Ann Natl Acad Med Sci (India), **47(1&2):** 13-28, 2011

Neurobiology of Food Intake and Ecology of Hunger and Malnutrition

K.N. Sharma
M.S.Ramaiah Medical Institutions and Hospitals, Bangalore

ABSTRACT

The dual hypothalamic feeding-satiety centres, identified by Anand and Brobeck in 1951, laid the ground work to suggest that both detection and control of food intake was a central phenomena. In sixties it was realized that not only central structures but a variety of peripheral mechanisms are as critical and extend well beyond the classic sense of taste and olfaction and involve gastrointestinal signalisation, motivation and drive, and social and other environmental features. Later decades brought in implications of external features modulaing not only quantitative but qualitative components of feeding behavior, linked among other factors to ontogeny of feeding, nutritional profile of the individual, socio-economic influences and other environmental conditions. A more recent development has been the interfacing of disciplines such as physical sciences, agriculture, food sciences, economics, social and environmental sciences, information technology and others. It would appear that control and regulation of food intake is a multilevel, multifactorial closed feedback system with several stages ranging from afferent synthesis to stages of decision making and leading to levels of behavioural acts becoming imperative and satisfying specific needs.

Keywords : Neurobilogy of food intake, feeding and satiety centres, hunger, metabolic and energy pool, environmental factor in food intake, malnutrition.

Introduction

The classical paper of Anand and Brobeck in 1951 (1) identifying the dual hypothalamic feeding –satiety centres, showed that tiny discrete lesions of specific, localized zones in hypothalamus bring about aphagia or hyperphagia and obesity, depending upon the site of the lesion. This pioneering work set in motion a number of studies with the main stream of thought during fifties

Correspondence : Prof. K.N.Sharma, Executive Director, M.S.Ramaiah Medical Institutions and Hospitals, Bangalore.

being that both detection and control of food intake regulation lay in the central nervous structures in which hypothalamus plays a major and decisive role. In the sixties it was gradually realized that though hypothalamus plays such an important role, this itself is not only influenced from higher limbic and other central neural regions but is modulated by several factors such as nutrition itself, motivation and emotional factors, sensory qualities of food and hedonic matrix, as also the signalization particularly from oral and gastrointestinal level. The appraisal of food includes its taste, flavor, texture, viscosity, volume, temperature and other physicochemical characteristics.

Still a number of questions remained unanswered and pointed to the existence of peripheral mechanisms extending well beyond the classic sense of taste and olfaction, and extended to cover motivation and drive, social and environmental context and formed the major thrust of research activities in seventies and eighties. Later decades brought in further implications of external features modulating not only quantitative but qualitative components of feeding behaviour linked among other factors to ontogeny of feeding, the nutritional profile of the individual such as undernourished, obese or malnourished subjects, the sociocultural and economic influences, religious taboos or environmental features ranging from high altitudes, arid zones, desert areas or arctic / antarctic climatic requirements to extreme tropical climate. A more recent development has been the interfacing of disciplines such as physical sciences, agriculture, food sciences, economics, social and environmental sciences, information technology and if I may say the addition of politico-economic influences by acknowledged Global Institutions and Agencies.

Orogastric Appraisal

Oral sensory appraisal of food is the first step in feeding and leads to its acceptance or rejection, and when accepted, is eaten in definite amounts. Through the second step of action of foods in feeding process, these orally determined responses to food are regulated. At the post absorptive and systems level, food as a nutrient, acts as a metabolic signal on the regulatory centres and ‘modulates’ oral feeding responses (2). The sensory signals not only become important in controlling intake, but feedback into the efferent system controlling the ‘energy pool’, producing some of the metabolic changes originally controlled biochemically at cellular level, and behaviourally signaling satiety. Thus satiety cues are produced in two phases, first as anticipatory reflex, initiated by the taste of food, and secondly by the post absorptive metabolic consequences. The flow of information from alimentary afferents has shown a number of features influencing gastro-gustatory interactions in taste (3-6). It is quite likely that the changes seen in intakes of sweet and salt solutions in vagotomised animals are predominantly due to loss of vagal afferents from the stomach (7). The flow of information from the alimentary receptors to the brain, are not all in one direction but is rather achieved by 'tuning' of the receptor systems through use of centrifugal controls. These controls allow sensory pathways to act as variable filters so that stimuli tagged with a particular attribute or feature are alone allowed through for a detailed analysis. By such means it is possible to attenuate or amplify afferent signals, or switch on or off the inputs, thereby selecting a particular input at a particular time. It seems these gastric and intestinal sensory mechanisms, are concerned with the 'sensory' appraisal of food including its texture, viscosity, volume, temperature, and other physico-chemical properties of food, and share in large measure the organizational control characteristics of oral sensory system (8, 9).

