bilateral hypothalamic lesions in the region of the ventromedial nuclei. Later on other authors confirmed that such obesity is due to "hyperphagia" (overeating) and not due to any disturbance of metabolism per se.

As detailed earlier, during Dr Anand's stay at Yale University in 1951 in Brobeck's Laboratory, he demonstrated that, while bilateral lesions in rats in the ventromedial regions produced "hyperphagia", lesions in lateral hypothalamus lead to complete `aphagia' and death of the animal due to starvation (12, 13). Further, he found that medial hypothalamic lesions produced hyperphagia only when the LHA was intact.

If the lateral areas are bilaterally lesioned following medial lesions, hyperphagia is immediately changed to complete aphagia. If medial lesions follow lateral lesions, aphagia is still maintained. The lateral hypothalamic area, bilateral destruction of which results in aphagia, is a discretely located, well-defined, very small region, in the same rostro-caudal plane as the ventromedial nucleus. If this region is intact even on only one side complete aphagia does not result. Lesions in any other region of the hypothalamus do not produce any quantitative changes in food intake. He also observed that lesions between the medial site and the lateral site also result in hyperphagia, indicating lateral projections from medial area. Because these results obtained in rats were later confirmed in many other species of animals (14-18), they established the role of hypothalamus in the regulation of food intake. Stimulation of these hypothalamic regions in unanaesthetised animals, through chronically implanted electrodes, produces effects on food intake, which are opposite to those produced by lesions (19,20). When stimulation of the LHA was initiated, the animal would start eating immediately, irrespective of whether it had been fasted or previously fed. Similarly initiation of stimulation of the medial area stopped eating even when the animals were hungry and eating. These particular behavioural changes lasted only during the period of stimulation. But if stimulation of the LHA was carried out for a longer period (about one hour or so), then the total food intake for that day remained higher (19, 20).

All these studies have provided evidence that there are two opposing mechanisms in the hypothalamus that regulate food intake, namely a mechanism in the lateral region of the hypothalamus which initiates feeding and is therefore designated as the "feeding centre", and one in the medial part of the hypothalamus which brings about satiety after a meal has been taken and is thus termed the "satiety centre". The satiety centre is connected by lateral projections to the feeding centre (21). The feeding centre has the basic hunger mechanism which provides `drive' to eat and thus results in motivated feeding behaviour, and its activity is inhibited when the satiety centre is activated after a meal has been taken.

(b) Brain-stem Mechanisms

Feeding behaviour is based on feeding reflexes operating through the spinal cord and brain stem levels. These reflexes are activated by sensory stimuli that make the animal aware of the presence of food. These reflexes are facilitated by the feeding centre and inhibited from the satiety centre by way of the projection of descending influences from the hypothalamic centres onto the brain-stem mechanisms (22,29). Thus, when the feeding centre is active it sends descending influences, which facilitate the feeding reflexes. In this state of hunger, the animal starts eating when it becomes aware of the presence of food through various peripheral sensations. On the other hand, when the satiety centre has been activated (by mechanisms described below), it inhibits the feeding centre through lateral projections and thus eliminates the hunger state. It also inhibits the feeding reflexes. This produces the state of satiation during which the animal will not eat even when it is aware of the presence of

food. In case the brain-stem mechanisms are separated from the hypothalamic and other cerebral regulations, as in a decerebrate animal, the feeding reflexes are still possible. When such animals are fed purring is also noted, suggesting a state of satiation.

(c) Higher Cortical Mechanisms

Although the hypothalamic mechanisms provide the basic states of hunger and satiation, these are further modulated and influenced from the limbic system of the brain, which modifies food intake through a discriminative selective mechanism, that is through a "discriminative appetite" (23-27). Lesions of the limbic system produce only small and temporary changes in the amount of food intake. On the other hand such lesions result in loss of animals power to discriminate between edible and non-edible objects. Such monkeys will put anything edible or non-edible, into their mouth. In fact monkeys which are ordinarily vegetarian, can be fed on meat after such limbic lesions. Conversely, stimulation of these areas produces "eating automatism" without any quantitative change in food intake.

(d) Necortical regions

Neocortical regions also modify the functional activities of these regulatory mechanisms, by way of habit formations and conditioning (14,28). This may explain why inspite of the hypothalamic centres providing subjective states of hunger or satiety, human beings, and animals with higher encephalisation can alter their feeding behaviour in a manner not extremely consonant with the subjective state.

(iii) Regulation of Activities of Central Nervous Mechanisms Related to Feeding (Signals for the Regulating System).

Adjustment of food intake to energy expenditure is a hypothalamic function. As a result of feeding, certain changes are produced in the body, which directly, or indirectly, stimulate the activity of the hypothalamic satiety centre (and possibly also the higher cerebral regions). The satiety centre, by suppressing the activity of the feeding centre, brings about the state of "satiation". Subsequently, when the food eaten is disposed of through conversion to heat, work, or some form of stored energy, activation of the satiety centre is removed and the feeding centre becomes more active, thus leading again to the state of "hunger". According to this concept, satiety is regulated rather than hunger. This conclusion is in keeping with the observation that, after destruction of the satiety centre, the rate of feeding in the feeding period is not much affected, but the animals no longer show normal satiety periods. Moreover, the observed constancy of body weight and energy reserves, inspite of great variations in energy expenditure, shows that there are regulatory mechanisms that adjust food intake to energy expenditure.

This regulation can be subdivided into two components working within biometrically defined limits. The first and possibly the most important is the short-term regulation, the other, operating over a longer period, may correct the errors of the short-term regulation.

SHORT TERM REGULATION

Various suggestions have been put forward regarding the nature of the change, or changes, produced as a result of feeding, which signal to the regulating system that further feeding should be stopped. The principal mechanisms for short-term regulation include, first of all, nervous afferents coming from the gastrointestinal tract, which provide information about the acts of eating, swallowing, and the presence of food in the stomach and intestines. Later on, changes in the internal environment, produced as a result of eating, provide information about energy balance. Because considerable delay is involved before precise information is supplied through the latter channel, sensory information from the alimentary tract plays a role as adjustment of feeding behaviour, till the changes introduced in the milieu interiuer.

(a) Signals During Intake of Meals

There is some suggestive evidence that a certain amount of motoring during the passage of food through the oropharyngeal region affect the satiety centre as demonstrated by electroencephalographic recordings from these centres during the act of swallowing (30). With the distension of stomach brought about by intake of food, direct activation of the satiety centre, with a simultaneous inhibition of the feeding centre, occurs. This was shown experimentally by distending the stomach through inflation of intragastric baloons. This resulted in a significant increase in the electrical activity of the satiety centre, recorded electroencephalographically through implanted electrodes. Also, when the activity of a single neuron in the hypothalamic centres was recorded through stereotaxically guided microelectrodes, distension of the stomach was observed to increase firing rate of satiety neurons and simultaneously to inhibit the neuronal discharge from the feeding centre (31). These results followed specifically by the distension only of the stomach, as distension of the adjoining peritoneal cavity with balloons did not produce this response. Information about distension of the stomach is passed on to the hypothalamic centres through gastric branches of vagus as stimulation of these neurons duplicated the hypothalamic effects of gastric distension. On the other hand, when the gastric branches of the vagus were cut, gastric distension no longer activated the satiety neurons. This effect is produced only through the activation of gastric branches of vagus and not through projections through lower central nervous regions, as this is still maintained even after cutting through the brain stem (decerebration).

Normal gastric hunger contractions, on the other hand, do not produce any changes in the electrical activity of the hypothalamic centres (32). But if the satiety centre is activated by some other means, this leads to inhibition of the gastric hunger contractions. This means that when the stomach is empty and the satiety centre is not active, gastric hunger contractions merely add 'objective' feeling of hunger to the 'subjective' feeling produced through activation of the feeding centre.

