"HIGHER NERVOUS CONTROL OVER FOOD INTAKE"*

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(Received on October 1960)

INTRODUCTORY

During the course of the 19th century a number of scientists had suggested a "central" mechanism for hunger. Others believed that hunger had a "peripheral" origin. The "peripheral" theory appeared to receive support when Cannon (1915) demonstrated rhythmic contractions of the stomach accompanying hunger feelings, and on the basis of this, Carlson (1916) built an entire theory of the regulation of appetite. Subsequent events showed, however, that the gastric mechanism was overemphasized and experimental observations began to accumulate which showed that elimination of gastric hunger contractions by a variety of ways did not alter hunger sensations (Grossman *et al.*, 1947; Adolph, 1947).

Meanwhile attention was focussed on the hypothalamus with the discovery by Hethrington and Ranson (1940) that obesity could be produced by lesions confined to hypothalamus, and the observations of Brobeck *et al.*, (1943) that such obesity was a result of hyperphagia. Subsequently hypothalamic hyperphagia was produced in several species of animals such as the rat, cat, dog and monkey.

ROLE OF HYPOTHALAMUS

Anand and Brobeck (1951) observed that hypothalamic injuries in rats could produce not only hyperphagia but also aphagia. Bilateral lesions in a restricted area of the lateral hypothalamus in the same rostrocaudal plane as the ventromedial nucleus (Fig. 1), led to complete aphagia and death of the animal from starvation. On the other hand lesions restricted to the medial hypothalamic regions of the ventromedial nuclei, and the regions in between
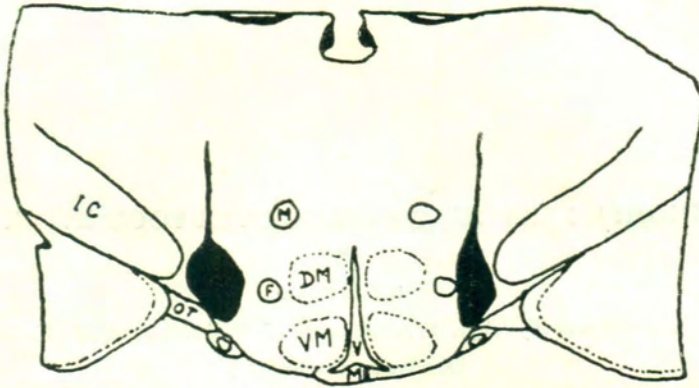

Fig. 1. Section through rat's brain passing through the hypothalamus in the tuberal region, rostral to the pituitary stalk and caudal to the optic tract. The heavy shaded areas represent bilateral lesions in the lateral hypothalammus, lateral to the fornix and medial to the internal capsule. The dorsal prolongations represent electrod tracks. (From Anand and Brobeck 1951).

these and the lateral hypothalamic areas, led to hyperphagia and obesity (Fig. 2), provided the lateral hypothalamic centres were undamaged. It was
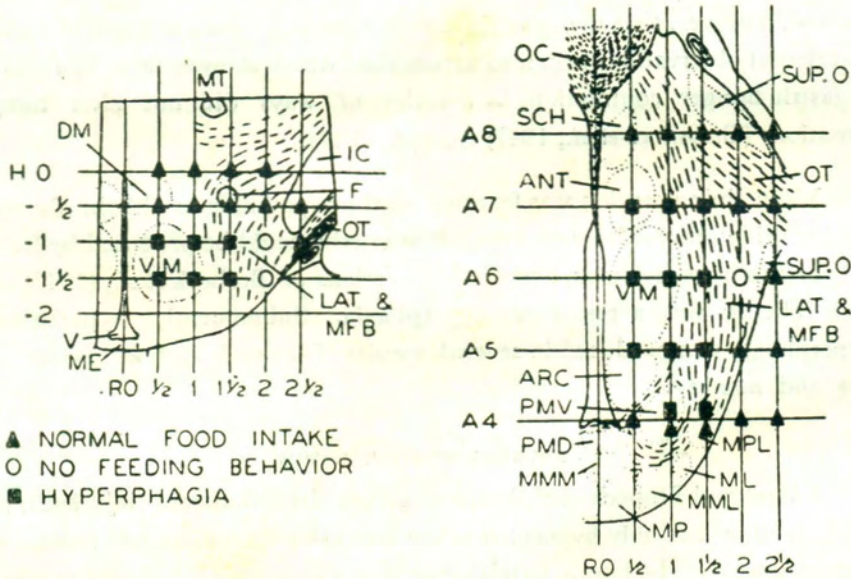

▲ NORMAL FOOD INTAKE
O NO FEEDING BEHAVIOR
▩ HYPERPHAGIA

Fig. 2. Diagram representing right side of rat's hypothalamus in horizontal and vertical plane of ventromedial nucleus. Horsley clarke coordinates are superimposed, and feeding behaviour of rats with small, bilaterally symmetrical lesions in each area is indicated. (From Anand and Brobeck 1951 A).

suggested that the lateral hypothalamic area be designated "feeding centre" and the medial one "satiety centre".

Anand, *et al.*, (1955) extended these studies to cats and monkeys (Fig. 3), confirming the dual hypothalamic mechanism regulating food intake. It was also demonstrated by Delgado and Anand (1953), and Anand and Dua (1955), that electrical stimulation for one hour of the lateral hypothalamic areas in cats markedly increased their daily food intake on the days of stimulation (Fig. 4), while stimulation of the medial hypothalamic areas for one hour produced only a slight decrease in daily food intake on the days of stimulation - never complete aphagia. This was confirmed by Larsson (1954) in goats.