Ontogeny of Feeding

Ontogenetic analysis suggests that each stage of development appears complete. Observations on ontogeny of saccharine preference in neonate rats clearly pointed that the apparent learning curves for saccharine, were infact maturation curves (10) and were linked to the maturation of gustatory system (11). It appears that neonate is primarily dependent upon 'taste', rather than 'calories', a feature also seen in adults under certain conditions of nutritional stress, food deprivation, metabolic disorders and psycho-sociocultural overtones. Need-related changes in palatability and taste sensitivity are well known and have been shown in normal adult rats and dogs, hypothalamic hyperphagic rats as also in neonate rats (12). Neonate rats can eat enough at least to double average growth rate if competition for food is eliminated by limiting the litter size. It is suggested that young rats lack active satiety systems (13).

An alternative possibility has also been proposed. Our approach has been to vary hunger by mealtime restriction, graded food deprivation, insulin or thyroxin injection. Food intake and preference shifts were, then observed to 'liked' items, e.g. fat, glucose or saccharue or 'disliked' items like cellulose, NaCl or quinine which were added to stock diet or put into solution. The results show that need-related changes in palatability and taste sensitivity are basically present all the time and are modulated linked to the prevailing circumstances. This is interfaced with developmental changes in the taste receptors and CNS, and in physiological and behavioural patterns in fetus and postnatal animals. Tongue epithelial cells are modified into taste buds only with innervations and are seen to degenerate on denervation. This in turn seems to show gradual transitions in electrical responses to taste stimuli from foetal to adult stage. Behaviourally, human foetus and neonatal mammals showed increased swallowing movements on sweet taste and decreased movements with bitter taste which is somewhat at variance with electro-physiological evidence and reflects on the multimodal involvement of taste cell functional and behavioural dynamics with age (14).

Multilevel Signals Related to Food Intake

The fact that the changes introduced in the internal environment by the feeding ultimately adjust subsequent feeding (15,16) places control of food intake in the same category as the control of various other visceral activities. The pattern of control of visceral activities is similar in many ways and parallel to that of somatic activities. The sensory inputs come from various regions of the body which make the animal aware of food. The hypothalamus provides quantitative control by 'facilitating' or 'inhibiting' feeding reflexes. Further, discriminative control of food intake is influenced from limbic level, and habit and conditioning from the neocortical regions (15). This scheme exemplifies the organization of neural substrates encompassing peripheral receptor mechanisms and interconnected systems situated at several levels of neuraxis. Through the functioning of these multiple neuronal systems the integration is achieved so that the organism is directed to the fulfillment of biological needs. Thus, the concepts of 'multiconstancy', 'multifactors', and 'multilevels' are all enshrined in the idea of homeostatic control of food intake (8), and indicate that the multilevel analysis, priorities, and competitions are essentially linked to internal (energy pool) and external (environmental) factors. This analysis of location, internal state and stimulus variety provides a basis that must be taken into account in any model of food intake regulation.

How does high altitude stress effects human taste intensity and hedonics? We conducted an extensive study on human volunteers at high altitude. The taste intensity ratings showed a linear relationship with increasing logarithmic molar concentration of each solution (sweet, sour, salt, bitter) as compared with taste hedonicity which showed an inverted 'U' type function. High altitude hypoxic stress brings about changes in hedonic responses, primarily an increased palatability for sweetness and suggests that the mechanism may be anorexia – linked nutritional stress. The high altitude stress appears to influence food intake in a manner that sensory cues (e.g. preference for sweet substances) become more important. (17,18).