After food passes on from the stomach into the intestine, further sensory information is provided for the activation

of satiety centre through the mesenteric nerves as their stimulation evokes electrical potentials in the region of the satiety centre (33, 34). The activation of mesenteric afferents is possibly produced through products of digestion present in the small intestine, as there is experimental evidence suggesting the presence of chemoreceptors in the intestinal mucosa, which are sensitive to products of digestion. This sensory information bridges the time lag (i) between the passage of food from the stomach into intestine and its digestion there, and (ii) changes in the milieu interieur result from absorption of products of digestion.

(b) Between Meal Information to the Hypothalamic Feeding Centres

Absorption of the products of digestion causes changes in the internal environment (milieu interiuer) which then provide specific information to the hypothalmic feeding centres (35). The ingestion of even a single meal is accompanied by a number of changes in the body, both chemical and thermal that alone or together may act as signals to the nervous regulating mechanisms. Available experimental evidences, however, suggest that such a regulation is mainly 'chemostatic' especially 'glucostatic', rather than 'thermostatic'.

(i) Chemosensitive mechanisms related to feeding

The hypothalamic centres contain sensitive neurons capable of responding to chemical qualities (signals) of the circulating blood (36-38). Among the important signals proposed are availability or utilisation of glucose, concentration of amino acids and water concentration as a result of shifts of water among the several compartments of the body.

(ii) Glucostatic or glucosensitive mechanisms

Mayer in 1953 postulated that in the hypothalamus there are "glucoreceptors" sensitive to blood glucose in the measure that they can utilize it. Dr Anand's group conducted a large number of experimental studies to test this hypothesis. These studies provided conclusive evidence for a direct relationship between the electrical activity of cells in the hypothalamic satiety and feeding centres, and the levels of glucose utilisation worked out from the arteriovenous glucose differences, thus firmly establishing the mechanisms of "glucostatic" regulation. Electroencephalographic activity recorded in unanaesthetized animals through depth electrodes chronically implanted in these centres, showed that the activity of satiety centre was significantly and selectively affected by changes in the blood sugar level (37,39). In another set of experiments where electroencephalographic activity of these regions was recorded in animals at different intervals after normal feeding, it was shown that the activity of the satiety and feeding centres changes in a reciprocal manner depending upon the state of hunger or satiety, and also that this activity correlates with the arterio-venous glucose differences (40).

Electrical activity of single neurons in hypothalamic satiety and feeding centres was also recorded before and after exposure to intravenous infusions of glucose, or insulin, or combinations of both (41). In fasted animals the activity of satiety centre

neurons was slower than that obtained from feeding centre neurons. Frequency of spikes recorded from satiety neurons increased and that of feeding centre neurons decreased significantly after glucose was given intravenously. Spike activity was specific to the satiety and feeding centre neurons as spike activity of neurons in adjoining hypothalamus and cerebral regions did not show any change. The spike activity of hypothalamic centres was also more closely related to the magnitude of arteriovenous glucose differences (levels of glucose utilisation in the body), rather than to the levels of arterial blood glucose per se. It was also interesting to observe that immediately after infusion of insulin,for the first few minutes the frequency of spikes of the satiety neurons was increased before a decrease in their activities was registered. This was due to an initial increase in glucose utilisation produced by insulin injection followed by hypoglycaemia and decrease in glucose utilisation. Unit activities recorded of these neurons in response to production of glucopenia, therefore, resulted in changes in frequencies opposite to this following glucose infusion (42).

The dependence of the activity of satiety centre neurons on the levels of glucose utilisation in the body has been further confirmed by the experimental use of chemical preparations that influence glucose utilisation. For example, after the injection of 2-Deoxy-D-glucose (which decreases glucose utilisation and simultaneously raises blood glucose level to some extent) the firing rate of satiety neurons were decreased and those of feeding neurons were increased (43). This conclusively suggests that it is the level of glucose utilisation (44), and not the level of arterial blood glucose, which activates the hypothalamic centres. After administration of pharmacological preparations like cyproheptadine, which increases appetite and causes a decrease in A-V glucose differences (glucose utilisation) the activity of the satiety area was again decreased and that of feeding area increased (45). Studies with other pharmacological preparations, which depress appetite, such as fenfluramine (46-47), and nialamide (48) suggest that they actively increase glucose utilisation in the body. Recording from these centres further indicated that reserpine, rastinon and preludin, also produced comparable results (49,50).

Respiration studies were also conducted in Warburg manometers on tiny slices of hypothalamus containing the satiety and feeding regions, obtained from hungry and fed animals. In fed (satiated) states both glucose and oxygen uptake were higher in the satiety region than in the feeding region, whereas conversely, during fasting (hungry) states both glucose and oxygen uptake were higher in the feeding centre region (51).

Further it was reported that single unit recordings from the hypothalamic centres after mid collicular transverse cuts through the brain stem (52), the changes in the unit activities of the satiety and feeding centre neurons in response to glucose and insulin infusions still could be reproduced. This conclusively proves that changes in the level of glucose utilisation act directly on nerve cells of the brain and not though any chemosensitive mechanisms which may be present at the periphery, say in the liver.

The different kind of experimental evidence presented above all clearly indicate that there is some kind of thermosensitive mechanism in the satiety centre. It increases the activity of these neurons when increased glucose utilisation in the body results from absorption of digested food. These results also further confirm the hypothesis that when energy intake (food intake) has to be adjusted to caloric requirement the best information about caloric balance in the body at any time is provided by the level of glucose utilisation, glucose being the ready supplier of energy.

(iii) Lipostatic Mechanism

Kennedy suggested that the hypothalamic mechanisms are concerned only in the prevention of an overall surplus of energy intake per expenditure which would cause deposition of fat in depots. He believed that this lipostasis is achieved through sensitivity of hypothalamic centres to varying concentrations of circulating metabolites (unspecified) related to the size of bodily reserves of fat. Electrophysiological studies by Dr Anand's group, however, did not demonstrate any sensitivity of hypothalamic mechanisms to any metabolite other than glucose, nor to any other chemical changes occurring in the blood.

(iv) Mechanisms sensitive to amino acids

A reciprocal relationship has been suggested between serum amino acid concentrations and appetite. Electrophysiological studies by Dr Anand's group again did not provide any evidence for the specific sensitivity of the central nervous mechanisms to amino acids (53).

(v) Mechanisms sensitive to water concentration

The hypothalamic mechanisms (regions) regulating food intake (hunger) and water intake (thirst) have been experimentally shown to be distinct from each other even though anatomically they are situated adjacent to each other (54,55). Nevertheless the regulation of food intake is correlated with the regulation of water exchange. After feeding there is movement of fluid out of the rest of the body into the digestive tract. It has been suggested that this temporary withdrawal of liquid from some selected tissues may be one of the factors causing satiety. It has also been suggested that, in as much as shifts of water that occur during digestion are similar shifts that are associated with regulation of body temperature, body activity, storage of protein and to some extent, fat synthesis. The water shifting may serve as a common denominator necessary for interrelationships in the control of feeding, drinking, body temperature, body activity, body size, and energy intake. However electrophysiological studies have not confirmed this correlation.