These observations provided an anatomical basis for a possible central mechanism in the hypothalamus regulating food intake. It seemed that the lateral "feeding" mechanism was the basic urge, while the medial "satiety" mechanism acted by inhibiting the lateral mechanism for the following reasons:— (i) Injury to the lateral regions invariably produces complete
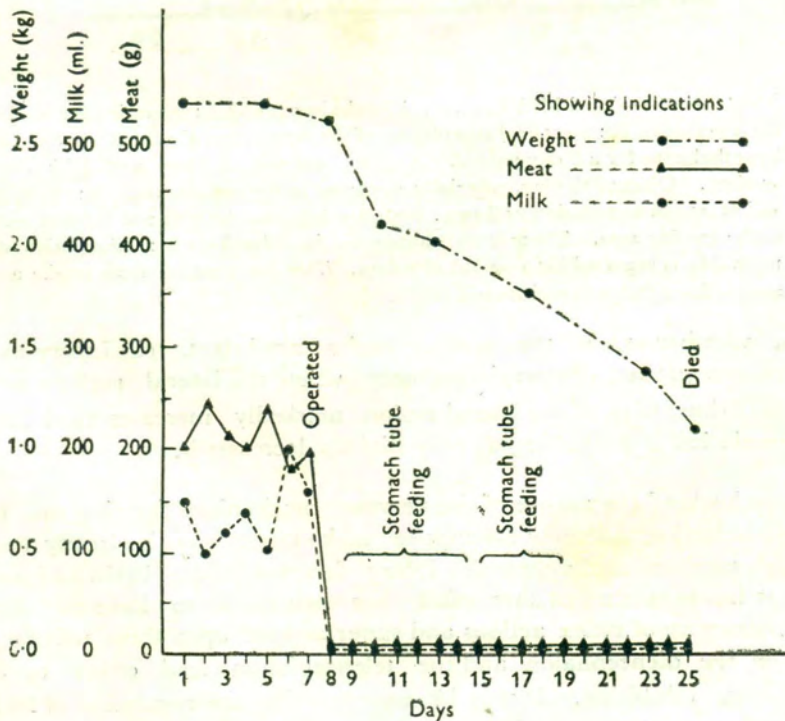

Fig. 3. Food intake (spontaneous) and weight chart of cat 11 which developed complete aphagia after hypothalamic lesions. (From Anand, Dua and Shoenberg 1955).
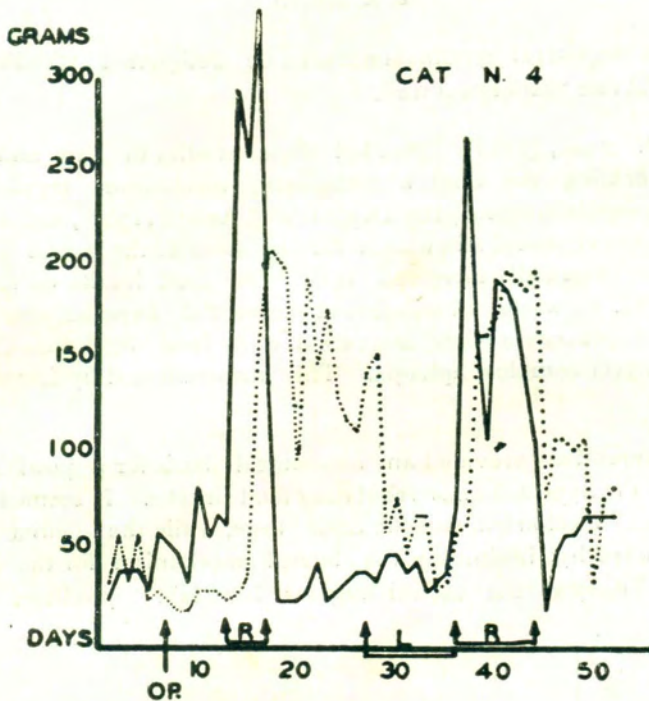
Fig. 4. Meat (————) and Milk (..........) intake in cat 4. O.P.: operation for implanting the electrodes. R : electrical stimulation of the most external part of the right lateral hypothalamus for a 5 day pariod. A great increase of meat and milk intake is evoked. Observe the lag, especially apparent in the milk intake. L: Stimulation of left lateral hypothalamus 2 mm. posterior 1.5 mm. inferior and 0.5 mm. external to the specific area. There is no change in food intake. R: stimulation of the right side is repeated for a period of 9 days. The increase in food intake appears again (From Delgado and Anand 1953).

aphagia, whether or not the medial regions are intact. (ii) Injury to the medial regions produces hyperphagia, only when the lateral regions are intact. (iii) Stimulation of the lateral region markedly increases food intake, while stimulation of medial region only slightly decreases it.

To understand the nature of the nervous mechanisms forming the basis of feeding behavior, one may attempt to make use of what is already known about such mechanisms in general. Every function of the brain and spinal cord that has been studied successfully, has been shown to have an important sub-structure of reflex actions and superimposed upon these reflexes, the brain stem, the diencephalon and the telencephalon lead either to their facilitation or inhibition. It may be suggested that the regulation of feeding also is reflex in nature, with superimposed 'facilitation' and 'inhibition'

from higher centres including the hypothlamaus. From what has been stated already, it would appear that the lateral hypothalamic mechanism is 'facilitatory' and the medial one 'inhibitory' to the feeding reflexes.

The level of the central nervous system most directly concerned with feeding reflexes is probably the brain stem containing the nuclei of the cranial nerves, motor and sensory components of which take part in normal feeding reflexes which aid in chewing, salivation, swallowing, as also in rejection of unacceptable objects. This was indicated as early as 1961 by Miller and Sherrington in decerebrate animals.

Brobeck (1955) has proposed two different tentative classifications of feeding reflexes. One is based upon the nature of the stimulus inducing the reflex which may be tactile, gustatory, auditory, olfactory or visual, making the animal aware of food. Enteroceptive reflexes initiated, for example, by distension of the stomach or duodenum or the contractions of gastric hunger pangs could also be integrated in the feeding reflexes. Second classification is based on the sequence of behaviour in normal feeding, including reflexes of attention, approach, examination, incorporation, and rejection.