The studies were also conducted to evaluate the effect of continuous exposure to hypobaric hypoxia on the feeding behavior and taste responses of rats, under simulated conditions of high altitude of 7,620m for 21 hours a day and consecutively for 18 days, which more closely resembled actual field conditions. The results showed a decrease in daily food and water intake and body weight and a preference for sweet solutions. High-altitude stress appears to influence food intake such that sensory cues assume greater significance during feeding behavior, and thus supported the observations obtained in humans at high altitude (19).

Dual Detector System

What are the consequences of food ingestion? How does an organism being fed adlib or under conditions of food deprivation, or in varying states of hunger, handle the information from dietary source. How does in fact the state of 'energy-homeokinetics' – surfeit or deficit state, interface with external dietary and environmental cues to guide the feeding behavior? How indeed feeding fits in the domain described under the rubric of homeostatic motivations? These and allied questions have attracted the attention of several workers during the last few decades.

It seems physicochemical information from the diet feeds into two detector systems – sensory and metabolic systems (Fig. 1). Whether the nervous system makes use of either set of signals in monitoring further intake is a function of the state of energy balance. The 'energy pool' acts as a biasing system, assigning priority to taste (sensory qualities) when the animal is in a deficit and to calories (metabolic properties) when it is in balance or surfeit (Fig. 2). The assumption is that organic needs alter perceptual bias on an innate basis so that animal seeks out and ingests the needed food on the basis of its sensory qualities. The fact that