(vi) Thermosensitive mechanisms related to feeding

Brobeck proposed the concept of a 'thermostatic' (thermosensitive) regulation of food intake, by suggesting that the animals eat to keep warm, and stop eating to prevent hyperthermia. It was suggested that regulation is achieved through the agency of small changes in body temperature produced by the "specific dynamic action" (SDA) of the food eaten, and that this extra heat possibly signals the

hypothalamic mechanisms. Dr Anand recorded single neuron spike activity from the satiety and feeding centres and exposed them to localised heating of the order of 0.5 –10 °C, through implanted thermodes. They found that spontaneous activity of neurons in these centres was not affected in any way by small local changes of temperature (56). However as shown by others direct cooling of anterior hypothalamus resulted in eating, whereas warming the same area inhibited eating. Thus it appears that whatever relationship may exist between the SDA of the ration and the amount of food eaten, it is probably operating indirectly through, the anterior hypothalamic temperature sensitive mechanisms. This demonstrates that there is integration between the thermosensitive anterior hypothalamic region and the satiety and feeding centres in the medial hypothalamus.

It thus appears that the hypothalamic mechanisms related to feeding are ordinarily directly influenced through expenditure (energy balance) only through changes in the level of glucose utilisation. In those circumstances in which this may tend to upset the temperature regulation, however, the heat-regulating centres would also influence the nervous mechanisms for feeding (energy intake).

LONG-TERM REGULATION

A long-term regulation corrects errors introduced over a period of time through the short-term mechanisms. That such errors occur, is a common observation. Very often, especially in higher mammals and human beings, food intake does not exactly correspond to energy output, and this changes the reserve stores of energy in the body. At the same time, it is well known that most adult men and animals maintain their body weight at the same level, sometimes for years. This shows that long-term regulation must also be playing an important and precise role. Very little experimental work is available to suggest how such a long-term regulation functions. It must be based ultimately on some information provided to the nervous mechanisms from the energy stores present within the body, presumably the fat depots. Some experimental evidence has been provided that, other things being equal, animals may mobilise each day a quantity of fat dependent on and increasing with, the total fat content of the body.

In conclusion, information about both energy intake and energy utilisation is provided to the hypothalamic centres related to feeding. During the intake of meals, signals go up to the hypothalamic centres through the afferent nerves from the gastrointestinal tract. Food absorption then further suppresses feeding by activating the satiety mechanism in response to chemical changes produced in the body, mostly increased glucose utilisation (57). It may be that increased heat production in response to SDA, and changes in the amino acid and fatty acid levels of the blood, also some how triggers the satiety mechanism, although direct experimental evidence in support of these is lacking. When these changes gradually disappear, the animal is hungry again.

Possibly some regulatory mechanisms are operating on a long-term basis also to keep the body weight constant over long

periods. These mechanisms come into operation whenever stored energy tends to change.

Again, in those situations in which body temperature tends to change, food intake is appropriately adjusted so that the body temperature is kept normal. This may create situations in which demands for increased energy intake may be sacrificed for prevention of hyperthermia. For example, physical exercise in a hot environment may not increase food intake to the same extent as such exercise in a cold environment. This calls for integration of the central mechanisms regulating body temperature and those regulating food intake.

Finally, it has been stressed that, in spite of the requirements of food intake in response to energy expenditure, feeding is very closely correlated with water exchanges in the body.

It thus appears that the central nervous mechanisms related to feeding are influenced, not only by the sensory afferents from the alimentary canal, and by chemical and thermal changes produced in the body as a result of eating, but also by many other external and internal environmental changes that are integrated with other regulating mechanisms in maintaining the homeostasis of the body. These are further influenced from higher mechanisms.

As long as all these mechanisms are in a state of equilibrium, the energy balance in the body is maintained. On the other hand, when this equilibrium is disturbed, either by involvement of nervous mechanisms, or by metabolic changes of the body, or even under the effect of psychological stresses (higher nervous modulating influences), this may upset the energy balance and so lead to conditions of obesity or cachexia.

(e) *Clinical applications:* These studies also provide basic scientific evidence about mechanisms for controlling and treating clinical "Obesity" which is associated with many, especially cardiovascular disturbances. These appear to have also provided clues for understanding the causative factors for "anorexia nervosa" (58,59). Further, changes in food intake and body weight in pathological and endocrine abnormalities can now be attributed to by hypothalamic involvement.

(2) HIGHER NERVOUS REGULATION OF AUTONOMIC AND VISCERAL ACTIVITIES

During recent years many experimental data have accumulated on the involvement of various central nervous structures in the regulation of visceral activities, which thereby influence the "homeostasis" of the body. Information about the levels of the central nervous system concerned in such regulation has been derived from experiments in which different parts of the central nervous system have been either destroyed or stimulated. From these results a functional analysis can be made, and complex regulatory mechanisms can be localised.

A very large number of early studies have shown that the regulation of various visceral activities, through autonomic outflows, depends upon the completion of

reflex arcs in the spinal cord and brain-stem. In addition to segmental and inter-segmental reflexes operating through the spinal levels, there are "centres" in brain stem which integrate sensory information and ultimately direct it towards the adjustments of certain visceral activities by way of autonomic outflows.

However, reflex mechanisms operating through the brain stem and spinal cord do not, on their own, provide efficient regulation for adjustment of homeostasis. This was demonstrated by the discovery that completely decerebrate preparations, in which all connections of the brain-stem and spinal cord with the rest of the brain are severed, are able to adjust reflexely various visceral activities per se, but cannot integrate the functioning of different visceral systems so as to maintain homoeostatic conditions under diverse environmental situations. It has been further shown that when the connections of hypothalamus with the brain stem and hypophysis are left intact while its connections with the rest of the brain are severed, homeostatic mechanisms can be maintained under basal conditions. However, such preparations also fail to maintain homeostatic conditions in certain stressful situation. These results indicate that the hypothalamus not only regulates and adjusts the activities of different visceral systems, but also integrates these with each other, the sum total of all these integrated responses preserving body homeostasis in basal conditions. Hypothalamus was thus designated as the "Head Ganglion" of the autonomic system. Further, when the connections of the limbic system of brain with the hypothalamus and the rest of brain stem and spinal cord are left intact and only neocortical regions are removed, the animal can adjust all of its visceral systems for the efficient maintenance of homeostasis even in all diverse situations. Thus the regulation of visceral activities is functionally organised at different levels of the central nervous system.

(i) Regulation of Visceral Activities by the Hypothalamus and the Limbic System

Autonomic reflexes mediated from the spinal cord and brain stem levels and also the organisation of the visceral integrating centres in the brain stem have been thoroughly studied for many years. However, experiments demonstrating that the hypothalamus and limbic system take part in autonomic regulation are more recent.

Experimental stimulation of hypothalamus mostly demonstrates a pattern of localisation for producing sympathetic and parasympathetic effects on the activities of different viscera. The anterior and medial hypothalamic regions usually give parasympathetic responses, while the posterior and lateral areas generally produce sympathetic responses. These responses involve almost all visceral systems of the body, including cardiovascular, respiratory, gastrointestinal, and excretory systems, and general metabolism. Experimental studies of the limbic system, by contrast, provide a picture of 'unspecificity' of such responses. Either stimulation or ablation of various limbic structures may be followed by changes in the various visceral systems, but in the

different limbic structures there is no specific localisation for the different functions. In this respect the "specific" localisation in the hypothalamus is somewhat similar to what is observed in the motor areas of neocortex and "nonspecific localisation" in the limbic system is similar to responses from the necortical association areas, for somatic activities.

As stated earlier, a large number of scientific studies on these higher nervous mechanisms for regulation of autonomic and visceral activities have been conducted at many centres during the last 4-5 decades. Dr Anand's group has also carried out detailed studies for understanding these central nervous regulating mechanisms. Some of their more important observations are highlighted here (6,15,23,24,27,60).

(a) Regulation of cardiovascular activities

Experimental procedures applied to the hypothalamus and limbic structures gave rise to changes in heart rate, blood pressure, tone of peripheral blood vessels, and level of blood flow through different structures.