CEREBRAL INFLUENCES

Experimental work has also suggested cerebral influence over normal feeding responses. Pribram and Bagshaw (1953) reported increased food intake after surgical lesions involving temporal polar - amygdaloid formations in monkeys. Anand *et al.*, (1955) had observed that bilateral destructions of 'feeding' centres in some monkeys produced a slightly modified response to that seen in cats and rats after similar lesions - such monkeys would not eat the food available in the cage but if it was put directly into their mouth, they would swallow it. Aphagic cats and rats with similar lesions would always reject the food even when it was put into their mouth. It was presumed that this difference in the monkey was due to higher encephalisation, suggesting that at least in primates, control over food intake was also mediated through "higher" cerebral centres. Anand *et al.*, (1958) further demonstrated that bilateral lesions in some structures of the limbic system changed the food intake in monkeys and cats. Frontal lobe lesions, including or restricted to the posterior orbital cortex, led to a decrease in food intake (Fig. 5), while those involving only the frontal tips and sparing the posterior orbital cortex led to an increase in intake (Fig. 6). Lesions restricted to anterior cingulate gyri had no effect. Lesions in the amygdaloid and periamygdaloid regions of the temporal lobe produced temporary aphagia for a few days (Fig. 7). Extensive temporal lobe lesions, on the other hand, led to an increase in food intake (Fig. 8). Such changes in food intake were more marked in monkeys than in cats; were never so
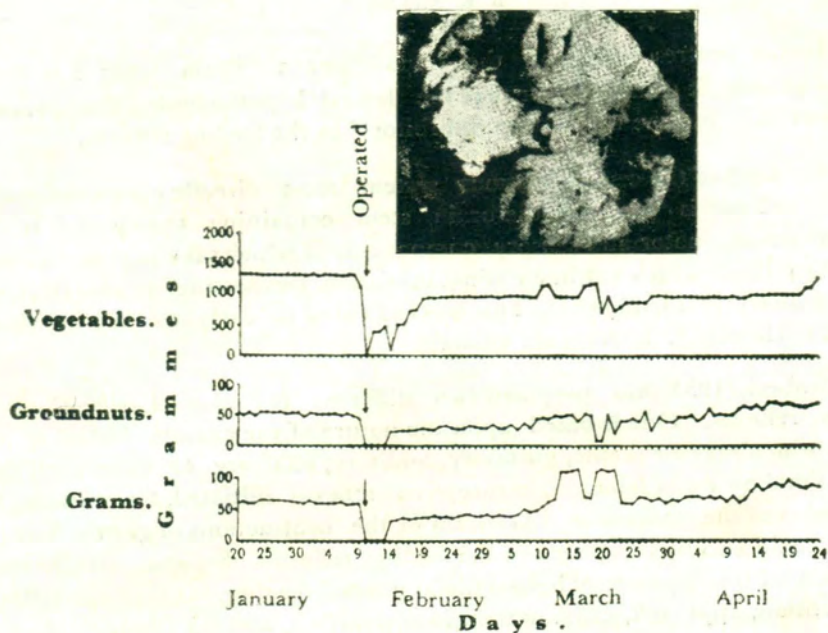
Fig. 5. Food intake chart and brain photograph of monkey 21, after extensive surgical lesions of frontal lobes including the posterior orbital surface. This monkey developed hyperactivity post operatively (From Anand, Dua and Chhina 1958).
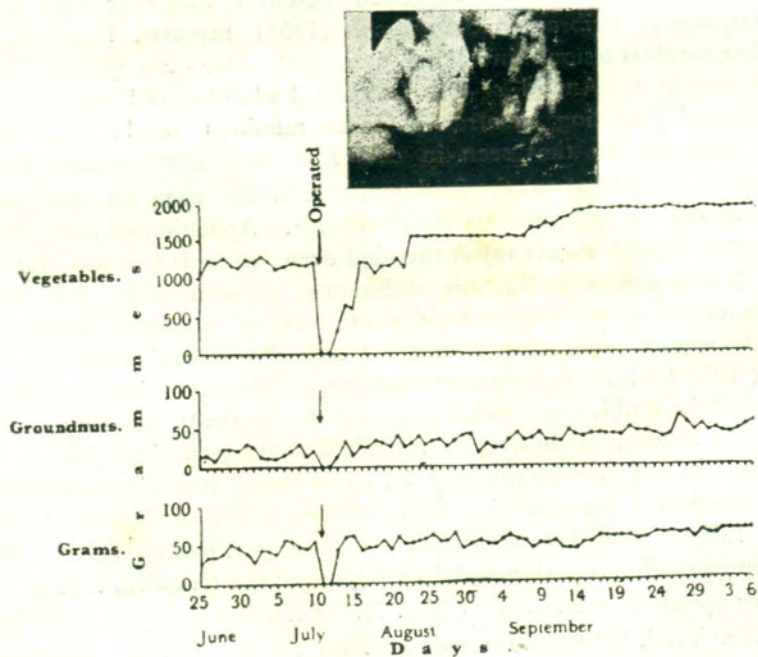