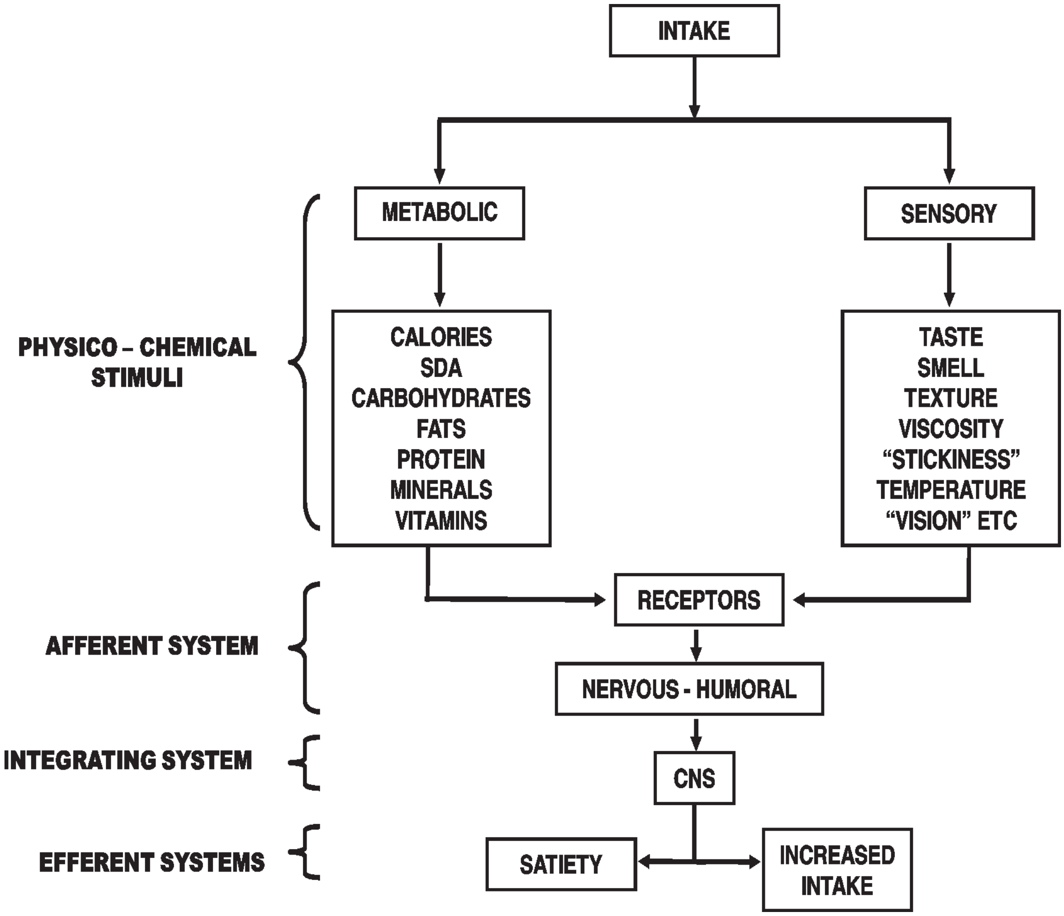

Fig. 1: Generalized scheme of sensory and metabolic feedback systems in food intake (23).

food contains nutrients is considered coincidental (20,21,22).

There has been yet another important dimension added as a result of the studies in sixties and seventies. Two problems have been separated – control of input and regulation of energy level. Available diet provides both sensory and nutrient signals that the brain in turn compares to other signals coming from the energy – nutrient pool, which provide information about the sensory and metabolic consequences of these nutrients (23). The brain then uses this information in modulating food intake or learned food related behaviours. It is easy

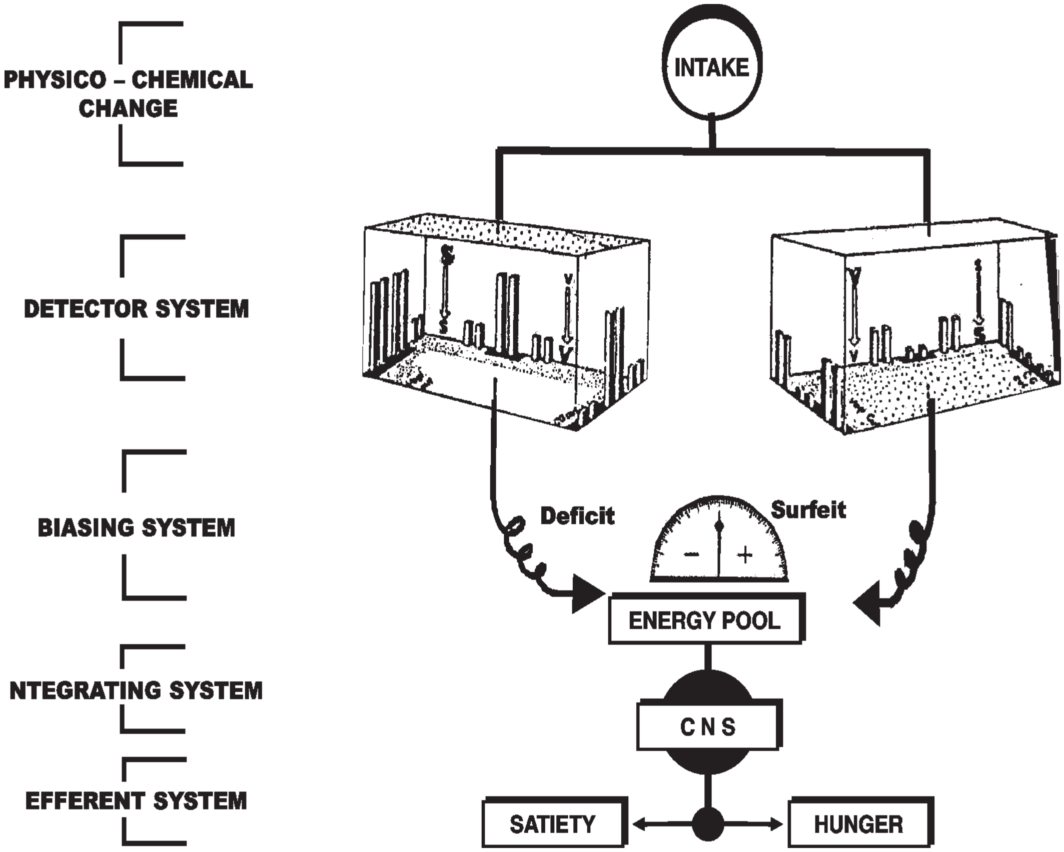

Fig. 2: Model showing the dual detector system and the role of the energy pool as a biasing system, in the overall control of food intake (From: Sharma et al. *J Neural Transmission,* **33:** 113-154, 1972).