Hypothalamus

Stimulation of posterior and lateral regions of the hypothalamus produced rises in blood pressure and increase in heart rate, and occasionally, fibrillation of the heart. Stimulation of anterior and medial hypothalamic regions, including the preoptic and septal areas, on the other hand, resulted in fall of blood pressure and a slowing of heart rate (4,6). Either lesions or stimulation in the preoptic region and anterior hypothalamus sometimes results in pulmonary oedema.

It was also interesting to observe that after the injection of reserpine (a therapeutic substance, which lowers B.P.) the threshold for eliciting pressor responses from the posterior hypothalamic areas was raised while the threshold for eliciting depressor responses from the antero-medial regions was lowered (61). This suggests that, in addition to neuronal interaction and integration between the different hypothalamic regions, hypothalamic neurons producing different responses may have somewhat different metabolic parameters.

Limbic System

When various limbic structures were stimulated systematically in the unanaesthetised animals (4,6,61,62), it was observed that stimulation of frontal lobe structures usually produced a rise in blood pressure accompanied by peripheral vasoconstriction, whereas stimulation of limbic structures contained in the temporal lobe, including the head of caudate nucleus (60), usually resulted in a fall in blood pressure accompanied by peripheral vasodilatation. Changes in the heart rate, however, were quite variable. On the other hand, when the different limbic regions were stimulated in anaesthetised animals, stimulation of either frontal or temporal lobe structures resulted in a fall in blood pressure, although vasoconstriction or vasodilatation still occurred, respectively (62). This emphasises that studies on visceral responses are best made on unanaesthetised preparations.

Surgical lesions involving frontal lobe structures produced a small drop in blood pressure, while similar lesions affecting temporal lobe structures resulted in a slight rise in blood pressure. A relationship between the ontogenetic development of cardiac cavity and cerebrum has also been shown by studying responses in chick embryos.

(b) Regulation of Respiratory Activities

Experimental procedures involving the hypothalamus and the limbic system have also been shown to change the frequency and the depth of respiration.

Hypothalamus

Like cardiovascular effects, changes in respiratory activity are also observed in stimulation or ablation of any hypothalamic region (4,6). Posterior hypothalamic stimulation generally increased the rate of ventilation. Stimulation of the medial part of anterior hypothalamus decreased the rate and amplitude of respiration.

Most of the respiratory responses were accompanied by cardiovascular changes and may, therefore, represent a necessary interrelation in regulation of the functions of these two vital systems.

Limbic System

In unanaesthetised animals, stimulation of frontal lobe structures generally produced quickening of respiration, and stimulation of temporal lobe structures, including head of the caudate nucleus, resulted in inhibition of respiration, including apnea (4,60,62,63). However, following anesthesia either frontal or temporal lobe stimulations inhibited respiration (62). Excitation of carotid body influenced the neural regulation of respiration (65).

(c) Regulation of Gastro-Intestinal Activities

Stimulation or ablation of hypothalamus and limbic system produced all kinds of changes in the secretary activity and motility of the alimentary tract. Further, experimental involvement of hypothalamic and limbic structures invariably led to the production of petaechial haemorrhages in the mucous membrane of the alimentary tract and the presence of blood in the stools. Involvement of certain brain structures led to the production of acute haemorrhagic ulcers of various sizes.

Hypothalamus

Stimulation of anterior hypothalamus generally produced an increase in gastric secretion, tone, and motility, while that of posterior hypothalamus resulted in relaxation of the stomach, including its pyloric end, and diminution in its secretory activity (66). Intestinal and colonic motility was inhibited by stimulating anterior hypothalamus. Salivation and licking was also observed on hypothalamic stimulation. Stimulation of the hypothalamus also resulted in gastric ulceration (66) as did the production of hypothalamic lesion (67).

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Stimulation of different limbic structures resulted in changes in the motility and tone of different parts of alimentary tract, the

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Limbic System

Stimulation of different limbic structures resulted in changes in the motility and tone of different parts of alimentary tract, the

results being often variable (68). Such stimulation or ablations also led to significant changes in the gastric secretory activity. However, acute haemorrhagic ulcers were produced only on stimulation of the amygdaloid nuclei (69). Even stimulation of dorsomedial thalamus also changed gastric secretory activity (70).

These experimental observations seem to explain the hyperchlorhydria, and even peptic ulceration, that result from stressful situations in which limbic structures are involved.

(d) Regulation of Liver and Kidney Functions and changes in Blood Chemistry

Stimulation or ablation of either hypothalamus or limbic structures produced changes in the functioning of the liver, as demonstrated by changes in serum bilirubin, alkaline phosphatase, plasma proteins, and carbohydrate metabolism (4,6). Changes in liver blood flow were also observed after hypothalamic stimulation. The observation that lesions in the ventromedial hypothalamus of monkeys blocked the development of liver necrosis that results from the massive haemolysis produced by malarial parasites (71), suggests a relationship of this area with the blood circulation through the liver.

Similar experimental procedures applied to limbic structures also disturbed renal function, as shown by changes in urea clearance, glomerular filtration rate, and renal plasma flow (6).

They also observed that lesions or stimulation of hypothalamic and limbic areas often disturbed the chemical composition of the blood, producing variations in its glucose content (72-73), as well as its sodium, potassium, and plasma protein content (6,27). Not only was the total quantity of plasma proteins affected, there were also disturbances of albumin: globulin ratio. All such changes could be related, not only in the changed functional activity of liver, kidneys and other visceral organs, but also to changes in the endocrine secretions (as brought out later).

(e) Regulation of visceral activities by cerebellum

Although cerbellum is not a part of the limbic system, certain parts of it, especially the paleocerebellum, has to and fro connections with the limbic system as first shown by Dr Anand and his colleagues (74,75). Since neocerebellar structures which are connected with neocortex, influence somatic activities mediated through neocortex, it is reasonable to expect that the paleocerebellum influences visceral activities through the limbic system

Stimulation of paleocerebellum in anaesthetised animals usually produced a rise in blood pressure, an increase in heart rate and rise in urinary bladder pressure (76-78). If the same stimulation was repeated after giving an anaesthetic, the blood pressure fell and the respiratory activity decreased. Stimulation of paleocerebellum also resulted in movements of alimentary tract.

(3) HIGHER NERVOUS REGULATION OF ENDOCRINE ACTIVITIES

Hypothalamic connections with the anterior pituitary gland, through the portal

vessels, enable this region to regulate hypophyseal activities, which it does by elaborating releasing factors. These then regulate the secretion of the tropic hormones of the pituitary. They include adrenocorticotropic hormone (corticotropin ACTH), thyroid stimulating hormone (thyrotropin, TSH), and the gonadotropins (FSH, LH), and prolactin. In addition, the hypothalamus has direct neuronal connections with posterior pituitary gland, so that some hormones synthesised in hypothalamus, like the antiduiretic hormone (ADH), are released there.

Many studies by a number of workers have demonstrated that the hypothalamus regulates the secretion of tropic hormones of the pituitary gland. The limbic system might also be expected to influence the secretion of these tropic hormones through the hypothalamus, but such studies on the limbic system are relatively few and non-conclusive.

A number of studies were also conducted on these nervous regulatory mechanisms. Some of the important contributions in this field are reported here.

(i) Regulation of ACTH

Stimulation and ablation studies demonstrated that hypothalamus exercises dual control over the secretion of ACTH. Stimulation of the median eminence increases the secretory activity, whereas stimulation of the anterior hypothalamus decreases it (79,80).