Fig. 6. Food intake chart and brain photograph of monkey 2, after less extensive surgical lesions of frontal lobes (mainly the frontal tips) excluding the posterior orbital surface. There was no hyperactivity. (From Anand, Dua and Chhina 1958).
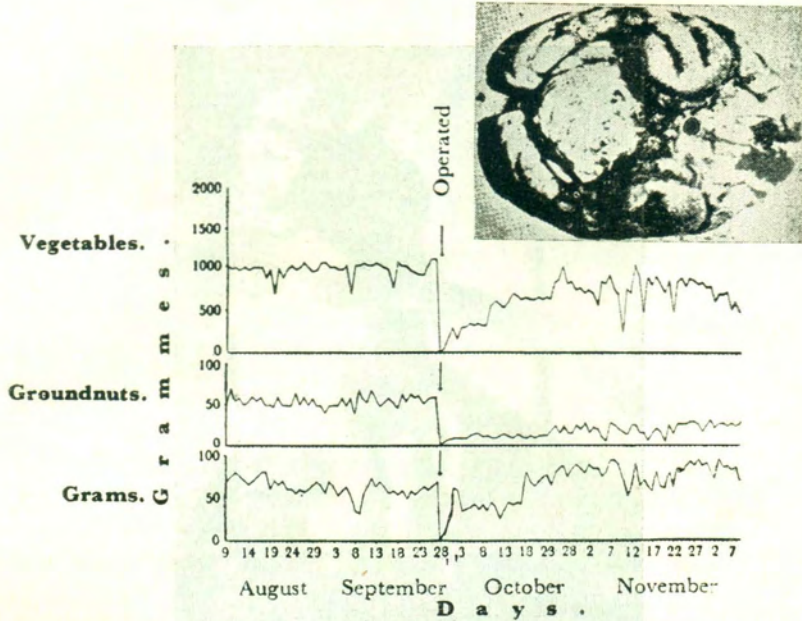
Fig. 7. Food intake chart and brain photograph of monkey 29 after surgical lesions restricted to the posterior orbital cortex. (From Anand, Dua and Chhina 1958).
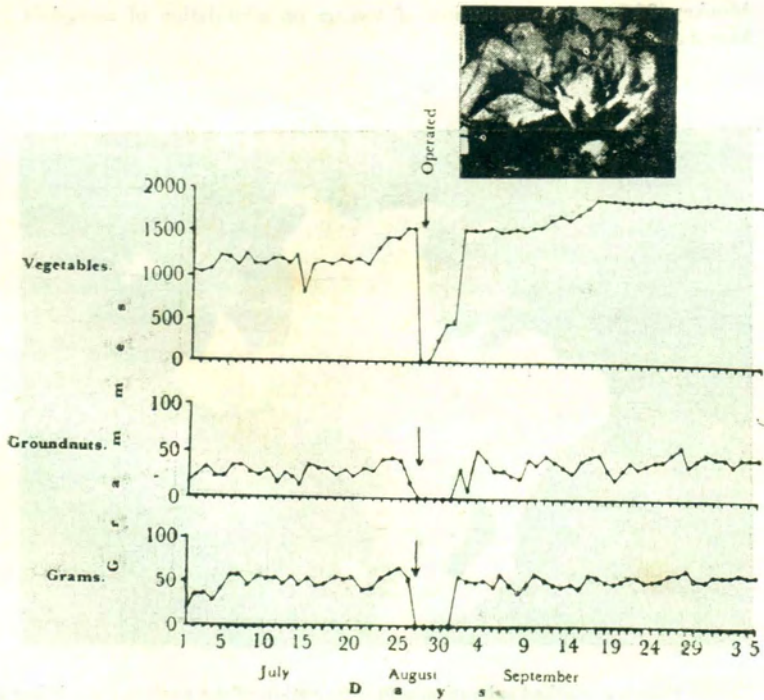
Fig. 8. Food intake chart and brain photograph of monkey 3 after extensive superficial surgical lesions of the temporal lobes excluding the amygdala. (From Anand, Dua and Chhina 1958).

Fig. 9. Monkey 26 showing protrusion of tongue on stimulation of amygdala. (From Anand and Dua 1956).

Fig. 10. Cat 96 showing marked salivation and assumption of the posture of defaecation on stimulation of right anteromedial amygdala (From Anand and Dua 1956).

pronounced as those associated with lesions of the hypothalamus; and also
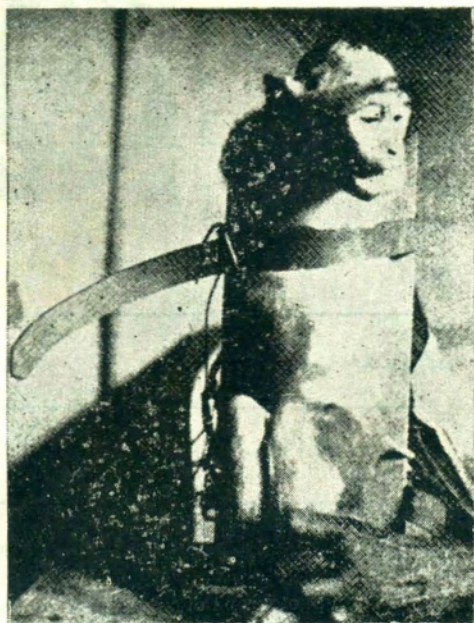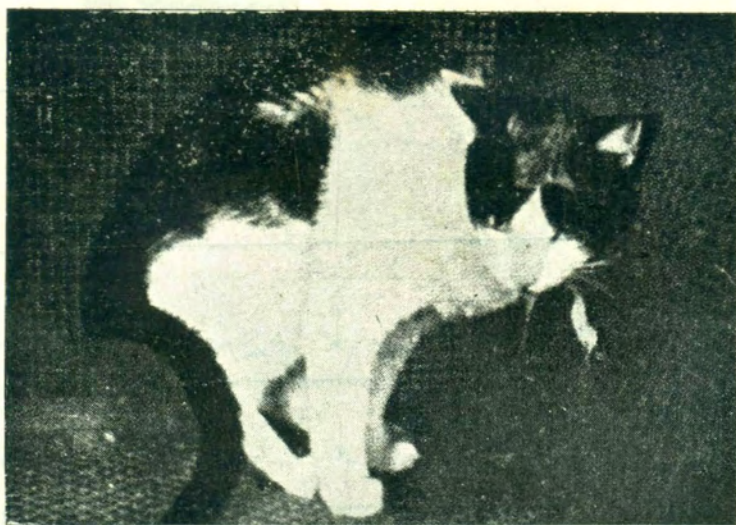tended to disappear after some weeks. Following such lesions in cats, pre-
operative daily variations in food intake also tended to disappear.
It was, therefore, concluded that the limbic structures in the frontal and
temporal lobes modified intake through a discriminating mechanism
("appetite"), while the primitive urge ("hunger") originated at the hypotha-
lamic levels. From experiments with rats, Bruce and Kennedy (1951) postu-
lated a similar hypothesis. The cerebral influences are possibly mediated
through the hypothalamus, modifyng the effects of hypothalamic factors.

Stimulation of the various limbic structures did not produce any change
in the daily food intake. On the other hand, such stimulations produced
responses consisting of chewing, licking, sniffing, repetitive opening and
closing of mouth with protrusion of the tongue (Fig. 9) and even salivation
(Fig. 10)-such responses being grouped under the heading of 'eating' automa-
tisms (Anand and Dua, 1956). It may be noted here that such 'eating'
responses were also produced during stimulation of the lateral hypothalamic
'feeding' centres (Delgado and Anand, 1953; Anand and Dua, 1955), accom-
panied by a marked increase in the daily food intake. In a recent study
Anand *et al.*, (unpublished) carried out bilateral lesions in some
neocortical regions and observed that there was a slight change in food
intake of a short duration after lateral frontal lesions only, while lesions in
the lateral parietal, occipital and temporal neocortical regions did not pro-
duce any change in intake.