to see that the combined action of gastric emptying time, intestinal absorption rate, efficiency of food utilization and metabolic activity, and the behavioural output of muscular work and general activity can be important in regulating the energy – nutrient pool. Thus in this scheme, body weight is not only influenced by food intake and changes in output, but also by taste-induced appetite shifts from energy nutrient pool (Fig. 3).

Recent Studies

During the last two decades or so, systems approach has been applied inkeeping with the technological advances, and include role of emotions and motivations, neuro-humoral

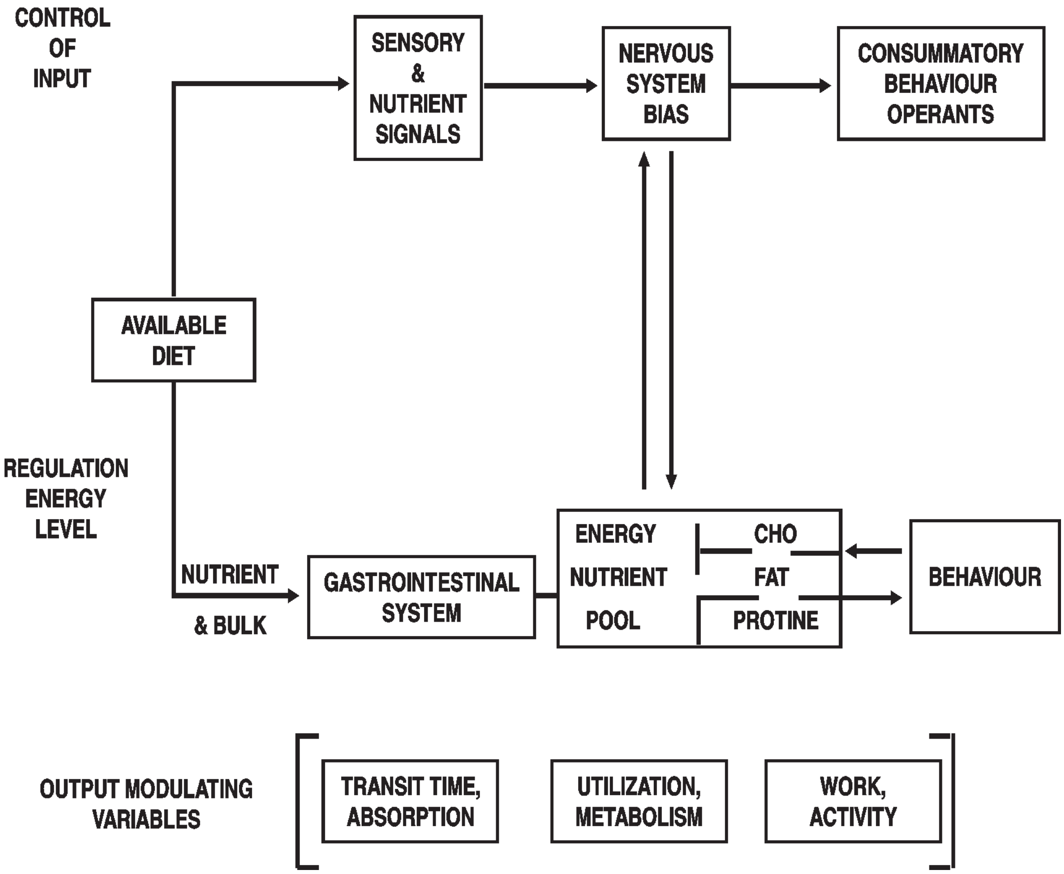

Fig. 3: Scheme of input control (top) and energy regulation (bottom) as interacting systems involved in homeostatic regulation of consummatory behavior (From: Sharma KN, In: Advances in Physiological Sciences, New Delhi: Macmillan India, pp. 639-647,1992).