(ii) Regulation of TSH

Similarly, the hypothalamus was shown to exercise a dual control over the secretion of TSH. Stimulation of the median eminence increases its secretion, and stimulation of the preoptic area and posterior mamillary region leads to inhibition of secretion (81-82).

(iii) Regulation of secretion of sex hormones and reproductive behaviour

(a) Ablation studies conducted on rats demonstrated that the median area of hypothalamus controls the oestrus cycle (83).

(b) Stimulation or ablation of this hypothalamic region in female monkeys established its control over ovulation and oestrogen secretion (84-86).

(c) In the rats and especially in monkeys, the involvement of hypothalamic region in regulating reproductive (sex) behaviour through gonadal hormones was established (87-90).

(d) Electroencephalographic and single neuron unit activity recorded from hypothalmic regions and from some limbic structures of sexually mature male monkeys, exposed to genital stimulation, demonstrated that the neural feed-back from the reproductive organs reaches mainly the preoptic area of the hypothalamus. When these experiments were repeated in sexually immature male monkeys, the electrical responses of the hypothalamic regions were not produced. However, after pretreatment of these immature monkeys with gonadal hormone (testosterone), genital stimulation then produced typical responses from the

preoptic area (91-93). These experiments demonstrated that the feedback by gonadal hormones also reaches the preoptic area, and further, that the priming of the nervous regulating mechanisms with gonadal hormones is essential before sensory nervous inputs into these regions can result in the sex (reproductive) behaviour.

(4) HIGHER NERVOUS REGULATION OF AFFECTIVE BEHAVIOUR

A large number of workers, as a result of studies originally restricted to ablations and later extended to stimulations, both electrical and chemical, have shown that many structures in the frontal and temporal regions of forebrain, along with the hypothalamus, take part in the elaboration of affective behaviour. The frontal and temporal lobe structures bring out an integration of affective behaviour and take part in the "feeling" of emotions, while the hypothalamus possibly creates an "exteriorisation" (expression) of emotions.

A large number of experimental studies on monkeys cats and rats were carried out by stimulating and lesioning the different limbic structures and then studying changes in the affective behaviour (2,26,54,63,84,94-96).

(i) Temporal Lobe

Restricted amygdala lesions, as well as surgical temporal lobectomies, generally made both monkeys and cats fearless, non-aggressive, and calm. These animals also showed loss of distinction between edible and non-edible objects and put even noxious objects into their mouth. Stimulation of amygdala, pyriform cortex, and hippocampal formation produced in a majority of animals a picture of appearing frightened and running away into a corner. Stimulation of temporal polar region, on the other hand, made the animals very irritable and violent. Lesions involving the head of caudate nucleus made the monkeys hypermotile. Surgical lesions of temporal lobes in monkeys produced a response of hypersexuality, with the male monkeys constantly trying to "mount", a female neighbour, or even a toy monkey.

(ii) Anterior Cingulate Gyurs

Restricted anterior cingulate lesions in both monkeys and cats mainly led to fearlessness and docility, and also made the animals hypermotile. Stimulation of this gyrus in cats made them vicious and violent, throwing some of them even into convulsions. Monkeys, after such stimulations, merely developed more irritable and angry behaviour, but did not develop typical rage reaction.

(iii) Posterior Orbital Gyrus

In some animals with lesions in this region, both hyperactivity and hypersexuality was produced. Stimulation of this region made both monkeys and cats very quiet.

The variability of the affective behaviour resulting form experimental involvements of the several component parts of the limbic system, suggest that possibly all these regions act together as one functional integrating unit and not as separate

entities. Their normal physiological functioning is responsible for the "normal" affective behaviour of the individual. Because of differences observed in animals of different species the direct application of these studies to human behaviour would have some limitations.

It has been suggested that more rostral parts of the limbic region may be responsible for "preservation of self" (feeding, drinking, searching, defence reaction), and more caudal parts may be responsible for "preservation of species" (Reproductive behaviour).

(5) NERVOUS INTEGRATING MECHANISMS FOR MAINTENANCE OF HOMEOSTASIS

One should recognise that observations made from a number of autonomic, endocrinal, and visceral responses obtained by experimental studies on the hypothalamus and limbic system may not give us a complete picture of how homeostatic conditions are maintained through nervous regulating mechanisms. These provide us however, with enough evidences to suggest that the pattern of regulation of our 'internal environment' is on lines similar to the pattern of nervous regulation of those somatic activities, which determine our behaviour in relation to 'external environment'. Sensory inputs from various internal organs form the basis of reflexes which are completed through spinal and brain-stem levels. The afferents ascend and have relay centres in the brain stem for "specific" reflex activities. Finally, most of these afferents project to the hypothalamus, and possibly some into limbic regions. The hypothalamus is like the motor area on the somatic side, in as much as it executes the different activities which ultimately regulate the autonomic outflows and thus modifies reflex activities mediated from the brain-stem and spinal levels. The secretion of hormones through the pituitary gland is also regulated. The hypothalamus is extensively interconnected with the various limbic structures and these regions, therefore, may serve functions of integration and modulation similar to those of the neocortical association areas. In addition to afferents coming from the visceral structures, any change in the internal environment (blood composition) also feeds back information into these nervous regulating mechanisms. The limbic structures, being also involved in the feeling and affect of emotional states and behaviour, further integrate visceral activities with the emotional states of the individual. All these integrations in the nervous system provide the complex mechanisms, which bring about the constancy of the 'milieu interieur' and thus maintain normal homeostasis. Any disorder involving these structures and mechanisms will lead to a disturbed condition of homeostasis.

(6) PHYSIOLOGICAL ADAPTATIONS AT HIGH ALTITUDE

With the invasion of our Northern Borders in 1962, national need arose for stationing a large number of our troops at high attitude positions. This required scientific investigations to be carried out on the mechanisms of physiological adaptations at various levels of high altitudes, with concomitant environmental exposures to hypoxia and cold. These studies have been

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mainly carried out by Medical Officers of Defence Services, with whom Dr Anand was associated in an advisory and consultant capacity. The results of these studies naturally belong to the Defence Services. They have published some of them.

Where the results involved adaptative mechanisms, Dr Anand has reported some of them (97-99).

(7) SOME SCIENTIFIC INVESTIGATIONS ON YOGIS

During the last 3 to 4 decades Yoga and Yogic practices have elicited worldwide interest, and have provided necessary impetus for scientific research to quite a few professional scientists. Dr Anand's group became interested in undertaking such studies from the early fifties, and were probably among the first few workers to undertake such scientific investigations. Their main interest has been to study effects of Yogic practices on the central nervous regulating mechanisms.

Although modern scientists feel least competent to interpret what Yoga really stands for, it seems that the physical Yogic practices mainly aim at achievement of positive bodily health, while meditative practices aim at influencing the mind and states of consciousness. In fact, it is essential first to "purify, ripen, and vitalise" the body through Pranayamas and Mudras, before undertaking Concentration, Meditation and Samadhi. By following physical Yogic disciplines the body develops positive physical fitness, whereas meditative practices, in addition, further improve bodily functions, including visceral functions, through their influence on the mind. There are thus three aspects of Yoga: such as Yoga and the Body, Yoga and the Mind, and Yoga and Consciousness. The study all these three in some respects was undertaken by Dr Anand's group.

(i) Yoga and the Body

Several investigations that describe the effects of various Yogic Kriyas that appeared from time to time from different centres, have provided conclusive positive evidence of the beneficial results of such Yogic exercises on the functioning of the muscular, cardiovascular, respiratory and gastrointestinal systems and other. Because in addition to the improvement in physical efficiency, such practices also produce a more relaxed mental state, this toning effect on the mind is the major argument of Yoga enthusiasts for preferring Yogic exercises to other forms of physical exercise. A large number of such studies were also conducted (107).