Enough evidence is thus available to classify the central nervous mecha-
nisms regulating food intake in a manner similar to the regulatory mecha-
nisms for other autonomic and visceral activities, such as the regulation of
blood pressure, pulmonary ventilation, and body temperature. Feeding
behaviour is probably regulated by certain reflex mechanisms mediated
from the spinal cord and brain stem levels, which are definitely facilitated
and inhibited from the hypothalamic regions, and further regulated from
the higher cerebral limbic and neocortical regions. In common with the
other visceral reflexes, the regulation from the limbic levels is more pronoun-
ced than from the neocortical levels.

MECHANISM OF NERVOUS REGULATION

It is well known that adult men and animals can maintain their body
weights, and growing organisms continue to grow at well defined rates, in
spite of marked variations in energy expenditure. Food intake, regulated
through central 'appetite' or 'hunger' mechanisms, must therefore be adapted
to caloric needs. Cowgill (1928) demonstrated that under a variety of
circumstances and on a variety of diets, "animals eat for calories". Gasnier

and Andre' Mayer (1939) further demonstrated that animals varied their food intake in a way which indicated that two regulations were at work, one, more important than the other, adjusts the calories eaten to the calories spent from day to day, and the other, working more slowly, corrects over a period of time whatever error the rapid mechanism could have been guilty of.

A simplified explanation to these adjustments would be that when food is eaten by a normal animal, there occur within the body certain changes which either directly or indirectly affect the hypothalamic centres and possibly also the higher cerebral centres, and through these change the feeding reflexes. These changes stimulate the activity of the medial or inhibitory hypothalamic mechanisms and suppress the lateral facilitatory mechanisms, thus producing satiety. On the other hand, when the food eaten is disposed of, through conversion to heat, work, or some form of stored energy, the changes produced by the feeding tend to disappear and so activation of satiety mechanism is removed and the lateral facilitatory mechanism becomes more active leading to a state of hunger. Thus, as a result of changes produced by feeding, the animal will remain satiated for most of the time and even in the presence of food behave as though unaware of it. When these changes disappear, the animal will be ready to eat again.

Various suggestions have been put forward regarding the nature of the change or changes, produced as a result of feeding, which influence the regulating system. The factors suggested by various workers are: (i) the specific dynamic action of food, increasing the heat stress of the body as a whole (the thermostatic hypothesis of Strominger and Brobeck, 1953); (ii) the availability and utilization of glucose from body fluids (the glucostatic hypothesis of Mayer, 1953); (iii) the concentration of certain metabolites, as yet unspecified (the lipostatic hypothesis of Kennedy, 1950); (iv) the concentration of serum amino acids (Mellinkoff et al., 1956); (v) the water concentration, or shifts of water among the compartments within the body (suggested by experiments of Adolph, 1947; Strominger, 1947; & others); and (vi) sensations from the digestive tract associated with eating, swallowing, and the presence of food in stomach and intestine (Janowitz and Grossman, 1949; Share et al., 1952). The ingestion of a single food is accompanied by a number of changes in the animal body and more than one such change could act as a signal to the regulatory mechanism. On the basis of existing evidence, it would seem unwise to incriminate a single specific factor. A multiple factor theory of regulation appears to be most reasonable.

The two hypotheses of regulation of food intake, which today compete for emphasis, are the 'thermostatic' regulation hypothesis, and the 'chemostatic', specially 'glucostatic', regulation hypothesis.

THERMOSTATIC REGULATION OF FOOD INTAKE.

Brobeck wrote, "animals eat to keep warm, and stop eating to prevent hyperthermia". Brobeck and his colleagues (Strominger and Brobeck, 1953; Strominger *et al.*, 1953) concluded that the day to day regulation of food intake is not in terms of a definite quantity of energy—a quantity equal to the total energy expenditure—but the specific dynamic action of the ration determined the amount of food eaten. Rats put on a high fat diet often ingested three times their normal caloric intake on the first day following the change in diet. Another point in favour of the thermostatic regulation put forward by Brobeck (1955) is that there is no direct evidence for a specific sensitivity of hypothalmic neurons except only to temperature change.

A serious criticism against the thermostatic theory is the observation that the addition of thyroprotein, or of substances with similar effect, to a ration results in increased food intake. Since the addition of this substance increases specific dynamic action of the ration, it should have decreased the intake.

CHEMOSTATIC REGULATION OF FOOD INTAKE

For short term regulation of energy intake, Mayer (1953, 1955, 1957) put forward the "glucostatic" theory, which postulates that somewhere, possibly in the hypothalamus, there are glucoreceptors sensitive to blood glucose in the measure that they can utilise it. He reasoned that during the interval between meals the body contents of fat and proteins, which are proportionately enormous, would decrease insignificantly, while body stores of carbohydrates, which are limited, would decrease proportionately more. Glucose is the essential fuel of the central nervous system. It seemed reasonable to postulate, therefore, that hypothalamic centres may be glucoreceptors.