networking, and unraveling of intimate mechanisms involved in control and regulation of feeding, so as to give a more detailed holistic picture. In this complex organization of systems approach, afferent synthesis forms the first step in which juxtaposition, selection and synthesizing of functionally diverse inputs linked to the dominant need, past experience or memory, simultaneous presence of other afferent stimuli, and straight through hotline passage of information are all taken into consideration (Fig.4). This stage then determines the subsequent stages of the systems organization of the behavioural act and underlines the formation of purposive behavior crucial for survival and adaptation, and show a well defined line up of hierarchical dependence (20).

The next stage bring into focus the preparedness of the individual and triggers the behavioural response activation time and determining the whole act to include initial and subsequent stages of decision making, formation of mechanisms of predicting results, and satisfying the specific needs. Interlinked with this is the next stage of decision-making in a manner that the behavioural act becomes imperative, and shapes the significance of resultant activity in need reduction or satisfaction,

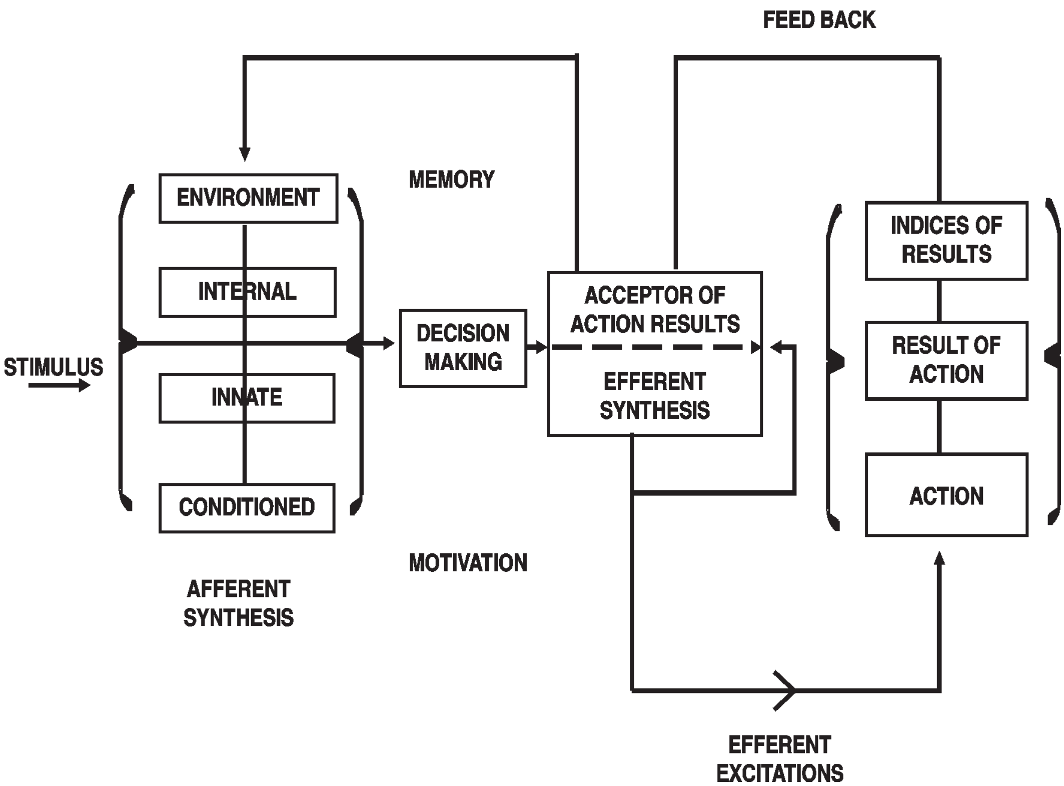

Fig. 4: Schematic block diagram showing various interlinked and interacting stages depicting the relationship of stimulus characteristics, afferent synthesis, decision making, efferent excitations, and the role of feedback control system and memory mechanisms in guiding the motivational behavior (From: Sharma KN, In: Advances in Physiological Sciences, New Delhi: Macmillan India, pp 639-647, 1992).

correct behavioural errors and bring about behavioural acts to their precise end point.