Some practitioners of Hath Yoga tend to develop their physical and muscular powers for performing certain extreme forms of physical feats. There have been reports that some Hath Yogis are capable of stopping the heart, even certified as such by some medical practitioners. This group' studies, however, indicated that they are not able to stop the heartbeats. But they do build up a high intrathoracic pressure (Valsalva), thus cutting out the venous return to the heart. Because of the drop in cardiac output the arterial pulse cannot be felt, and heart valves do not close and so mostly absence of heart sounds (100).

(ii) Yoga and the Mind

Sufficient scientific information has been provided to show that certain meditative practices result in improvement of various visceral functions, through their influence on the central nervous system.

(a) Autonomic Balance

Quite a few studies have indicated that yogic practices correct the equilibrium in the functioning of the sympathetic and parasympathetic nervous system. This is very beneficial to individuals who are in stressful situation, which results in sympathetic dominance, as meditative practices gradually diminish this sympathetic dominance and result in a better autonomic balance (100).

(b) Voluntary Control of Autonomic Functions

It has been claimed that some Raj Yogis, who have been meditating for prolonged periods of years, develop the capacity consciously and voluntarily to control their visceral functions, including their metabolic rate. Physiologists generally believe that this is not possible, as the neocortical regions (which consciously control our voluntary activities) cannot influence the functioning of limbic regions of brain, (which unconsciously influence visceral responses).

It has not been easy scientifically to substantiate such claims, since it is difficult to persuade Raj Yogis to agree to be investigated in the laboratory. However, in some rare studies, this group obtained scientific evidence to substantiate some such claims. Although, as stated earlier, complete voluntary stoppage of the heart was not confirmed by them in any Yogi, one Yogi could voluntarily produce slowing of heart, confirmed by ECG to be due to "complete heart block" (increased vagal tone); which would last for about 15 seconds at each attempt (101, 102).

A Yogi, whose metabolic activity was studied while he meditated in a completely sealed (metal) box, provided the most remarkable evidence. During meditation he could reduce his metabolic activity to a level some 40% below his expected basal metabolic rate (103).

(iii) Yoga and Consciousness

The question of consciousness has been exciting the interest of religious and learned men over centuries, and has now evoked tremendous interest among scientists. However, scientific studies so far have failed to provide any correlation between the activity of the brain and the different levels of consciousness. Raj Yogis claim that, by meditation, they can achieve a state of "super consciousness" or "Nirvana", when they are oblivious of the external world, but are very much conscious.

Electroencephalography (EEG) is the only important technique that has been used by scientists for determining changes in brain activity. Alpha activity is observed when the brain is conscious (awake) but is not exposed to strong peripheral stimuli, or involved in serious thinking. In such a state any exposure to peripheral sensory inputs results in desynchronised fast EEG activity, as a result of stronger activation of the reticular activating system, which to a great extent determines EEG patterns recorded from brain (104).

EEG investigations carried out by this group on very few Yogis, who had been meditating for much longer periods, have provided very interesting results. During meditation they showed a prominent alpha activity (indicating they were awake and conscious) and this alpha activity could not be desynchronized by exposing them to strong peripheral sensory inputs, such as photic, auditory, thermal and noxious (105). The peripheral stimuli, which one would expect to activate the activating reticular system, did not project to neocortex (conscious brain), meaning that the meditating yogis were oblivious to external stimuli.

As some suggestions had been made that Yoga may be a state of hypnosis, Dr. Anand's group carried out EEG studies on a hypnotised individual (106), and showed that the pattern was different.

(d) Yoga and Medical Sciences

The ultimate aim of both medical science and yogic practices is the attainment of optimum physical and mental health for the individual. Medical science tries to achieve this through preventive, curative and promotive means, although for a long time medical professionals have emphasised the curative aspect, with some attention to the preventive aspect. On the other hand in yogic practices the stress is mainly on the promotive aspects (108). Some Yogic methods are also prescribed for curative purposes, but these mainly produce their beneficial effects, if any, on the psychosomatic disorders.

Enclosed with this is a list of a large number of publications, emanating from all these studies. This write up only summarises the conclusion drawn. For details of these studies one has to read the publications referred.

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REFERENCES

1. Anand BK. Structure and functions of the limbic system (visceral brain)- A review. *Indian J Physiol Pharmacol* 1957; 1: 149–158.
2. Anand BK. Studies on the limbic system of brain (visceral brain). *Physiol Expntal Sci (Annual Volume)* 1957; 58: 103.
3. Anand BK. Recent trends in neurophysiology of the visceral nervous system. *Indian J Physiol Pharmacol* 1960; 4: 80–83.
4. Anand BK. Functional importance of limbic system of brain. *Indian J Med Res* 1963; 51: 75.
5. Anand BK. Functional importance of limbic system of brain. *J Sci Industri Res* 1966; 25: 506–507.
6. Anand BK. Regulation of visceral activities by the central nervous system. In Wolstenholme GEW and Knight J, eds. Ciba Foundation Symposium on Control Process in Multicellular Organism. J&A. Churchill Ltd., London, 1970; 356–381.
7. Anand BK. Visceral brain and its functions. *Armed Forces Med J* 1972; 27: 6–13.
8. Anand BK. Motivation and drives. *IBRO Bulletin,* 1968; 7: 64–65
9. Anand BK. Limbic system in Innate Animal Behaviour. *Proceedings of the International Union of Physiological Sciences-XXIV-International Congress, Washington, D.C.* 1968; 7:432.
10. Anand BK. Nervous regulation of food intake. *Physiol Rev* 1961; 41: 677–708.

11. Anand BK. Central chemosensitive mechanisms related to feeding. *In Handbook of Physiology, Section 6; Alimentary Canal, Vol. 1, American Physiological Society , Washington DC,* 1968; 249–263

12. Anand BK, Brobeck JR. Localization of a "feeding centre" in the hypothalamus of the rat. *Proc Soc Exp Biol Med* 1951; 77:323–324.

13. Anand BK, Brobeck JR. Hypothalamic control of food intake in rats and cats. *Yale J Biol Med* 1951; 24: 123–140.

14. Anand BK, Dua S, Shoenberg K. Hypothalamic control of food intake in cats and monkeys. *J Physiol (London)* 1955; 127: 143–152.

15. Anand BK, Dua S, Chhina GS. Higher nervous control over food intake. *Indian J Med Res* 1958; 46: 277–287.

16. Anand BK. Higher Nervous Control Over Food Intake - *XXI Internatinal Congress of Physiological Sciences - Buenos Aires - Abstracts of Symposia and Special Lectures.* 1959; 196–202.

17. Anand BK. Nervous regulation of food intake. *Am J Cli Nutr* 1960; 8: 529–534.

18. Anand BK. Higher nervous control over food intake. *Indian J Physiol Pharmacol.* 1960; 4: 215–233.

19. Delgado JMR, Anand BK. Increase of food intake induced by electrical stimulation of the lateral hypothalamus. *Am J Physiol.* 1953; 172:162–168.

20. Anand BK, Dua S. Feeding responses induced by electrical stimulation of hypothalamus in cat. *Indian J Med Res* 1955; 43: 113–122.

21. Anand BK. Intrahypothalamic connections between the two sides. *Indian J Physiol Allied Sci* 1954; 8: 50–154.

22. Nayar U, Chakrabarty KK, Anand BK. Effects of stimulation of brain-stem reticular formation on food intake. *Indian J Physiol Pharmacol* 1971; 15: 67–73.

23. Anand BK, Brobeck JR. Food intake and spontaneous activity of rats with lesions in the amygdaloid nuclei. *J Neurophysiol* 1952; 15: 421–430.