Mayer and Bates (1952) showed that in normal and diabetic animals and in animals subjected to various hormonal treatments, decreased glucose availability or utilization correlated well with increased food intake. It was also shown that there was good correlation between decreased liver glycogen and feeding behaviour. It was pointed out that for studying the influence of the blood glucose on appetite, absolute blood levels by themselves do not give a measure of availability of glucose. A generally reliable representation of glucose utilization can be obtained from the arteriovenous glucose differences (Van Itallie *et al.*, 1953). It was demonstrated that 'hunger' state is the one in which the $\triangle$–glucose tends towards zero, while in the 'satiety' state there is an appreciable $\triangle$–glucose. Stunkard and Wolff (1954) found that small $\triangle$–glucose coincided generally with hunger gastric contractions and subjective feelings of hunger in human beings, while large $\triangle$–glucose accompanied satiety and disappearance of stomach contractions.
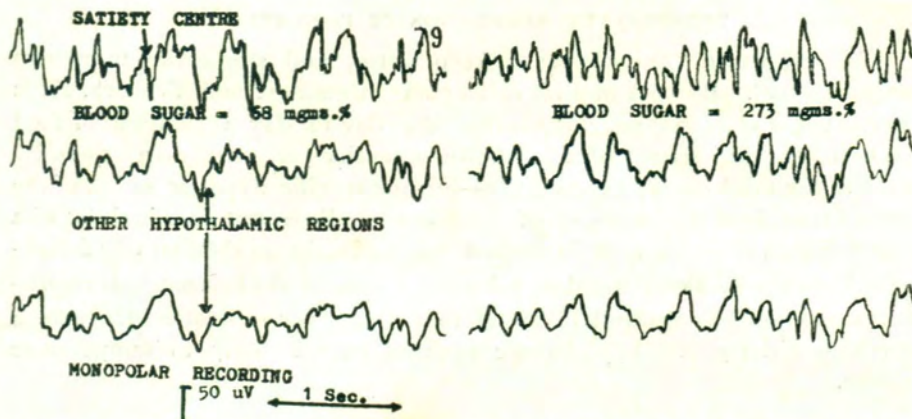
Fig. 11. Monopolar recordings from a cat with reference electrode on the left ear, before and after I.V. glucose injection. Hyperglycaemia has increased the frequency of the electrical activity of the satiety centre from 6—7 waves/sec. to 9—10 waves/sec. without changing the amplitude. No significant change in the electrical activity of other hypothalamic regionis seen. (From Anand, Dua and Baldev Singh 1960).

Mayer and Marshall (1956) have also demonstrated that injection of goldthioglucose in mice produced overeating and obesity by causing selective destruction in the medial satiety centres of the hypothalamus. On the other hand, a large number of other goldthiocompounds tested did not produce any hypothalamic lesions and obesity. Since the general toxicity of many of the other compounds was about the same as that of the effective dose of goldthioglucose, it has been suggested that the affinity of glucoreceptors in the ventromedial nuclei of the hypothalamus for the glucose moiety of the compound causes them to accumulate damagingly high quantities of gold.

Anand, et al., (1959) have studied this problem in another manner. Depth electrodes were implanted in the lateral ‘ feeding ’ and medial ‘satiety’ hypothalamic centres of monkeys and cats and the activity of these regions recorded electroencephalographically. After taking the normal recordings blood glucose levels were changed either by intravenous infusion of glucose saline or by intravenous injection of insulin. Control electrodes were also implanted in the other hypothalamic as well as cortical regions. It was observed that with the production of hyperglycaemia the activity of the ‘satiety’ centre was increased (Fig. 11) while that of ‘feeding’ centre was slightly decreased (Fig. 12). With hypoglycaemia, the activity of ‘satiety’ centre was slowed down (Fig. 13) while that of ‘feeding’ was increased. These changes were observed both in monkeys and cats. Changes in blood glucose levels did not alter the activity recorded from the other hypothalamic regions and cortical areas. Intravenous transfusion of protein hydrolysate (aminoacid mixtures) and fat emulsion (Lipomul) did not alter the activity
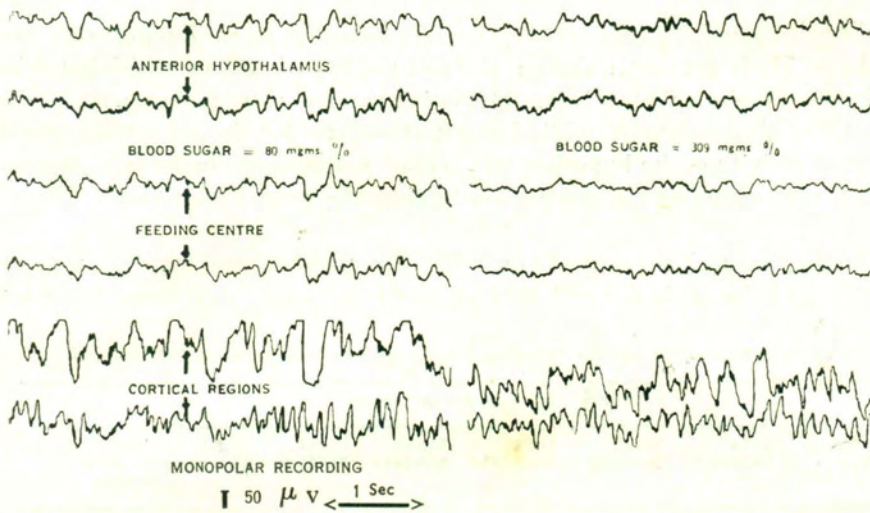
Fig. 12.   Monopolar recordings in a cat, with reference electrode on left ear. Hyperglycaemia
has reduced the voltage of the electrical activity of the feeding centres; From 70—75
μv to 20—25 μv.   No significant change is observed in the electrical activity of the
anterior hypothalamus and cortical regions.   (From Anand, Dua and Baldev Singh
1960).
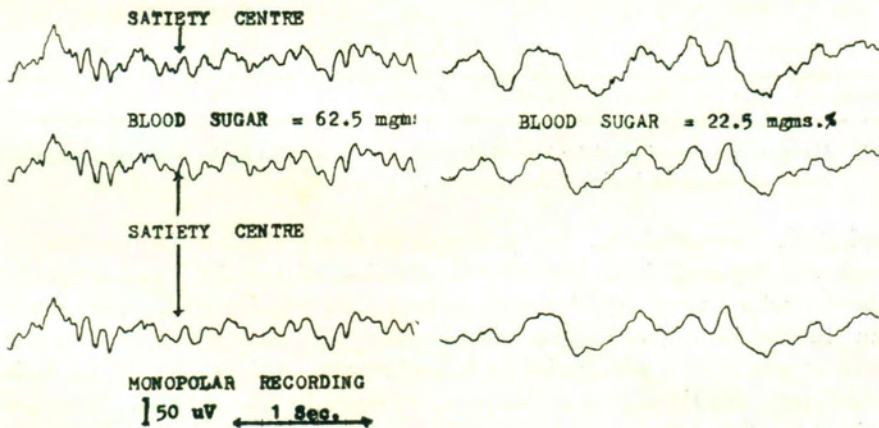
Fig. 13.   Monopolar recordings in a monkey with reference electrode on left ear.   Hypogly-
caemia has diminished the frequeney of the electrical activity of satiety centre from
6—7 Waves/Sec. to about 2—3 waves/sec.   The amplitude of the slow waves is
increased from about 50—60 μv to 80—90 μ_{v}. (From Anand, Dua and Baldev Singh
1960).

either of the 'feeding' or of the 'satiety' centres.   Our studies to date lend
support to the hypothesis that the hypothalamic centres are sensitive to
changes in blood glucose, rather than to changes in the blood protein or fat
contents.