Thus it would seem that food intake is regulated by a closed-feedback system, with regulated input as well as output. There is a distinct relationship between sensations (eg. hunger) and drives (eg.food intake). Stimuli (internal or external) adequate to elicit a sensation also elicit activities directed towards reducing the intensity of such sensations. In other words, the stimuli for those sensations induce motivational states that drive the individual, to provide whatever is felt to be lacking. Viewed in this respect, physico-chemical signals from food form a base that controls food acceptance, choice and intake (8). The interfacing of these signals with the changing needs of the individual, include the concept of priorities, competition and compromises in regulation of several factors contributing to homeostasis (20). The fact an identical stimulus may be handled differently by the nervous system depending upon the variety and the complexity of the existing variables, is all well enshrined in the capacity and the plasticity of the nervous system and linked to the requirements of internal and external environment (23,24,25).

Econutrition

With this background let me bring to your attention another perspective which is becoming important and relevant as never before. Do we not realize that traditional agricultural and food sciences disciplines have to dovetail with human nutrition and health by forging explicit linkages not just in a linear fashion but in a truly integrated manner, and use food-based, systems approaches to meet human nutrition goals. For instance, the current focus on micronutrients for people globally may form a part of the effective inter-disciplinary research, teaching and extension activities directed towards sustainable improvements in human nutrition and health. In this task the paradigms of agriculture, human nutrition and public health, will have to be shifted from linear approaches to integrated and interactive long-term efforts. In other words econutrition should integrate environmental health with human health with a particular focus on the interactions among the fields of agriculture, ecology and human nutrition, and thereby help alleviate not only extreme poverty but would appear also fundamental to linking basic sciences understanding in multiple areas. Can we ignore the relationship between environmental degradation, develop-ment, world poverty and hunger and social justice. The struggle to preserve the environment is unavoidably intertwined with the struggle to improve the conditions under which the poor of many third world countries live.

Put in other words, as Kristensen argues (26), hunger, satiety and appetite can be seen as a central research subject for the social sciences, both as the locus where food consumption is bodily regulated and the nexus where biology, social praxis and cultural meanings meet and are negotiated by the individual. For instance, the number of people developing overweight and obesity is increasing as is the prevalence of eating disorders and weight preoccupation. These tendencies can be considered as expressions of a polarization of eating habits in modern societies. These tendencies could as well be seen as a result of a more general ambivalence in relation to food, which influences the experiences of hunger, satiety and appetite and their regulating effect on food consumption. It would be worth exploring to link traditional agricultural production disciplines to the food sciences and the various disciplines concerned with human nutrition. Cornell University has developed a new programme to cover 'Food Systems for Health', and fosters effective inter-disciplinary research, teaching and extension activities directed towards sustainable improvement in human nutrition and health (27). Similarly, the United Nations Millenium Development

MDGs sets targets related to important global poverty, health and sustainability issues, and seeks to improve survival through environmental and nutritional interventions (28). For instance, to estimate the reduction in child mortality as a result of interventions related to environmental and nutritional goals like improving child nutrition and providing clean water, sanitation and house hold fuels, coupled with the magnitude and distribution of the effects of interventions vary largely based on the economic status of intervention recipients, and therefore calls forth for an integrative approach which should prioritize the poor.

Implementing interventions that improve child nutrition has shown considerable reduction in child mortality as shown by the results from Latin America and the Caribbean, South Asia and Sub-Saharan Africa, and indicated that the three regions show larger than expected improvement if the interventions are implemented among the poor first, and this needs to be emphasized and taken note of. Contrast this with the aggregate human impact on the environment now exceeding the limits of absorption. The resultant global environmental changes include altered atmosphere composition, widespread land degradation, depletion of fisheries, fresh water shortages, and biodiversity. Disturbances of the Earth's life-support systems will affect disproportionately the resourcepoor and geographically vulnerable populations particularly in many tropical countries, and lead to, among other hazards, to food insecurity and water stress, thus causing various health consequences.