24. Anand BK, Dua S. Electrical stimulation of the limbic system of brain (visceral brain) in the waking animals. *Indian J Med Res* 1956; 44 107–119.

25. Anand BK, Dua S, Chhina GS. Changes in affective behaviour produced by lesions in the frontal and temporal lobes. *Indian J Med Res* 1957; 45: 353–357.

26. Anand BK, Chhina GS, Dua S. Effects of lesion in the limbic system on the affective behaviour and visceral responses in the monkeys and cats. *Indian J Med Res* 1959; 47: 51–59

27. Anand BK, Chhina GS. Visceral and metabolic changes on stimulation of limbic system of brain of monkeys. *Indian J Physiol Pharmacol* 1959; 3:27–38.

28. Anand BK, Dua S, Chhina GS. Effect of neocortical lesions over food intake. *Indian J Med Res* 1961; 49:491–497.

29. Subberwal U, Anand BK. Role of reticular formation of brain stem in regulation of food intake. *Indian J Med Res* 1965; 53: 440–448.

30. Pillai RV, Chakrabarty AS, Anand BK, Singh B. Activity of hypothalamic feeding centres. *Indian J Physiol Pharmocol* 1967; 11: 35.

31. Anand BK, Pillai RV. Activity of single neuron in the hypothalamic feeding centres: effect of gastric distension. *J Physiol (London)* 1967; 192: 63–77.

32. Sharma KN, Anand BK, Dua S, Singh B. Role of stomach in the regulation of activities of the hypothalamic feeding centres. *Am J Physiol* 1961; 201: 593–598

33. Kumar VM, Chhina GS, Anand BK. Evoked responses from hypothalamus in response to stimulation of mesenteric nerves. *Indian J Physiol Pharmacol* 1970; 14: 27–28.

34. Kumar VM, Chhina GS, Anand BK. Effect of different substances on the responses evoked in the hypothalamus by the stimulation of mesenteric nerves. *Indian J Physiol Pharmacol* 1971; 15: 14.

35. Anand BK. Influence of internal environment on the nervous regulation of alimentary behaviour. In Brazier MAB, ed. Brain and Behavior. Vol. II American Institute of Biological Sciences - Washington DC. 1963; 43–116.

36. Anand BK. Influence of metabolic changes on the nervous regulation of food Intake - Symposium on the regulation of food intake. *Procedings of XXII International Congress of Physiological Sciences, Leiden, Abstracts of Lectures and Symposia* 1962; 1: 680–685

37. Anand BK, Dua S, Singh B. Electrical activity of feeding centres under the effect of changes in blood chemistry *Electroencephalogr Clin Neurophysiol* 1961; 13: 54–59.

38. Anand BK. Regulation of nervous drives in feeding behaviour. *Totus Homo* 1971; 3: 59–66.

39. Anand BK, Chhina GS, Singh B. Effect of glucose on the activity of hypothalamic "feeding centres". *Science* 1962; 138: 597–598.

40. Anand BK, Subberwal U, Manchanda SK, Singh B. Glucoreceptor mechanism in the hypothealamic feeding centres. *Indian J Med Res* 1961; 49: 717–724.

41. Anand BK, Chhina GS, Sharma KN, Dua S, Singh B. Activity of single neurons in the hypothalamic feeding centres: effect of glucose. *Am J Physiol* 1964; 207: 1146–1154.

42. Desiraju T, Banerji MG, Anand BK. Unit activity of hypothalamic neurons sensitive to glucopenia *Indian J Physiol Pharmacol* 1968; 12; 38–39.

43. Desiraju T, Banerji MG, Anand BK. Activity of single neurons in the hypothalamic feeding centres: Effect of 2-Deoxy-D-Glucose. Physiol Behav 1968; 3:757–760.

44. Chhina GS, Anand BK. Mode of action of glucose utilization on the electrical activity of hypothalamic feeding centres. *Indian J Physiol Pharmacol* 1969; 13: 9.

45. Chakrabarty AS, Pillai RV, Anand BK, Singh B. Effect of cyproheptadine on the electrical activity of the hypothalamic feeding centres. *Brain Res* 1967; 6:561–569.

46. Khanna S, Nayar U, Anand BK. Effect of fenfluramine on single neuron activities of hypothalamic feeding centres. *Physiol Behav* 1972; 8: 453–456.

47. Chhina GS, Kang BK, Singh B, Anand BK. Effect of fenfluramine on the electrical activity of the hypothalamic feeding centres. *Physiol Behav* 1971; 7: 434–438.

48. Manchanda SK, Subberwal U, Anand BK, Singh B. Effect of nialamide on the electroencephalographically recorded activity of brain. *Arch Int de Pharmacodyn Therapy* 1963; 143: 408–420.

49. Anand BK, Malhotra CL, Dua S, Singh B. Electrical activity of hypothalamic feeding centres under the effect of reserpine, rastinon and preludin. *Indian J Med Res* 1961; 49: 152–157.

50. Kang HK, Singh B, Anand BK. Effect of some appetite depressing substances on the EEG activity of brain. *Indian J Physiol Pharmacol* 1971; 15: 3.

51. Anand BK, Talwar GP, Dua S, Mhatre RM. Glucose and oxygen consumption of hypothalamic feeding centres. *Indian J Med Res* 1961; 49:725–732.

52. Chhina GS, Anand BK, B.Singh, Rao PS. Effect of glucose on hypothalamic feeding centres in deafferented animals. *Am J Physiol* 1971; 22: 662–667.

53. Anand BK, Banerji MG, Chhina GS. Activity of single neurons in the hypothalamic feeding centres: effect of protein hydrolysate. *Indian J Med Res* 1965; 53:1172–1179.

54. Anand BK, Dua S. Hypothalamic control over water consumption in the rat. *Indian J Med Res* 1958; 46: 426–430.

55. Anand BK, Dua S. Effect of cerebral lesions over water intake in the rat. *Indian J Med Res* 1961; 49: 834–836.

56. *Anand* BK, Banerjee MG, Chhina GS. Single neuron activity of hypothalamic feeding centre. *Brain Res* 1966; 1: 269–278.

57. Anand BK. Nervous mechanisms involved in maintaining energy balance. *Bull All India Institute of Medical Sciences, New Delhi.* 1968; 2(1): 4–16.

58. Singh B, Anand BK, Malhotra CL, Dua S. Stress as an aetiological factor in the causation of anorexia nervosa. *Neurology* 1958; 6: 50–52.

59 Anand BK. Experimental observations on anorexia. *Adv Psychosom Med* 1972; 7: 243–256.

60 Subberwal U, Anand BK, Singh B. Effect of caudate stimulation on some vegetative functions. *Indian J Med Res* 1965; 53: 1034–1039.

61. Anand BK, Dua S, Malhotra CL. Effect of reserpine (serpasil) on blood pressure responses evoked from hypothalamus. *British J Pharmacol Chemotherapy* 1957; 12:8–11.

62. Anand BK, Dua S. Circulatory and respiratory changes induced by electrical stimulation of the limbic system. *J Neurophysiol* 1956; 19: 393–400.

63. Anand BK, Dua S. Stimulation of the limbic system of brain in waking animals. *Science* 1955; 122: 139.

64. Anand BK, Dua S, Chhina GS. Changes in visceral and metabolic activities after frontal and temporal lobe lesions. *Indian J Med Res* 1957; 45: 345–352.

65. Khetarpal K, Manchanda SK, Anand BK. Carotid bodies in the neural regulation of respiration. *Indian J Physiol Pharmacol* 1971; 15:52.