Forssberg and Larsson (1954) demonstrated that in hungry rats the uptake of 32_P is greater in those regions of the hypothalamus which have the feeding mechanisms than others. Mayer interpreted this as supporting the existence of glucoreceptors, while Larsson thought that it indicated overall increased activity of the hypothalamic region containing the 'feeding' centre. Their studies on uptake of glucose containing 14_C were inconclusive.

Studies upon the uptake of glucose by the 'feeding' and 'satiety' regions of the hypothalamus in fed and starving monkeys have also been made by

Oxygen Consumption of the 'feeding' and 'satiety' centers in Fed Monkeys

Monkey No.	QO_2 in μl of O_2 / μg DNA/hour						Center which is more active
	Left Satiety	Left Feeding	Left Control	Right Satiety	Right Feeding	Right Control	
2.F	0.46	0.32	1.34	0.50	0.30	—	Satiety
4.F	0.17	0.07	0.12	0.20	0.15	0.23	Satiety
5.F	0.31	0.27	0.28	0.29	0.27	0.25	Satiety
6.F	0.40	0.45	0.83	0.31	0.37	0.35	Feeding
8.F	0.23	0.45	0.21	0.29	0.34	0.35	Feeding
9.F	1.77	0.72	1.16	0.79	0.49	1.21	Satiety
10.F	0.49	0.57	0.55	0.37	0.48	0.49	Feeding
Mean	0.54	0.40	0.64	0.39	0.74	0.48	

Fig. 14.   Oxygen consumption of the hypothalamic centres studied in the warburg apparatus, taken out from the brains of fed monkeys.

Anand *et al.*, (unpublished). In the first series of experiments, 14_C containing glucose was injected into the carotid arteries of both fed and starving monkeys who were guillotined immediately afterwards, the brain frozen in liquid air, and then pieces from the 'satiety' and 'feeding' regions, as well as two other adjacent hypothalamic regions, studied for their radioactivity. No significant activity was detected in any region. In other experiments, the glucose and oxygen uptakes of various hypothalamic regions in fed and starving monkeys have been investigated with the Warburg technique. Preliminary observations suggest relatively increased oxygen and glucose uptake per unit nucleic acid by the 'satiety' region (Fig. 14 & 15) in the fed state, as compared with 'feeding' region. In the starving state the oxygen as well as glucose utilisation of the 'feeding' centre is more than that of 'satiety' centre (Fig. 16 & 17). These denote the presence of glucoreceptor mechanism in the 'satiety' region of the hypothalamus. They would also support the original hypothesis of Anand and Brobeck (1951),

Glucose Consumption of 'feeding' and 'satiety' centers in Fed Monkeys

in $\mu g/\mu g$ DNA/2 hours

Monkey No.	Left Satiety	Left Feeding	Left Control	Right Satiety	Right Feeding	Right Control
1.F	12.5	10.7	10.0	—	11.4	17.3
2.F	11.4	Nil	6.0	21.33	12.3	Nil
4.F	1.196	—	2.800	0.671	2.359	—
5.F	2.95	3.53	Nil	2.84	0.95	2.35
Mean	7.0	4.74	4.7	8.3	6.75	6.55

Fig. 15.   Glucose consumption of the hypothalamic centres studied in the warburg apparatus, taken out from the brains of fed monkeys.

that basic urge to eat is located in the lateral hypothalamic regions, while the medial regions are activated as a result of (blood sugar) changes produced by food intake, which in turn by inhibiting the lateral mechanisms produce

Oxygen Consumption of the 'feeding' and 'satiety' centers in 48 Hours Starving Monkeys

QO_2 in μl $O_2/\mu g$ DNA/hour

Monkey No.	Left Satiety	Left Feeding	Left Control	Right Satiety	Right Feeding	Right Control	Active Centers
2.S	0.26	0.45	0.77	0.24	0.58	1.02	Feeding
4.S	0.21	—	0.33	0.17	0.43	0.37	Feeding
5.S	0.36	0.37	—	0.32	0.28	0.35	Equal activity
6.S	0.19	0.46	0.29	0.45	0.52	0.39	Feeding
8.S	0.65	0.33	0.18	0.33	0.29	0.41	Satiety
9.S	1.05	1.20	1.18	0.90	0.60	0.72	L.Feeding
10.S	0.38	0.44	0.30	0.36	0.47	0.38	Feeding
Mean	0.44	0.54	0.49	0.39	0.45	0.52	

Fig. 16.   Oxygen consumption of the hypothalamic centres studied in the warburg apparatus taken out from the hrains of 48 hours starving monkeys.

satiety and abolition of further eating.   The electroencephalographic recordings from feeding and satiety centres under conditions of hyper and hypoglycaemia referred to earlier lend further support to this hypothesis; as changes in the activity of satiety centres are more pronounced than changes in the activity of feeding centres.

Glucose Consumption of the 'feeding' and 'satiety' centers in Starving Monkeys

in µg/µg DNA/2 hours

Monkey No.	Left Satiety	Left Feeding	Left Control	Right Satiety	Right Feeding	Right Control
1.S	Nil	8.20	Nil	4.686	3.99	12.1
2.S	11.8	8.5	10.2	7.5	7.0	7.2
4.S	2.125	—	2.785	1.439	—	1.368
5.S	2.17	1.88	2.91	1.44	1.27	Nil
Mean	4.02	6.01	3.973	3.76	4.8	5.167

Fig. 17.   Glucose consumption of the hypothalamic centres studied in the warburg apparatus taken out from the brains of 48 hours starving monkeys.