In short, as Jaffe (29), summarises, there are a variety and complexity of factors which in one way or the other influence on the selection and acceptability of foods such as:

(i) physiological and psychological aspects, to include genetic factors, neurophysiological factors, emotional factors, perceptive factors; and

(ii) at another plane, physical and ecological aspects; or

(iii) the domain of social and cultural aspects – habits and traditions, religious believes, taboos, nutrition faddism; prejudice, aversions and pervertions; social value of food, industrialized foods, or

(iv) at still other plane, economic aspects, and

(v) finally the frame work of educational aspects.

It would therefore be safe to conclude that feeding behavior is regulated by a multiple-sensor, closed-feedback system, with regulated input as well as output. The driving biological need, linked to the internal physiological deficits or biologically relevant events in the external environment is reflected in the changes in different major homeostatic indices determining the normal metabolism, and interact with the environmental factors to form the basis of the biological motivation. There is a distinct relationship between sensations (e.g. hunger) and drives (e.g. food intake). Stimuli (internal or external) adequate to elicit a sensation also elicit activities directed towards reducing the intensity of such sensations, i.e. the stimuli for those sensations induce motivational states that drive the organism, to provide whatever is felt to be lacking. Viewed in this respect, chemosensory signals from food provide the sensory basis of hedonic matrix that controls food acceptance, choice and intake. The interfacing of these signals with the changing needs of the organism, include the concept of priorities, competition and compromises in regulation of several factors contributing to homeostasis. The fact that an identical stimulus may be handled differently by the nervous system depending upon the variety and complexity of existing variables or the capacity of the nervous system to make continuous appraisals and instant decisions in order that the organism can react in strict accordance with the requirements of internal and external environment and should form a base for us to follow. This is the central message.

It would thus become clear that in this closed feed back system regulating food intake, afferent synthesis is the first stage. This afferent synthesis leads to the specific states of readiness in which both motivation and environmental stimuli interact as activated by memory mechanisms and bring into focus the preparedness of the organism. This in turn leads to triggering of the behavioural response activation time and determining the whole act to initial and subsequent stages of decision making, formation of mechanisms of predicting results, and satisfying specific needs. Dovetailed with this is the next stage of decision making in a manner that the behavioral act becomes imperative and bring about behavioral acts to their precise end point. Some of the recent findings have laid a fairly good groundwork indicating that the control and regulation of sensory and metabolic events resulting in the particular feeding behaviour, may come from higher levels of the same sensory pathways, from motor pathways, from pathways mediating other modalities and a number of other sources. Extending these studies further to neuronal level, it could be seen that sensorimotor cortical neurons (SMC) would show excitatory responses in hungry animals when Lateral Hypothalamic (LH) neurons were stimulated and the animals would vigorously eat food; but if the food was withheld and not presented to the animal, the same SMC neurons now showed an inhibition rather than excitation (25). These types of results quite clearly indicated that there was reorganization of neuronal activity for decision making and thereby differentially influencing the motivational and reinforcing components of the composite feeding behavior. Extending the work to humans it has become clear that nutritional background (internal state), previous dietary history (ontogeny of feeding), and external environmental factors interact in such a way that the prepotent sensory properties of food and experiential factors subserve to bring about relevant metabolic adaptive changes, taste preferences, and food habits.

In conclusion, it may be surmised that whether the sensory or the metabolic cues become prepotent to guide the motivational behavior towards need reduction or homeostatic regulation of feeding, is a dynamic process in which both sets of cues ie sensory or metabolic cues, are involved, and it is the interaction of internal milieu with the external environmental factors impinging upon the innate and experiential correlates which appear to determine the degree and the direction of feeding behavioural act, visa vis nutrition and energy balance.

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