66. Sen RN, Anand BK. Effects of electrical stimulation of the hypothalamus on gastric secretory activity and ulceration. *Indian J Med Res* 1957; 45: 507–515.

67. Sharma KN, Dua S, Anand BK. Effect of hypothalamic lesions on experimental gastric ulceration in rats. *Indian J Med Res* 1963; 51: 708–715.

68. Anand BK, Dua S. Effect of electrical stimulation of the limbic system (visceral brain) on gastric secretion and motility. *Indian J Med Res* 1963; 51: 708–715.

69. Sen RN, Anand BK. Effect of electrical stimulation of the limbic system of brain (visceral brain) on gastric secretory activity and ulceration. *Indian J Med Res* 1957; 45: 515–521.

70. Sen RN, Anand BK. Effect of stimulation of frontal cortex and dorsomedial parts of thalamus on gastric secretory activity. *Indian J Physiol Pharmacol* 1957; 1: 4.

71. Ray AP, Anand BK, Dua S, Sharma GK. Pathogenesis of liver injuries (Part III) – *Bull Nat Soc India Malarial Mosquito Dis* 1958; 6: 173–175.

72. Anand BK, Dua S. Blood sugar changes induced by electrical stimulation of hypothalamus in cat. *Indian J Med Res* 1955; 43: 123–127.

73. Anand BK, Dua S. Blood sugar changes induced by electrical stimulation of the limbic system (visceral brain). *Indian J Med Res* 1956; 44: 121–124.

74. Anand BK, Malhotra CL, Singh B, Dua S. Cerebellar projections to the limbic system. *J Neurophysiol* 1959; 22: 451–457.

75. Anand BK, Singh B, Malhotra CL, Dua S, Sharma KN. Electroencephalographic studies of spontaneous and activated patterns in the cerebellum and its projections. *Indian J Physiol Pharmacol* 1960; 4: 113–114.

76. Rasheed BMA, Manchanda SK, Anand BK. Effects of stimulation of paleocerebellum on certain vegetative functions in the cat. *Brain Res* 1970; 20:293–308.

77. Manchanda SK, Rasheed BMA, Bhattarai A, Anand BK. Vegetative functions of cerebellum. *Proceedings International Union of Physiological Sciences Regional Congress Breasov* 1970; 172.

78. Singh B, Chhina GS, Anand BK. Effects of anaesthesia, mid-collicular section and variation in blood glucose on spontaneous EEG activity of the cerebellum in cats. *Neurology (India)* 1970; 28: 97.

79. Anand BK, Raghunath P, Dua S, Mohindra S. Hypothalamic control of the pituitary adrenocortical response to stress stimuli. *Indian J Med Res* 1954; 42: 231–248.

80. Anand BK, Thomas S. Effect of hypothalamic involvement in the pituitary adrenocortical response. *J Physiol (London)* 1955; 127: 155–156.

81. Anand BK, Thomas S. Effect of hypothalamic stimulation on TSH secretion. *Proceedings of the International Union of Physiological Sciences XXIV International Congress Washington DC.*1968; 5: 432.

82. Thomas S, Anand BK. Effect of electrical stimulation of the hypothalamus on thyroid secretion in monkeys. *J Neurovisceral Relations* 1970; 31: 399–408.

83. Anand BK, Malkani PK, Sikand S. Hypothalamic control over estrus cycle in the rat. *Indian J Med Res* 1957; 4:503–506.

84. Anand BK, Malkani PK, Dua S. Effect of electrical stimulation of the hypothalamus on menstrual cycle in monkey. *Indian J Med Res* 1957; 45: 499–502.

85. Chatterjee S, Anand BK. Effect of hypothalamic lesions and stimulation on urinary estrogen excretion in female monkeys. *Indian J Med Res* 1967; 55:981–990.

86. Anand BK, Malkani PK, Dua S, Sikand S. Hypothalamic control over estrous in rat and ovulation in monkey. *Proceedings World Congress Fertility and Sterility* 1961; 3:992.

87. Chhina GS, Kaur K. Baijal ND, Chowdhury G, Singh B, Anand BK. Neuroendocrinal participation in the reproductive activities. *Indian J Physiol Pharmacol* 1968; 12:39.

88. Chhina GS, Chandra S, Anand BK. Studies of normal sex behavior patterns in monkeys. *Indian J Physiol Pharmacol* 1968; 12:49.

89. Anand BK. Nervous regulation of reproductive behaviour. *Bull Nat Inst Sc of India* 1964; 27: 20–27.

90. Chhina GS, Anand BK. Regulation of reproduction by central nervous system. *Society of Biological Chemists of India. Symposium on Regulatory Mechanisms* 1965; 3–4.

91. Chinna GS, Chakrabarty AS, Kaur K, Anand BK. Electroencephalographic responses produced by genital stimulation and hormone administration in sexually immature rhesus monkeys. *Physiol Behav* 1968; 3: 579–584.

92. Chhina GS, Anand BK. Responses of neurons in the hypothalamus and limbic system to genital

stimulation in adult and immature monkeys. *Brain Res* 1969; 13: 511–521.

93. Kang HK, Singh B, Anand BK, Chhina GS. Effect of gonadal hormones on electrical activity of brain in adult monkeys. *J Repro Fertil* 1971; 27: 298–299.
94. Chhina GS, Thomas S, Kang HK, Anand BK. Effect of sub-cortical lesions on feeding and emotional behaviour. *Indian J Physiol Pharmacol* 1968; 12:40.
95. Chhina GS, Nayar U, Anand BK. Nervous control of emotional behaviour in rats. *Indian J Physiol Pharmacol* 1968;12: 41–42.
96. Anand BK, Limbic system in innate animal behaviour. *Proceedings of International Union of Physiological Sciences, XXIV International Congress, Washington DC, 1968 Vol VII, pp 432.*
97. Anand BK. Neurophysiological problems at high altitudes. *Indian J Physiol Pharmacol* 1964; 8: 40–48.
98. Anand BK. Physiological responses to high altitudes – *Symposium on Problems of high altitude, Armed Forces Medical College, Poona* 1965: 5–10.
99. Dikshit PK, Anand BK, Boparai MS. Oxygen requirements for thermogenesis during cold adaptation at high altitudes. *Indian J Physiol Pharmacol* 1972;16: 31–45.
100. Anand BK, Chhina GS. Investigations on yogis claiming to stop their heart beat. *Indian J Med Res* 1961; 49: 90–94.
101. Wenger MA, Bagchi BK, Anand BK. Experiments in India on "voluntary" control of the heart and pulse. *Circulation* 1961; 24: 1319–1325.
102. Wenger MA, Bagchi BK, Anand BK. Voluntary heart and pulse control by yoga method. *Int J Parapsychol* 1963; 5: 25–41.
103. Anand BK, Chhina GS, Singh B. Studies on Shri Ramanand Yogi during his stay in an air tight box. *Ind J Med Res* 1961; 49: 82–89.
104. Anand BK. Physiological concepts of consciousness. *Indian J Physiol Pharmacol* 1960; 4: 155–167.
105. Anand BK, Chinna GS, Singh B. Some aspects of electrocencephalographic studies in yogis. *Electrocencephalogr Clin Neurophysiol* 1961; 13: 452–456.
106. Anand BK, Chhina GS, Singh B. Electroencephalographic activity under hypnotism. *Indian J Physiol Pharmacol* 1961; 13: 452–456.
107. Chhina GS, Singh B, Anand BK. Some further studies on the physiological changes in yogis. *Indian J Physiol Pharmacol* 1968; 12:40–41.
108. Anand BK. Yoga and medical sciences. *Indian J Physiol Pharmacol* 1968; 12: 84–87.