Experiments have also been carried out with certain pharmacological preparations, which either change the appetite, or the blood glucose levels. Brobeck et al., (1956) reported that administration of amphetamine derivatives resulted in an increase in the recorded activity of the medial regions of the hypothalamus.   Anand et al., (unpublished) conducted similar experiments with another drug, Preludin, which also decreases appetite, and observed a similar desynchronized fast activity.   Studies were also made with Rastinon, an oral anti-diabetic drug used for lowering blood sugar. No change was produced in the activity of the 'feeding' or the 'satiety'

RIGHT AND LEFT SATIETY CENTRES

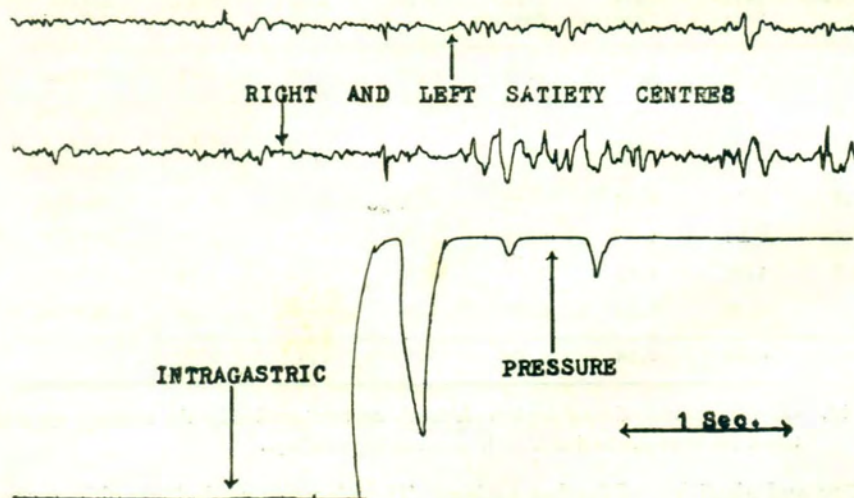INTRAGASTRIC   PRESSURE

1 Sec.

Fig. 18.   The Electroencephalographic activity of the left and right satiety contres correlated with the pressure of a balloon introduced into the stomach.   It is observed that with rise of intragastric pressure the activity of the satiety centres become more marked.

centres immediately after intravenous administration, but after the lapse of an hour to an hour and a half, the activities of the 'feeding' and 'satiety' centres were similar to those observed in hypoglycaemia.

AFFERENTS FROM STOMACH

Evoked potential studies are being conducted to see if the gastric afferents, travelling centrally through the vagus, project to the hypothalamic centres. Preliminary studies have shown a projection into the medial hypothalamus just anterior to the 'satiety' centre (Gill and Anand – unpublished). Sharma *et al.*, have also observed that ballooning of the stomach *in situ*, also evokes potentials in the 'satiety' regions of the hypothalamus, which correlate well with increasing intragastric pressure (Fig. 18).

CORRELATION OF WATER INTAKE WITH FOOD INTAKE.

Strominger (1947) had noted that, within limits, the higher the water concentration of the diet, the greater the food intake ; animals given no water ate little or no dry food and those given no dry food drank little or no water. The regulation of food intake appears to be correlated with regulation of water exchange. A suggestion had also been put forward that, if these two are so intimately correlated, after hypothalamic lesions the changes in food intake may be the indirect result of changes in water intake which may be the primary function regulated from the hypothalamic levels. Anderson and McCann (1955) described a hypothalamic "drinking area" electrical stimulation of which produces polydipsia. Similar results were obtained by microinjection of hypertonic saline into the same regions. Montemurro and Stevenson (1955) demonstrated that the hypothalamic area regulating water intake was situated in the same region as the 'feeding' centre. Studies in rats with hypothalamic lesions spread over different regions (Anand and Dua, 1958) have demonstrated that, after hypothalamic lesions, the rats failed to show the correlation of water with food intake observed in normal animals. Lesions in the lateral hypothalamic 'feeding' centre, resulted in complete adipsia in addition to complete aphagia. Lesions near about this region (1 m.m. medial or anterior) produced hypodipsia, irrespective of increase in food intake (Fig. 19). Lesions further removed from this region, do not significantly change water intake, in spite of changes in food intake. It can be concluded, therefore, that the hypothalamic regions controlling water and food intake, although present in the adjacent regions, act separately and independently. Morrison and Mayer (1957) have also made similar observations. It may be noted here that lesions in the limbic structures of rats did not change their water intake (Anand and Dua – unpublished).

TABLE.

Average of food and water intakes of rats after hypothalamic lesions, compared with pre-operative period.

Location of lesions*.	Number of rats.	Duration, days.	Food. g./rat/day.	'Water. c.c./rat/day.	Water/food. c.c./g/.day.
$A_8R_1L_1$ ..	3	30	‡11·21±†2.00	18·13±0·24	1·61
$A_8R_2L_2$ ..	4	30	‡10·83±1·63	15·38±3·68	1·42
$A_7R_1L_1$ ..	3	30	‡11·92±0·93	18·64±3·67	1·56
$A_7R_2L_2$ ..	4	30	‡10·17±1·89	‡13·05±2·59	1·28
$A_6R_1L_1$ ..	4	30	‡12·10±3·7	‡13·22±3·96	1·09
$A_6R_2L_2$ ..	2		D I E D		
$A_5R_1L_1$ ..	4	30	‡10·82±1·54	16·21±2·26	1·49
$A_5R_2L_2$ ..	3	30	‡10·58±2·4	16·18±3·93	1·53
$A_4R_1L_1$ ..	2	30	‡11·93±0·74	21·00±3·55	1·76
$A_4R_2L_2$ ..	3	30	‡11·73±0·50	16·08±2·72	1·37
Control (before lesions) ..	25	30	9·05±0·81	16·95±3·49	1 87

*Horsley–Clarke Co-ordinates (see Fig. 1).   †Standard error of mean.
‡Statistically significant change from control.

Fig. 19.   Average of food and water intakes of rats after hypothalamic lesions compared with pre-operative period (From Anand and Dua 1958A.).

CONCLUSION

In this communication, experimental studies bearing on the nature and mechanism of nervous regulation of food intake in animals have been reviewed.   It was possible to say that this phenomenon was probably in the same category as the nervous regulation of most other visceral activities.   Experimental evidence was furnished suggesting certain modes of activation of the higher nervous mechanisms.   More knowledge is required before a complete picture of the nervous regulation of food intake is revealed.

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